ISSN 2409-9988

Inter Collegas

Experientia docet

2023

10(1)

INTER COLLEGAS

2023

Vol. 10 No.1

OFFICIAL JOURNAL OF
KHARKIV NATIONAL MEDICAL UNIVERSITY
ISSN 2409-9988

Recommended for publishing
by Scientific Council of Kharkiv
National Medical University

30 June 2023

Correspondence address:
61022, Kharkiv,
Nauki Avenue, 4

E-mail:
inter.collegas@knmu.edu.ua
as.shevchenko@knmu.edu.ua

URL: http://inter.knmu.edu.ua

Periodicity:
4 times a year

INTER COLLEGAS, VOL. 10, No.1 (2023)
ISSN 2409-9988

Table of Contents

https://doi.org/10.35339/ic.10.1

HYGIENE & OCCUPATIONAL MEDICINE

THEORETICAL AND EXPERIMENTAL MEDICINE

THERAPY

SPORT MEDICINE & REHABILITATION

EPIDEMIOLOGY & PUBLIC HEALTH

DENTISTRY

PSYCHIATRICS & MEDICAL PSYCHOLOGY

NURSING

TEACHING ISSUES & LECTURES

LIFE HISTORIES OF THE FOUNDERS OF KHARKIV SCHOOL OF HYGIENE

Kapustnyk V.A., Korobchanskiy V.O., Rezunenko Y.K., Shcherban M.H., Gerasymenko O.I., Oliinyk Y.O.

Kharkiv National Medical University, Kharkiv, Ukraine

https://doi.org/10.35339/ic.10.1.kkr

Abstract

This article describes the life history of the founders of Kharkiv school of hygiene Arkadiy Ivanovich Yakobiy (1827–1907) and Ezro Musiyovych Kahan (1887–1948). It is dedicated to the 150th anniversary of the Department of Hygiene and Ecology No.1 of Kharkiv National Medical University (KhNMU) and the 100th anniversary of Research Institute of Occupational Hygiene and Occupational Diseases.

Both of these talented individuals left their places of birth, secondary and higher education at some point, due to certain unfavorable consequences of regional life, and arrived in prosperous Kharkiv. Having a wide range of knowledge, both worked in a wide aspect of science and practice that relate to the general well-being of various categories of the population, including environmental, household, epidemic, production, family and other statuses of human life. Both came to the conclusion that identifying and overcoming risk factors for health deterioration is a very promising direction for achieving global well-being of humanity. Based on this, both became the founders of the Kharkiv School of Hygiene.

Yakobiy A.I. founded the first department of hygiene at Kharkiv University on February 1, 1873, and headed it for the following 12 years. Kahan E.M. headed specialized institute for workers' health problems (the first on the territory of the USSR), namely the Institute of Occupational Medicine, in May 1923, and managed it until 1931. During the term of their work at Kharkiv hygienic institutions, these professors provided a methodological basis for the multi-decade development of the corresponding scientific, pedagogical and practical field of state health care.

Keywords: *historical aspects, scientific research, health care, lifestyle, professor Yakobiy A.I., professor Kahan E.M.*

Arkady Ivanovich Yakobiy was born on September 22 (October 4), 1827, in Kazan. Having received a home education, he entered the faculty of physics and mathematics of Kazan University in spring of 1843. He graduated from this university in 1847 with the degree of a candidate of physics and mathematics (*Fig. 1*).

While working at Kazan University, he submitted an application for dismissal from this higher education institution among seven progressive professors in November 1871, criticizing its unfavorable educational conditions (*Fig. 2*).

Arriving in prosperous Kharkov, he received the status of extraordinary professor of the Imperial Kharkiv University at the Department of General Therapy and Medical Diagnosis on May 8, 1872.

Corresponding Author:
Gerasymenko Olga Igorivna – PhD, associate professor of the Department of Hygiene and Ecology No.1 of Kharkiv National Medical University.
E-mail: oi.herasymenko@knmu.edu.ua

Then working as a professor of the Department of Forensic Medicine and Hygiene of the Faculty of Medicine of the Imperial Kharkiv University since 1873, he recognized the concept of preventive medicine as a significant direction of health care. After that, Arkady Ivanovich Yakobiy founded the Department of Hygiene of Imperial Kharkiv University on February 1, 1873, was the first to occupy the chair of hygiene and headed it for 12 years (from 1873 to 1885). He received the academic title of ordinary professor on December 4, 1875.

In 1889, at the solemn meeting of Kharkiv University, he spoke about the tasks of the State Red Cross. In his report, he called for the organization of shelters and nursing homes for the sick and wounded, shelters for widows and orphans, the organization of manufacture of limb prostheses, and the establishment of stations for climatic treatment of the wounded (*Fig. 3*).

Arkady Ivanovich Yakobiy determined that the term hygiene comes from the Greek ύγετνός (healthy).

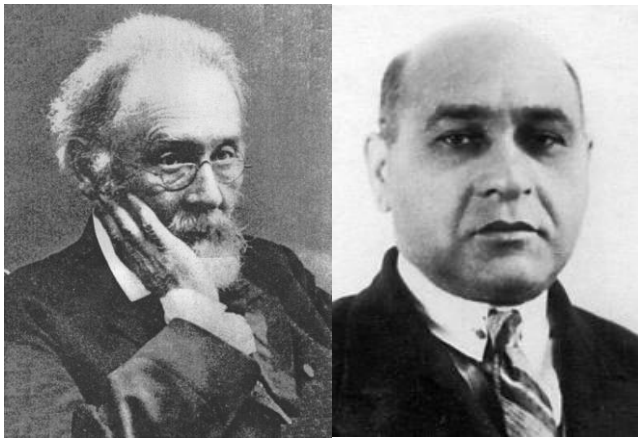

Fig. 1. Leading founders of Kharkiv School of Hygiene professors Arkady Ivanovich Yakobiy (1827–1907) Ezro Musiyovych Kahan (1887–1948)

Fig. 2. Professors of Kazan University who resigned (1871)

Fig. 3. The solemn meeting of Imperial Kharkiv University (1889)

According to the definition of Yakobiy A.I., hygiene is a science that studies the influence of environmental factors on the health, working capacity and life expectancy of a person and develops the measures to improve the conditions of his/her life and work.

Hygiene defines and evaluates risk factors for health and substantiates methods of managing them (modes of work and rest, sanitary norms and rules, individual regulations) as well as uses both specific methods of preventive medicine (epidemiological analysis, sanitary surveys and description, sanitary and hygienic expertise, laboratory and natural experiments), and those borrowed from other sciences [1; 2].

The field of scientific interests of Yacobiy A.I. was versatile. His works on the methodology of hygienic research were widely used in hygienic practice and provided the basis for development of preventive medicine, which has been implemented worldwide. He proved the relevant information related to the methodology of preventive medicine: the method of researching the porosity of bread in hygienic practice [3]; determination of the hygienic value of ventilation formulas, in relation to overcoming the relevant risk factors [4]; communal hygiene, ecological and psycho-emotional bases of stay of certain categories of population in different countries of the world [5–8]; proving a wide range of hygienic risk criteria for the development of a certain range of diseases, including epidemic and environmental diseases of a certain population [9–16].

In teaching of hygiene and scientific research, Yacobiy A.I. was guided by the idea that a person cannot be considered and studied outside the society, outside the social conditions. The lectures that the professor gave to medical students of Kharkiv University were called *A Course of Public Hygiene*. They were recorded by the student Okorokov and published in 1885 as a manuscript reproduced by lithographic method. The book, edited by professor Yacobiy A.I., includes the following sections: waste and its disposal; the history of development of sanitary facilities; soil; climate; ventilation; artificial climate; dwelling; feeding; starvation; water supply; population biology; places of imprisonment; diseases from the polluted air of closed premises; school; disinfection; epidemics; sexual activity [17]. He described the sanitary conditions and daily life, the economy of the examined communities, and even the policy of the royal officials in relation to certain categories of the population. His public lecture on March 16, 1869 *About happiness from the perspective of hygiene* received a disapproving assessment from Archbishop Antony of Kazan in a letter to the trustee of the educational district Shestakov P.D., because the lecturer indicated that "the only way to the happiness of mankind is in hygiene".

In addition, the hygiene methodology based on the implementation of the principles of disease prevention among different categories of the population was determined by the author at the expense of research in the field of sanitation, epidemiology, ethnography, state public organizations, including the Red Cross [18; 19].

To date, the significant historical contribution of professor Yacobiy A.I. is recognized. It was he, who created the methodological base for the further development of preventive medicine, performing scientific and pedagogical work at Kharkiv University [1; 20–23]. The first Ukrainian Department of Hygiene is celebrating its 150th anniversary in 2023.

During the entire history of the department, its employees conducted extensive scientific and research work on various hygienic problems (*Fig. 4*).

Fig. 4. The staff of the Department of Hygiene and Ecology No.1, which is located at KhNMU Research Institute of Occupational Hygiene and Occupational Diseases (2019)

The founder and first director of Kharkiv Institute of Occupational Medicine, Ezro Musiyovych Kahan, was born in July 1887 in Riga. In 1901, he left an elementary school, in 1910 he passed the exams for the matriculation certificate as an external student in Vitebsk. But the restless nature of the young man was cramped within the patriarchal environment. Since childhood, he was looking for an outlet for his boiling energy. And he found this way out in revolutionary activity, which at that time was gaining strength and recruiting personnel on the territory of the Russian Empire (*Fig. 1*).

It is quite logical that Ezro joined the ranks of the Jewish Socialist Party (Bund), which aimed to create national and cultural autonomy, according to the principle " There, where we live, that is our country" [24]. However, at the height of the revolutionary events of 1903–1905, arrests of Bundists became a daily occurrence. He stayed for four months in the royal prison and was released under police supervision.

Despite the state emergency, the mentally gifted young man entered the Yuryiv (Tartus) University. In 1910–1916, Kahan E.M. studied at the medical faculty of this prestigious educational institution. After graduating from the university, he worked as a doctor at Oryol Provincial Zemstvo Hospital. And then there was an appointment that determined the entire further professional path of doctor Kahan E.M. He was appointed to the position of doctor of Oryol hospital fund. It should be emphasized that these specialized institutions were first implemented in Germany, and on the territory of the Russian Empire they were implemented in 1912, according to the law "On insurance of workers in case of illness" dated June 22, 1912. From 1919, the so-called Kharkiv period of almost 20 years of the life of the outstanding doctor and organizer of national health care Kahan E.M. started. It contained the highest rise of his talent, as well as a deep personal tragedy. All this was shared with Ezro Musiyovych by his wife Berta Volodymyrivna and daughter Dina [25].

The very atmosphere of that time contributed to the discovery of the scientist's talent. It is known that in the USSR the 20s and 30s of the last century were a period of formation and rapid development of hygienic science and sanitary practice. It was Ukraine that took the lead in the organization of state sanitary supervision. The methodical and organizational center of this activity was in Kharkiv, that time the capital of the Soviet Ukraine. In April 1922, the fateful 3rd Congress of bacteriologists, epidemiologists and sanitary doctors took place in Kharkiv, at which the "Regulations on Sanitary Organization" were approved.

In June 1923, the resolution "On sanitary bodies of the republic" was signed by the Council of People's Commissars of the Ukrainian SSR. Having moved to Kharkiv, doctor E.M. Kahan continued his work in the field of occupational pathology as a doctor of the hospital fund. In 1920, he was appointed to the position of the chief physician of Kharkiv Workers Polyclinic, as the head of the consulting bureau of Department of Labor Protection of the People's Commissariat of Labor of the Ukrainian SSR.

Kahan E.M. began his pedagogical activity by lecturing on the course of hygiene and labor protection at Kharkiv Institute of Technology and Kharkiv Institute of National Economy (1921–1923). In 1923, Kahan was sent to Germany for an internship.

Upon arrival from the appointment, he was elected a professor of Kharkiv Medical Institute. Undoubtedly, organizational frivolities, broad erudition and practical knowledge on the basis of two indispensable directions in medicine – therapeutic and preventive – allowed Professor Kahan E.M. to take a fateful step for native medicine: to justify the feasibility of creating the Institute of Labor Medicine on the basis of Kharkiv Workers Polyclinic and in May 1923 to head this first on the territory of the USSR specialized institute for problems of health protection of workers [26]. On the initiative of Professor Kahan E.M., this institution had a complex structure, which included a hygiene department with relevant laboratories, a department of labor physiology (which, due to a coincidence of interests, was headed by him himself), a clinic of occupational diseases with a polyclinic.

Creative thinking of Professor Kahan E.M. also manifested when setting the main task of a fundamentally new institution: the study of topical problems that are on the border of natural and social sciences, physical, chemical, technological and other factors [27; 28]. How not to compare this with today's priority direction of the institution – the medicine of borderline conditions [29]. After five years of existence, in 1929, when the institute proved its viability, and the economic situation in the state somewhat stabilized, the collegium of the People's Commissariat of Health of the Ukrainian SSR took a decision to build a specialized building for the location of the Central

Institute of Pathology and Occupational Hygiene (CIP and OH) (this was the name of the institution in 1928–1939). All responsibility for construction was assigned to the director. The construction was difficult, accompanied by a reduction in funding, numerical checks and "organizational conclusions".

The institute building, designed by the architect Viktor Abramovich Estrovych (1881–1941), was commissioned in 1935. The Research Institute is still located in this building (*Fig. 5*).

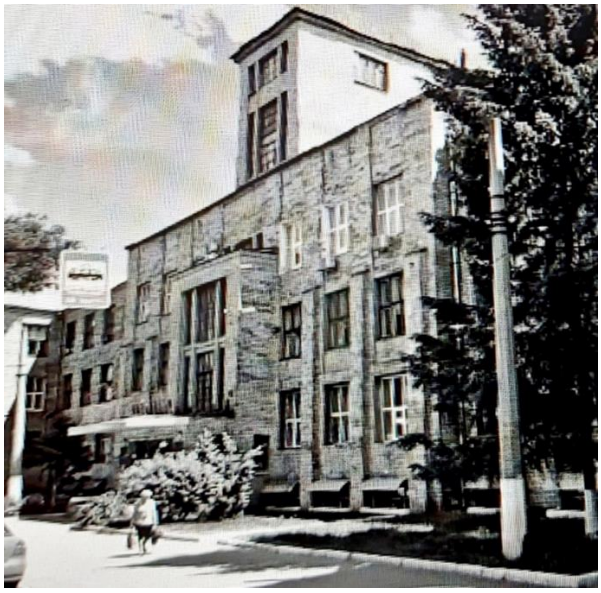

Fig. 5. The building of Central Institute of Pathology and Occupational Hygiene (1935)

Professor Kahan E.M. headed this institution until 1931, when the management of the institution was transferred to his successor Zinovy Davidovich Gorkin, after which he worked as a deputy director for research until 1938.

Professor Kahan's scientific interests covered a wide range of problems related to the systematic analysis of human labor activity, which, according to academician Kundiyev Yu.I. [30], was essentially the first epidemiological studies in occupational medicine aimed at multifactorial analysis of health risks in order to manage them.

The works of the scientist on in-depth analysis of the morbidity of workers [31; 32], problematic issues of toxicology [33–36], foundry production, which was covered by his doctoral dissertation (defended in 1925) [37], work on physiology [38; 39] are well-known. Professor Kahan E.M. founded the national school of occupational hygienists. Famous scientists, heads of departments and scientific institutions, including Abramovich M.O., Vasylevsky V.M., Gorkin Z.D., Miller S.V., Karminskyi M.S., Navrotskyi K.V., Neiman A.F., Sakhnovskyi Y.D., and others, graduated from his scientific school [40]. On the initiative of Professor Kahan, sanitary and hygiene faculties were opened in medical universities. It was the demand of the time, and for many years to come it determined the structure of medical education, the theory and practice of health care. Our present is making its own corrections to the structure of Ukrainian health care based on the European experience, but the long-term positive experience of the preventive direction of the native medicine gives reason to assert its expediency and perspective. The change of the existing paradigm of health care is envisaged precisely in the direction of preventive orientation (*Fig. 6*).

Taking into account the professor's services to health care, the People's Commissariat of Health of the Ukrainian SSR awarded Kahan E.M. the title of Honored Professor in 1934. It was state recognition and probably the peak of the master's career.

There were only a few years left before the period of oblivion... In February 1938, Professor Kahan E.M. was arrested, and in October 1939 he was imprisoned in a forced labor camp for 5 years "for belonging to a counter-revolutionary organization".

The tragic circle of fate closed in the camp located in the Kirov region. What the tsarism forgave at one time was not forgiven by the Soviet government. The Bolsheviks reminded the Bundists of the accusation of "usurpation of the will of the people" [24]. Presumably, the professor's foreign business trips were not left out of the attention of the punitive bodies. It is obvious that the strong will and endurance inherent in this intelligent man played a role during the period of the camp trials, during which the doctor Kahan did his job – treated. And there were many sick among the prisoners. Hard camp work, in conditions of daily supply shortages against the background of the Great War, exhausted people. The medical assistance provided by an experienced professional pathologist was all the more valuable.

In 1942, "for conscientious attitude to work as a doctor, excellent behavior in everyday life" [30] and at the request of the Camp Management, Professor Kahan E.M. got conditional early release.

Since that time, he worked in the hospital for freelancers of the Vyatlag Department of the People's Commissariat of Internal Affairs (PCIA) of the USSR, living at the station of Lisniy, Kaisky

Fig. 6. The staff of Central Institute of Pathology and Occupational Hygiene (1932)

District, Kirovohrad Region. But the fortunes of Professor Kahan E.M. did not end there. The famous professor did not remain unnoticed by his Russian colleagues. His own authority and the authority of his scientific school formed the prerequisites for overcoming the period of oblivion.

Professor Vinnikov M.E., deputy director of Omsk Medical Institute, addressed a letter to the head of the USSR PCIA Directorate for Omsk region. Justifying the expediency of appointing Professor Kahan to the position of head of the department of occupational hygiene, he referred to his experience as the director of Kharkiv Institute of Occupational Hygiene and Occupational Diseases and head of the department of hygiene.

Permission from the PCIA was received [41]. From this time, a new period of the professor's life, little studied by Ukrainian specialists, begins.

The occupational hygiene department of Omsk Medical Institute, which he headed in 1945–1948, was the first hygiene department at the sanitary-hygienic faculty of this university. It was organized on the initiative of the famous occupational hygienist Professor Israelson Z.I. in 1941. This gives reason to claim that Professor Kahan E.M. stood at the origins of its existence. Possessing a colossal pedagogical education and teaching skills, Professor Kahan E.M. immediately joined the work. It was he who created the program on the occupational hygiene course, which is the basis of the current educational programs [42]. It is with the name of Professor Kahan E.M. that the creation of the hygienic school of Western Siberia is connected, the priority direction of which is still hygienic provision of the oil-mining industry.

Such well-known professors as Dvoryaninova N.K., Demchenko V.G., Ogleznev G.O. and others graduated from this school [43]. After courageously overcoming the period of oblivion, the period of earthly nothingness came for the outstanding professor. He went to Eternity. On August 4, 1948, Ezro Musiyovych died and was buried at the Old Jewish Cemetery in Omsk.

And all of us, colleagues and followers of Professor Kahan E.M., are extremely grateful to the leadership of Omsk State Medical University for erecting a monument on the grave of the outstanding hygienist in 2010.

The chronicles of Professor Kahan's life show that this talented man devoted himself to his country and to the improvement of its state system. The system raised this individual to the heights of social recognition, and then turned him into camp dust.

The lesson is that in that era, this is how the Soviet people were "hardened". It is bitter to realize that the period of non-existence of a famous scientist was only occasionally broken by not numerous, but meaningful publications about him [30; 40–45]. According to the biblical story, when Jesus Christ, an already well-known preacher, returned to his homeland, to Judea, he was met there with distrust, and one of the Pharisees insisted that nothing good could come out of the worthless Nazareth. "...Jesus said to them: there is no prophet without honor, except only in his homeland and in his house" [46]. Centuries later, this phrase acquired the meaning of a catchphrase, which translating from the Old Slavic language sounds like this: "There is no prophet in his homeland". According to the conclusion of the Kharkiv Region Prosecutor's Office on May 4, 1989, based on Article 1 of the Decree of the Presidium of the Supreme Soviet of the USSR dated December 16, 1989, Kahan Ezro Musiyovych was rehabilitated.

Today, the Research Institute of Occupational Hygiene and Occupational Diseases of Kharkiv National Medical University is a powerful research institution that focuses on preventive and curative work to preserve the health of workers in

Thus, the leading founders of Kharkiv School of Hygiene, professors Arkady Ivanovich Yakobiy (1827–1907) and Ezro Musiyovich Kahan (1887–1948), made the methodological basis of scientific-pedagogical and research work of the relevant hygiene units of Kharkiv National Medical University, which were also improved during the respective 150 and 100 years of the Department of Hygiene and Ecology No.1 and Research Institute of Occupational Hygiene and Occupational Diseases (*Fig. 7*).

Fig. 7. The emblem of KhNMU Research Institute of Occupational Hygiene and Occupational Diseases (Author Korobchanskyi V.O.).

Based on the long history of Kharkiv hygiene science, practice and education, further successes of national preventive medicine aimed at identifying and overcoming risk factors for deteriorating health of various categories of the population are inevitable [47]. But today, the most urgent preventive measures are to overcome the risk factors of an emergency during military operations [48].

There is no **conflict of interest**.

References

1. Bulakh SM, Vilenskyi YuH, Kornilova LIe. Imena v medytsyni u vidhomoni chasu. 2012: kalendar znamennykh ta pamiatnykh dat [Names in medicine in the echo of time. 2012: calendar of famous and memorable dates]. Kyiv: National Scientific Medical Library of Ukraine; 2012. P. 56-59. [In Ukrainian].

2. Bondarchuk S. Profesor A.I. Yakobiy (1837–1907 rr.) - teoretik i praktik hihiienichnoi nauky Kharkivskoho universytetu druhoi polovyny XIX st. [Professor A.I. Yakobiy (1837–1907) as a theorist and practitioner of hygienic science at Kharkiv University in the second half of the nineteenth century]. The chronicle of Ukrainian history. 2014;30:133-7. [In Ukrainian].

3. Yakobiy AI. Metodyka doslidzhennia porystosti khliba [Methods for studying bread porosity]. Kharkiv: University print shop; 1877. 4 p. [In Ukrainian].

4. Yakobiy AI. Pro ventyliatsiini formuly. Matematychne doslidzhennia [About ventilation formulas. Mathematical research]. Kharkiv: University print shop; 1877. 6 p. [In Ukrainian].

5. Yakobiy AI. Zghasannia inorodnytskykh plemen Pivnochi [Extinction of foreign tribes of the North]. Kharkiv: University print shop; 1893. [In Ukrainian].

6. Yakobiy AI. Pro misionerskyi stan krainy Nadyma i pro mozhlyvu postanovku khrystyianskoi misii u krainakh rosiiskoi inorodnytskoi pivnochi [About the missionary situation in the country of Nadym and about the possible establishment of a Christian mission in the countries of the aliens' russian North]. Kharkiv: University print shop; 1895. [In Ukrainian].

7. Yakobiy AI. Zghasannia inorodnytskykh plemen Tobolskoi Pivnochi [Extinction of the foreign tribes of the Tobolsk North]. Kharkiv: Universytets′ka typohrafiya. Kharkiv: University print shop; 1900. [In Ukrainian].

8. Yakobiy AI. Tiurky stepiv Pivnichnoho Kavkazu [Turks of the steppes of the North Caucasus]. Kharkiv: University print shop; 1901. [In Ukrainian].

9. Yakobiy AI. Spektralnoe issledovanie pihmentov [Spectral study of pigments]. Diaries of the Kazan' Association of doctors, 1868-1869. P.62-69. [In russian].

10. Yakobiy AI. Ob izmenenii muti krovi [About the change in blood turbidity]. Diaries of the Kazan' Association of doctors. 1871. P. 37-44. [In russian].

11. Yakobiy AI. O chumnoi vetlianskoi epidemii. Otchet [About the epidemic in the Vetlyanskaya village. Report]. Kharkiv: University print shop; 1879. [In russian].

12. Yakobiy AI. O profilakticheskikh merakh protiv rasprostraneniia sifilisa [About preventive measures against the spread of syphilis]. Prylozhenie k protokolam Kharkovskoho Medytsynskoho Obshchestva [Annex to the minutes of the Kharkiv Medical Society]. 1885; IV. [In russian].

13. Yakobiy AI. Leuconostoe quercus. Hlava IV toma traktata prof. N.V. Sorokina o "Rastytelnykh parazytakh". [Leuconostoe quercus. Prof. Sorokin, N.V. treatise "Plant Parasites". Chapter of volume IV]. Kharkiv: University print shop; 1886. [In russian].

14. Yakobiy AI. Materialy k istorii razvytiia rysunka kryliev babochky [Materials for the history of the development of the pattern of butterfly wings]. Annex to the minutes of the Kazan Society of Natural Sciences. 1888. [In russian].

15. Yakobiy AI. Fidonia piniaria L., v Stolbyshchenskoi lesnoi dache, pry derevne Borovoe-Matiushkyno, Kazanskoho uezda [Fidonia piniaria L., in the Stolbishchenskaya forest dacha, near the village of Borovoe-Matyushkino, Kazan district]. Proceedings of the Kazan Society of Natural Sciences. 1890: XXI. [In russian].

16. Yakobiy AI. O volostnykh popechitelstvakh [About township trusteeships]. Russian wise; 1900. [In russian].

17. Yakobiy AI. Kurs suspilnoi hihiieny [Course in public hygiene]. Kharkiv: University print shop; 1885. [In Ukrainian].

18. Yakobiy AI. O rezultatakh sanitarnykh meropriiatii pri dyfteritnoi epidemii v Kharkovskoi hubernii [On the results of sanitary measures during a diphtheria epidemic in the Kharkov province]. Kharkiv: Publication of the Kharkov governor's zemstvo; 1875. [In russian].

19. Yakobiy AI. Zadachi russkoho Krasnoho Kresta. Rech na akte Kharkovskogo universiteta [Tasks of the Russian Red Cross. Speech on the act of Kharkiv University]. Kharkiv: University print shop; 1889. [In russian].

20. Entsyklopediia ukrainoznavstva: Slovnykova chastyna: [v 11 t.] Naukove tovarystvo imeni Shevchenka; hol. red. prof., d-r Volodymyr Kubiiovych. [Encyclopedia of Ukrainian studies: Dictionary part: [in 11 volumes] Shevchenko' Scientific Society; Gen. ed. Prof. Dr. Volodymyr Kubiyovych]. Paris – New-York: Young life. 2000;4:1506-9. [In Ukrainian].

21. Kotsur N. Stanovlennia i rozvytok vitchyznianoi hihiienichnoi nauky v universytetakh druhoi polovyny XIX st. [Formation and development of domestic hygienic science in universities of the second half of the 19th century]. Pereiaslav Chronicle. 2011;1:165-73. [In Ukrainian].

22. Bondarchuk S. Profesor A.I. Yakobiy (1837–1907) - teoretyk i praktyk hihiienichnoi nauky Kharkivskoho universytetu druhoyi polovyny XIX st. [Professor A.I. Yakobiy (1837–1907) as a theoretician and practitioner of hygienic science at Kharkiv University in the second half of the 19th century]. The chronicle of Ukrainian history. 2014;30:133-4. [In Ukrainian].

23. Abashnik V. Deutsche Einwirkungen auf Hygiene an der Universität Char'kov (1873–1920). In: Ortrun Riha, Marta Fischer, Hygiene als Leitwissenschaft. Die Neuausrichtung eines Faches im Austausch zwischen

Deutschland und Russland im 19. Jahrhundert. Shaker Verlag, 2014, p. 111-129. Available at: https://www.saw-leipzig.de/de/projekte/wissenschaftsbeziehungen-im-19-ahrhundert/relationes%2016

24. Boyko OD. BUND [Bund]. In: Smoliy VA and oth. Encyclopaedia of Ukrainian history. National Academy of Sciences of Ukraine. Institute of Ukrainian history. Kyiv: Scientific thought; 2003. 688 p. Available at: http://www.history.org.ua/?termin=Bund

25. Lichnoe delo Ezro Moiseevicha Kahana. Pervii Kharkovskii medytsynskii institut. Narodnii Komissariat zdravookhraneniia USSR [The personal file of Ezro Moiseyevich Kahan. First Kharkov Medical Institute. People's Commissariat of Health of the Ukrainian SSR]. [In russian].

26. Korobchanskiy VO. Minlyvosti doli profesora Kahana (1887-1948) do 130-richchia zasnovnyka vitchyznianoi medytsyny pratsi [Changes in the fate of Professor Kahan (1887-1948) to the 130th anniversary of the founder of national labor medicine]. Ukrainian journal of occupational health. 2017;1(50):82-7. [In Ukrainian].

27. Kahan EM. Struktura i deiatelnost Pervoho Ukrainskoho instituta rabochei meditsiny [Structure and activities of the First Ukrainian Institute of Working Medicine]. Kharkiv, Kharkivprint: 1925. 9 p. [In russian].

28. Kahan EM. Chto takoe institut rabochei meditsiny [What is the Institute of Working Medicine]. Kharkiv, Scientific thought: 1926. 30 p. [In russian].

29. Lisovyi V, Kapustnyk V, Korobchanskyi V. Medytsyna hranychnyh staniv: teoriia i praktyka donozolohichnoi diahnostyky [Borderline medicine: theory and practice of prenosological diagnostics]. Scientific journal of Ministry of Health of Ukraine. 2013;2(3):49-60. [In Ukrainian].

30. Kundyev YuI. Professor E.M. Kahan – vidnii deiatel profilakticheskoi meditsiny [Professor E.M. Kahan – a prominent figure in preventive medicine]. Ukrainian journal of occupational health. 2005;3-4:104-8. [In russian].

31. Kahan EM. Zabolevaemost kharkovskikh rabochikh v 1923 y 1924 hodakh [The morbidity of Kharkov workers in 1923 and 1924]. Kharkiv, Kharkivprint; 1926. 101 p. [In russian].

32. Kahan EM. Osnovnie elementy i postroenie ambulatorno-klinicheskoi orhanizatsii medpomoshchi zastrakhovannym [The main elements and construction of an outpatient-clinical organization of medical care for the insured]. Kharkiv, 4th Print shop "Kharkivprint"; 1923. 40 p. [In russian].

33. Kahan EM. Professionalnye intoksikatsii: programmnyi doklad [Occupational intoxications: keynote speech]. Kharkiv, Kharkivprint; 1926. 10 p. [In russian].

34. Kahan EM. Promyshlennye yady. Okys uhleroda. Svynets. Sernistyi haz [Industrial poisons. Carbon monoxide. Lead. Sulphur dioxide]. Kharkiv, Kharkivprint; 1926. 12 p. [In russian].

35. Kahan EM. Deistvie nitroproizvodnykh benzola na orhanism [The effect of nitro-derivatives of benzene on the body]. Kharkiv, Kharkivprint; 1935. 8 p. [In russian].

36. Kahan EM. Opredelenie vrednykh veshchestv v vozdukhe promyshlennykh predpriiatii [Determination of harmful substances in the air of industrial enterprises]. Kharkiv, Kharkivprint; 1937. 8 p. [In russian].

37. Kahan EM. Trud v liteinykh: opyt hihiienicheskoho issledovaniia liteinoho dela [Labor in foundries: experience of hygienic research of foundry business]. Kharkiv, Kharkivprint; 1926. 10 p. [In russian].

38. Kahan EM. Fiziolohiia truda v metalloobrabatyvaiushchei i metallurhicheskoi promyshlennosti [Physiology of labor in the metalworking and metallurgical industry]. Kharkiv, Kharkivprint; 1935. 28 p. [In russian].

39. Kahan EM. Sootnoshenie mezhdu enerheticheskimi i hemodinamicheskimi pokazateliami vo vremia raboty i vosstanovleniia [Correlation between energy and hemodynamic parameters during work and recovery]. Kharkiv, Kharkivprint; 1935. 10 p. [In russian].

40. Kundiyev YuI. Institut skvoz prizmu epoch [Institute through the prism of epochs]. Ukrainian journal of occupational health. 2012;4(33):75-89. [In russian].

41. Toskaev I, Brodskyi I. Vozvrashchenie iz nebytiia [Return from oblivion]. Literary almanac of the Omsk State Medical Academy. 2012;41:88-93. Available at: http://kk.convdocs.org/docs/index-53374

42. Korobchanskyi VO. Minlyvosti doli profesora Kahana (1887–1948) do 130-richchya zasnovnyka vitchyznyanoyi medytsyny pratsi [Changes in the fate of Professor Kahan (1887-1948) to the 130th anniversary of the founder of national labor medicine]. Ukrainian journal of occupational health. 2017;1(50):85. [In Ukrainian].

43. Pertsev DP, Zavhorodnyi IV. Professor Ezro Moiseevich Kahan i eho rol v razvitii sovetskoi hihiieny truda [Professor Ezro Moiseevich Kahan and his role in the development of Soviet occupational health]. Collection of materials of the international conference "Medical professorship of USSR" (moscow, May 25, 2012). P. 219-221. [In russian].

44. Miller SV. Rol E.M. Kahana v razvitii sovetskoi hihieny truda (k 80-letiiu so dnia rozhdeniia) [The role of E.M. Kahan in the development of Soviet occupational health (on the occasion of his 80th birthday)]. Labour hygiene and occupational diseases. 1967;4:34-6. [In russian].

45. Idel'chik KhI. Professor E.M. Kahan – sotsial-hihiienist [Professor E.M. Kahan – social hygienist]. Soviet healthcare. 1989;11:69-72. [In russian].

46. New Testament, Gospel of Matthew, ch. 13, art. 57.26. Available at: http://slovopedia.org.ua/33/53405/33036.html

47. Korobchanskyi VO, Sarkis-Ivanova VV, Bohachova OS, Oliinyk YO, Bielecka SV. Implementation of the principles of the scientific concept "Medicine of borderline conditions", regarding donosological diagnosis and overcoming the risks of health deterioration in student youth (review). Medicni perspektivi. 2022;27(4):207-13.

48. Shcherban MH, Khoroshun EM, Kapustnyk VA, Miasoiedov VV, Korobchanskyi VO, Vorontsov MP, et al. Viiskova hihiiena (navchalnyi posibnyk) [Military hygiene (study guide)]. Kharkiv: KhNMU; 2022. 218 p. [In Ukrainian].

Received: 24 May 2023
Accepted: 26 Jun 2023

Cite in Vancouver style as: Kapustnyk VA, Korobchanskiy VO, Rezunenko YK, Shcherban MH, Gerasymenko OI, Oliinyk YO. Life histories of the founders of Kharkiv school of hygiene. Inter Collegas. 2023;10(1):5-14. https://doi.org/10.35339/ic.10.1.kkr

DETERMINATION OF ASPERGILLOSIS OF THE FEMALE GENITAL ORGANS IN WOMEN WITH IMMUNODEFICIENCY

Lytvynenko M.V.[1], Bondarenko A.V.[2], Bondarenko O.V.[3], Gargin V.V.[2], Katsap O.V.[4]

[1]Odessa National Medical University, Odesa, Ukraine
[2]Kharkiv National Medical University, Kharkiv, Ukraine
[3]Kharkiv International Medical University, Kharkiv, Ukraine
[4]MNPE "City Clinical Hospital No.1" of the Odessa City Council, Odesa, Ukraine

https://doi.org/10.35339/ic.10.1.lbb

ABSTRACT

Background. Morphological diagnosis of aspergillosis sometimes poses great difficulties due to the fact that molds of the genus Aspergillus are very sensitive to the use of antimicrobial therapy and change under its influence. In this regard, we provide information about aspergillosis of the female genital organs, discovered accidentally during an autopsy.

The purpose of the study is to conduct a complex pathomorphological analysis of biopsy, operative and sectional gynecological material of women with secondary immunodeficiency conditions, for early diagnosis of aspergillosis (which is the key to a favorable outcome of the disease), differential diagnosis and detection of invasive forms of aspergillosis.

Materials & Methods. We analyzed the autopsies of 4,796 women who died in Odesa region from 2009 to 2022. Autopsies revealed 7 cases of aspergillosis with damage to the female reproductive system. All of them were found in women who had confirmed HIV infection. In 5 cases, women additionally suffered from chronic alcoholism.

Results. Based on the results of these cases, it can be stated that the detection of characteristic mycelium in the preparations is a reliable sign of aspergillosis, but their absence does not deny this disease. Aspergillus hyphae change as the process develops: they can be weakly stained, and with dystrophic phenomena and the presence of necrotic fragments of mycelium, it can be almost colorless when using hematoxylin and eosin. While necrosis, tissue detritus is observed in the center of the granuloma, fibrous structures, fungal hyphae are formed perifocally. To confirm the diagnosis, it is important to detect granulomatous productive inflammation, conidial heads, inflammatory infiltration, microabscesses, foci of calcifications. However, against the background of immunodeficiency, it is not always possible to see the "classic morphological picture" of aspergillosis. In addition, detection of characteristic mycelium is possible only in a proportion of patients.

Conclusions. When examining the autopsy material of deceased women with immunodeficiency states, attention should be paid to the specific etiology of inflammatory processes of the reproductive system and the nature of the inflammatory process, the presence of Aspergillus hyphae and mycelia. The presence of morphological changes characteristic of aspergillosis allows to conduct a diagnostic search in the right direction. Detection of an invasive form of aspergillosis may indicate the presence of an immunodeficient state.

Keywords: *aspergillosis, female reproductive system, immunodeficiency state, HIV infection, uterus, mammary gland, drug addiction.*

Corresponding author:
Lytvynenko Marianna – Candidate of Medical Sciences, Associate Professor of the Department of Normal and Pathological Clinical Anatomy of Odessa National Medical University.
Address: Ukraine, 65000, Odesa, Valikhovsky lane, 2, ONMedU. E-mail: lytvynenko_marianna@ukr.net

Introduction

In recent years, an increase in immunodeficiency states has been noted in Ukraine [1]. The presence of an immunodeficiency condition affects a woman's body [2; 3], in particular, such women with immunodeficiency conditions are twice as likely to have pathological processes in the genital organs,

namely: dysfunctional uterine bleeding, endometrial hyperplasia, endometrial atrophy, pelvioperitonitis, actinomycosis of the uterus and appendages, dissemination of mycobacterium tuberculosis in the uterus and appendages, aspergillosis of the uterus and appendages, disseminated candidiasis, disseminated pneumocystosis, lymphoma, ovarian cystadenocarcinoma, squamous cell carcinoma of the cervix, acute and chronic non-specific salpingo-oophoritis, acute non-specific endometritis, cervical intraepithelial neoplasia, sclerocystic syndrome.

The course of the infectious process against the background of immunodeficiency has an atypical character. One of these processes is aspergillosis, which in the presence of an immune imbalance often takes on generalized forms [4].

The purpose of this work was to provide information about aspergillosis of the female genital organs, which was discovered accidentally during an autopsy.

Materials & Methods

To achieve this goal, we analyzed the autopsies of 4,796 women who died in Odesa region between 2009 and 2022. During this period, autopsies revealed 7 cases of aspergillosis with damage to the female reproductive system. All of them were found in women who had confirmed HIV infection. In 5 cases, women additionally suffered from chronic alcoholism. HIV infection was verified by enzyme-linked immunosorbent assay (ELISA). Chronic alcoholism was verified on the basis of catamnesis data and the establishment of alcoholic cirrhosis of the liver. In two cases, there was no prenatal data on the presence of aspergillosis. All autopsies were conducted in accordance with the order of the Ministry of Health of Ukraine (No.81 dated on May 12, 1992, and No.1877 dated on September 06, 2021). Pieces of organs were fixed in 10% neutral formalin, further processed according to generally accepted methods, and embedded in paraffin. Thickness sections were obtained on a microtome 5×10^{-6} m, which were placed on glass and stained with hematoxylin and eosin. To confirm aspergillosis, the sections were additionally stained by Shabadash, Foot's silvering. After identifying the morphological pattern characteristic of aspergillosis, the material was sent to the bacteriological center, where the presence of *Aspergillus spp.* was determined.

Results

We cite cases in which no lifetime data on the presence of aspergillosis were established.

Patient M., born in 1979, HIV-infected since 2004. She suffered from lymphoma for five years and underwent multiple courses of polychemotherapy. Remissions were short-lived. She was admitted to the hospital with complaints of headache, general weakness, low-grade fever. The examination revealed generalized lymphadenopathy, progression of the underlying disease with leukemia. The patient died 11 days after hospitalization. At the autopsy, the diagnosis of HIV infection, stage IV, terminal stage of lymphoma was confirmed, and generalized aspergillosis with lesions of the lungs, lymph nodes, brain, vagina, uterus was also revealed (*Fig.*).

Patient Z., born in 1973, has been taking narcotic drugs for 10 years, HIV-infected since 1999. She did not seek medical help. She died at her place of residence. HIV infection, stage IV, was detected at the autopsy; generalized aspergillosis: aspergilloma of lungs, mammary gland, vasculitis and thrombovasculitis of pulmonary vessels, aspergillosis abscesses of lymph nodes, aspergillosis sepsis. Among other AIDS-indicative diseases, candidal erosive esophagitis and bacterial pneumonia are documented.

The described observations illustrate the presence of different forms of aspergillosis (invasive and non-invasive) in persons with secondary severe immunodeficiency. At the same time, in both cases, the most affected organ of the female reproductive system was the uterus (*Fig.*). In both cases, the diagnosis was established only during the study of autopsy material. In both cases, histological examination of the endocervix and endometrium revealed the presence of fungal structures in the form of branched septate hyphae together with conidial forms, with ingrowth into the mucous membrane, with foci of necrosis. This was the basis for sending the material to the bacteriological laboratory, where the presence of *Aspergillus spp.* was established.

Discussion

The course of any pathological process against the background of immunodeficiency often has unexpected clinical manifestations. It is known that the presence of actinomycosis of the uterus and appendages, tuberculosis of the genital organs, aspergillosis, disseminated candidiasis, and pneumocystosis is significantly more frequent in HIV-infected patients [5–7]. While we found descriptions of only isolated cases of aspergillosis with extrapulmonary localization [8–10].

In the structure of chronic inflammatory gynecological diseases of the uterus, an additional

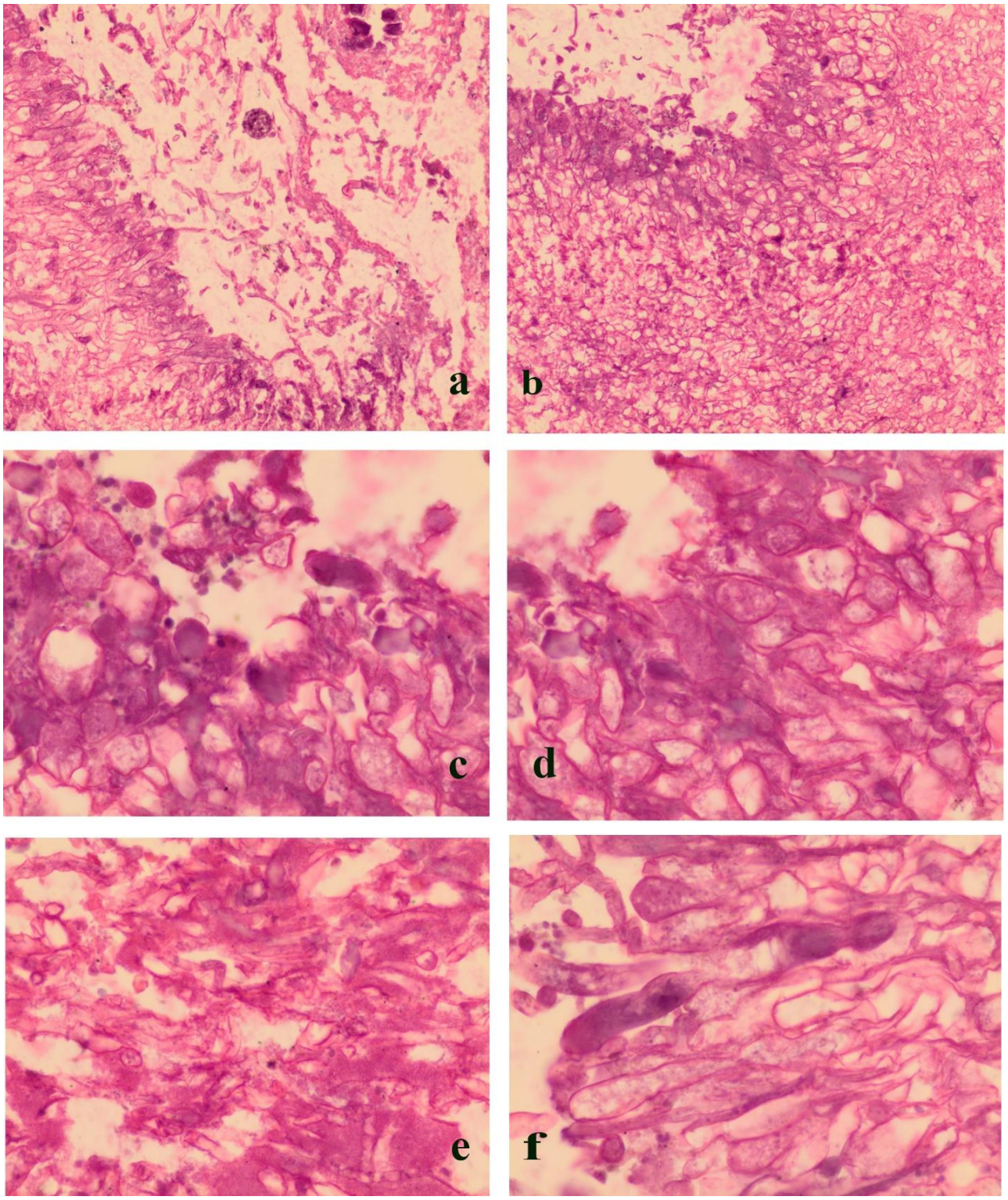

Fig. Aspergillosis of the female reproductive system: a) the presence of an *Aspergillus* conidial head in the center of the detritus when the uterus is affected. Magnification ×100; b) Multiple *Aspergillus* hyphae in the uterus. Magnification ×100; c, d) Radial arrangement of hyphae of the genus *Aspergillus* in the uterus. Magnification ×400; e) The presence of aspergillus mycelium in the center of mammary gland necrosis during the development of sepsis. Magnification ×400; f) aspergillosis salpingitis. Magnification ×400.

place is occupied by aspergillosis. Aspergillosis of the pelvic organs in women is also characterized by a long-term progressive course that leads to multiorgan complications.

Diagnosis of genital aspergillosis, as a rule, is based on the results of a histological examination of the surgical material, it is quite informative and important for differential diagnosis. However, the morphological diagnosis of aspergillosis sometimes presents greater difficulties due to the fact that aspergillus is very sensitive to the use of antibacterial drugs. Therefore, this disease remains undiagnosed during life. In this regard, when making a diagnosis, along with light electron microscopy and examination of micropreparations stained with hematoxylin and eosin, it is necessary to use additional research methods.

Detection of characteristic hyphae and mycelia of *Aspergillus* in preparations is the most reliable factor in the diagnosis of the disease. The cellular composition of a granuloma changes as the process of their development progresses. While necrosis is observed in the center of the granuloma, fibrous structures, xanthoma cells are formed perifocally. For diagnosis, it is also important to detect granulomatous productive inflammation, leukocyte infiltration, microabscesses, "cellular" tissue structure, specific granulomas that are surrounded by polynuclear, giant and plasma cells, lymphocytes and histiocytes. However, against the background of immunodeficiency, it is not always possible to see the "classic morphological picture" of aspergillosis. In addition, the detection of drusen is possible only in 25–60% of patients with actinomycosis, since these organisms are able to spontaneously lyse, calcify, deform and undergo other degenerative changes. The use of separate staining methods for diagnosis of aspergillosis does not always allow to increase the percentage of its detection. Considering the unfavorable state of reproductive health of women in Ukraine [11–13], we believe that the given data will help to establish a timely diagnosis and prescribe adequate treatment.

Conclusions

When examining the autopsy material of deceased women with immunodeficiency states, attention should be paid to the specific etiology of inflammatory processes of the reproductive system and the nature of the inflammatory process, the presence of *Aspergillus* hyphae and mycelia. The presence of morphological changes characteristic of aspergillosis allows you to conduct a diagnostic search in the right direction. Detection of an invasive form of aspergillosis may indicate the presence of an immunodeficient state.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Funding Sources

There are no external sources of funding.

Consent for publication

All authors give their consent to publication.

Received: 05 May 2023
Accepted: 22 Jun 2023

References

1. Krysko MO. Development of HIV-infection epidemic in Ukraine. Ukraine. The health of the nation. 2011;4(20):36-40. [In Ukrainian].

2. Demirdag Y, Fuleihan R, Orange JS, Yu JE. New primary immunodeficiencies 2021 context and future. Curr Opin Pediatr. 2021;33(6):657-75. DOI: 10.1097/MOP.0000000000001075. PMID: 34670265.

3. Lytvynenko MV, Gargin VV. Triple-negative transformation of the endometrium, cervix and mammary gland on the background of immunodeficiency. Med Perspekt. 2022;27(2):119-24. DOI: 10.26641/2307-0404.2022.2.260284.

4. Houbraken J, Kocsube S, Visagie CM, Yilmaz N, Wang XC, Meijer M, et al. Classification of Aspergillus, Penicillium, Talaromyces and related genera (Eurotiales): An overview of families, genera, subgenera, sections, series and species. Stud Mycol. 2020;95:5-169. DOI: 10.1016/j.simyco.2020.05.002. PMID: 32855739.

5. Francini B, Canepa MC, Lamonica C, Capece P, Posse G, Sanguineri V, et al. Histoplasmosis diseminada. Una infección oportunista en pacientes con infección por VIH. Experiencia en el Hospital Nacional Prof. A. Posadas, 2011–2017 [Disseminated histoplasmosis. An oportunistic infection in HIV positive patients Experience in the Hospital Nacional Prof. A. Posadas, 2011–2017]. Rev Chilena Infectol. 2018;35(6):671-9. DOI: 10.4067/S0716-10182018000600671. PMID: 31095188. [In Spanish].

6. Mendez-Samperio P. Diagnosis of Tuberculosis in HIV Co-infected Individuals: Current Status, Challenges and Opportunities for the Future. Scand J Immunol. 2017;86(2):76-82. DOI: 10.1111/sji.12567. PMID: 28513865.

7. Stepanova TV, Nedospasova OP, Golubchykov MV. Analysis of tuberculosis/hiv co-infection trends in Ukraine in 2008-2017. Wiad Lek. 2019;72(5 cz 1):903-7. PMID: 31175793.

8. Borsa BA, Ozgun G, Houbraken J, Okmen F. İmmün kompetan bir hastada Aspergillus protuberus'un neden olduğu ilk inatçı vajinit olgusu [The first case of persistent vaginitis due to Aspergillus protuberus in an immunocompetent patient]. Mikrobiyol Bul. 2015;49(1):130-4. DOI: 10.5578/mb.8397. PMID: 25706739. [In Turkish].

9. Jia J, Chen M, Mo X, Liu J, Yan F, Li Z, Xie S, Chen D. The first case report of kerion-type scalp mycosis caused by Aspergillus protuberus. BMC Infect Dis. 2019;19(1):506. DOI: 10.1186/s12879-019-4144-7. PMID: 31182059.

10. Sun B, Luo C, Bills GF, Li J, Huang P, Wang L, et al. Four New Species of Aspergillus Subgenus Nidulantes from China. J Fungi (Basel). 2022;8(11):1205. DOI: 10.3390/jof8111205. PMID: 36422028.

11. Antypkin YG, Gorban NEY, Borysiuk OY, Lynchak OV. The reproductive health of the female residents in the areas of Ukraine affected by the radioactive contamination (2007–2017). Probl Radiatsiinoi Med Radiobiolohii. 2019;2019(24):284-95. DOI: 10.33145/2304-8336-2019-24-284-295. PMID: 31841474. [In English, in Ukrainian].

12. Lyngso J, Ramlau-Hansen CH, Hoyer BB, Stovring H, Bonde JP, Jonsson BA, et al. Menstrual cycle characteristics in fertile women from Greenland, Poland and Ukraine exposed to perfluorinated chemicals: a cross-sectional study. Hum Reprod. 2014;29(2):359-67. DOI: 10.1093/humrep/det390. PMID: 24163265.

13. Zhylka NY, Slabkiy GO, Shcherbinska OS. The state of female reproductive health in Ukraine (literature review). Reprod Endocrinol. 2021;(60):67-71. DOI: 10.18370/2309-4117.2021.60.67-71. [In Ukrainian].

Cite in Vancouver style as: Lytvynenko MV, Bondarenko AV, Bondarenko OV, Gargin VV, Katsap OV. Determination of aspergillosis of the female genital organs in women with immunodeficiency. Inter Collegas. 2023;10(1):15-9. https://doi.org/10.35339/ic.10.1.lbb

PRINCIPLES OF EFFECTIVE USE OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

Meretskyi V.M., Meretska I.V.

I. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine

https://doi.org/10.35339/ic.10.1.mer

ABSTRACT

The article provides an overview of references on the rational use of nonsteroidal anti-inflammatory drugs (NSAIDs) in modern medicine. Nonsteroidal anti-inflammatory drugs are a group of drugs with different chemical structures (mostly acid derivatives) that have anti-inflammatory, analgesic, antipyretic, antiplatelet (acetylsalicylic acid, acetylsalicylate, ketoprofen, diclofenac sodium, niflumic acid, indomethacin) effects. NSAIDs are divided according to the selectivity of action relative to cyclooxygenase (COX) isoforms: non-selective COX inhibitors, selective COX-1 inhibitors, approximately equal inhibition of COX-1 and COX-2, selective COX-2 inhibitors. They are characterized by general pharmacological properties: high degree of absorption in the gastrointestinal tract; a high degree of binding to albumins; approximately the same volume of distribution; the ability to accumulate in the focus of inflammation. Indications for NSAIDs use are: acute arthritis and chronic arthritis; acute and chronic pain syndrome of various nature (lower back pain syndrome, joint and soft tissue injuries, migraine, dysmenorrhea, preoperative and postoperative pain, renal colic, fever in various rheumatic and non-rheumatic diseases). Additional indications for prescribing NSAIDs are: pleurisy, pericarditis, erythema nodosum, polycystic lung disease, sciatica. The most frequent and dangerous side effects include gastrointestinal, kidney complications. Special attention is paid to the cardiovascular safety of NSAIDs and, above all, COX-2 inhibitors because of risk of cardiovascular events. The most effective drug with the best tolerability should be selected for a specific patient. Before starting NSAID therapy, the patient's age, comorbidities, previous medical or surgical history, concomitant use of medications (including antiplatelet agents, anticoagulants, corticosteroids, ACE inhibitors, and selective serotonin reuptake inhibitors), H. pylori infection, and blood pressure monitoring should be considered.

Keywords: *inflammation, pain, side effects, gastropathy, selectivity*.

For the first time, the term nonsteroidal anti-inflammatory drugs (NSAIDs) was proposed by Flower J., who emphasized their fundamental differences from glucocorticoids [1]. In terms of frequency of clinical use, NSAIDs are second only to antibacterial drugs. According to World Health Organization, about 20% of the population around the world take NSAIDs. In particular, about 30 million people in the world use these drugs every day [2].

Corresponding author:
Meretskyi Viktor Mykolayovych –
Professor of the Department of Pharmacology and Clinical Pharmacology at I. Horbachevsky Ternopil National Medical University.
Address: Ukraine, 46001, Ternopil, Maidan Voli, 1.
E-mail: meretskyy@tdmu.edu.ua

NSAIDs are a group of drugs with different chemical structures (mostly acid derivatives) that have anti-inflammatory, analgesic, antipyretic, antiplatelet (acetylsalicylic acid, acetylsalicylate, ketoprofen, diclofenac sodium, niflumic acid, indomethacin) effects, as well as desensitizing effects (indomethacin, diclofenac sodium, acetylsalicylic acid) and stimulate the synthesis of interferon (mefenamic acid).

NSAIDs are classified according to their chemical structure as follows:

I. Derivatives of acids.

Arylcarboxylic acids.

Derivatives of salicylic acid or salicylates (acetylsalicylic acid, diflunisal).

Derivatives of anthranilic acid or fenamates (mefenamic acid, niflumic acid).

Arylalkanoic acids.

Derivatives of arylacetic acid (diclofenac sodium).

Derivatives of heteroacetic acid (ketorolac).

Derivatives of indole/indenoacetic acid (indomethacin, sulindac, etodolac).

Derivatives of arylpropionic acid (ibuprofen, naproxen, ketoprofen).

Enolic acids.

Pyrazoline derivatives (phenylbutazone, metamizole).

Oxicams (piroxicam, meloxicam).

II. Some other derivatives: nimesulide, colchicine, celecoxib, nabumetone.

III. Combined drugs:

- arthrotec (diclofenac + misoprostol), ambene (phenylbutazone + dexamethasone);

- aspifat (acetylsalicylic acid + sucralfate), dolaren (diclofenac + paracetamol).

The mechanism of action of NSAIDs was discovered by a group of scientists (Vane J., Smith J., Willis A.) in 1992, for which they were awarded the Nobel Prize. It consists in non-selective or selective inhibition of the cyclooxygenase (COX) enzyme, which inhibits the formation of prostaglandins (E1, I2, F2α), thromboxane, as a result of which the intensity of inflammation, pain, and fever decreases. Today, it is known about the existence of 2 isoforms of COX: COX-1 (constitutional), COX-2 (regulated). COX-1 is found in almost all organs and tissues, including the digestive tract, bronchi, kidneys, and platelets. It regulates the synthesis of homeostatic and cytoprotective prostaglandins (PG) in the mucous membrane of the gastrointestinal tract, bronchi, vascular endothelium, platelets, and kidney tubules. COX-2 is predominant in the brain, bone tissue, reproductive organs, juxtaglomerular apparatus of kidneys, monocytes and macrophages. COX-2 is normally found in small amounts, but the expression of this isoenzyme increases sharply in foci of inflammation. Inflammatory mediators (tumor necrosis factor, interleukin-1, etc.) can increase the level of COX-2 tenfold. According to modern ideas, it is believed that COX-2 is involved in the synthesis of "pro-inflammatory" prostaglandins, enhances the activity of inflammatory mediators, such as histamine, serotonin, and bradykinin. Regarding the existence of COX-3 (in animals, it is localized in the central nervous system (CNS), contributes to pain and fever, but does not affect the inflammatory cascade), there has been a debate in scientific circles for many years, and some researchers consider COX-3 to be a variant of COX-1, calling it COX- 1b or SOX 1v [3–5].

NSAIDs are divided according to the selectivity of action relative to COX isoforms:

- non-selective COX inhibitors: (diclofenac, ibuprofen, piroxicam, indomethacin) – the majority belongs to this group NSAIDs;

- selective COX-1 inhibitors: highly selective (low doses of acetylsalicylic acid), and selective (fenoprofen, piroxicam, sulindac);

- approximately equal inhibition of COX-1 and COX-2 (lornoxicam);

- selective COX-2 inhibitors: highly selective – coxibs (celecoxib, rofecoxib, valdecoxib, etoricoxib) and others (meloxicam, nimesulide, etodolac);

- selective COX-3 inhibitors (acetaminophen, metamizole).

COX-1-selectivity increases the likelihood of NSAID-gastropathies, chondrodestructive processes and causes renal toxicity, and COX-2-selective drugs increase the risk of cardiovascular side effects. In addition, COX-2 inhibitors, like other NSAIDs, slightly increase blood pressure. By blocking the formation of PG, NSAIDs reduce the permeability of the vascular wall and the penetration of plasma factors into tissues. At the same time, the activity of guanylate cyclase and the level of cyclic guanosine monophosphate (cGMP) decrease, the division of fibroblasts, the synthesis of collagen, mucopolysaccharides, and the formation of connective tissue are inhibited. The antiproliferative effect of NSAIDs is partly due to the inhibition of the activity of serotonin and bradykinin, which stimulate the division of fibroblasts. Destructive processes in cartilage and bone tissue are unfortunately not inhibited by most NSAIDs. In addition, against the background of the use of classic NSAIDs, the synthesis of proteins necessary for the regeneration of cartilage and bone tissue decreases [4; 6].

The anti-hyaluronidase activity of NSAIDs also helps to reduce the permeability (anti-edematous effect) of blood vessels and cell membranes in the focus of inflammation. NSAIDs reduce the energy supply of the inflammatory reaction, inhibit oxidative phosphorylation, which disrupts the synthesis of glycosaminoglycans and inhibits proliferation processes.

According to the degree of anti-inflammatory effect, non-steroidal anti-inflammatory drugs are divided into:

NSAIDs with significant anti-inflammatory activity:

- salicylates (acetylsalicylic acid, diflunisal);

- pyrazolidines (phenylbutazone);
- derivatives of indoleacetic acid (indomethacin, sulindac, etodolac);
- derivatives of phenylacetic acid (diclofenac);
- oxicams (piroxicam, meloxicam);
- alkanones (nabumetone);
- derivatives of propionic acid (ibuprofen, naproxen, fenopofen, flurbiprofen, ketoprofen, tiaprofenic acid);
- sulfonanilide derivatives (nimesulide);
- derivatives of other chemical groups (celecoxib).

NSAIDs with weak anti-inflammatory activity:

- derivatives of anthranilic acid (mefenamic acid);
- pyrazolones (metamizole sodium, propifenazone);
- derivatives of paraaminophenol (paracetamol);
- derivatives of heteroarylacetic acid (ketorolac).

By decreasing analgesic activity, NSAIDs can be arranged as follows: lornoxicam → ketorolac → diclofenac (aceclofenac) → indomethacin → ibuprofen → acetylsalicylic acid → ketoprofen; according to the risk of cumulation and unwanted drug interaction: piroxicam → aceclofenac → meloxicam → ketorolac → ibuprofen → diclofenac → lornoxicam. *According to the effect on the metabolism of hyaline cartilage*, NSAIDs can be classified as follows: drugs with chondronegative, chondroneutral and chondroprotective effects. Indomethacin, piroxicam, naproxen and some other traditional NSAIDs have a chondronegative effect on cartilage, chondroneutral – ibuprofen, diclofenac, chondroprotective – aceclofenac, ketoprofen and meloxicam.

The immunosuppressive effect of NSAIDs is moderately pronounced, appears with long-term use and is of a "secondary" nature: by reducing the permeability of capillaries, NSAIDs complicate the contact of immunocompetent cells with antigen and the contact of antibodies with the substrate [1; 4; 7–9].

Most NSAIDs are weak organic acids with a relatively low pH. They are characterized by general pharmacological properties:

- high degree of absorption in the gastrointestinal tract;
- a high degree of binding to albumins (with hypoalbuminemia, the concentration of the "free" drug increases, which can lead to increased toxicity);
- approximately the same volume of distribution;
- the ability to accumulate in the focus of inflammation.

The half-life of NSAIDs (T½) varies widely (from 0.2 h – acetylsalicylic acid to 35–45 h – piroxicam). Conventionally, they are divided into drugs with short T½ (<6 h) and long T½ (>6 h). However, the duration of the anti-inflammatory effect does not always correspond to T½, since the concentration of the drug in the focus of inflammation does not always correlate with the concentration in the blood plasma. Of great importance is the ability of NSAIDs to accumulate in the inflammation zone (for example, the joint cavity) and stay there for a long time in therapeutic concentrations. The therapeutic response also depends on the time required to reach stable (equilibrium) concentrations in the blood plasma (a level corresponding to 3–5 T½ periods). Often, taking drugs with a short T½ twice a day is as effective as multiple intake [4; 7; 10].

Indications for use of the nonsteroidal anti-inflammatory drugs are:

- acute arthritis (gout, exacerbation of chronic joint diseases – rheumatoid arthritis, osteoarthritis, spondyloarthritis, reactive arthropathy in non-rheumatic diseases);
- chronic arthritis (osteoarthritis, rheumatoid arthritis, seronegative spondyloarthritis, arthritis in other rheumatic diseases and non-rheumatic diseases);
- acute and chronic pain syndrome of various nature (lower back pain syndrome, joint and soft tissue injuries, migraine, dysmenorrhea, preoperative and postoperative pain (reduction in the need for narcotic analgesics), renal colic, fever in various rheumatic and non-rheumatic diseases);
- additional indications for prescribing NSAIDs: pleurisy, pericarditis, erythema nodosum, polycystic lung disease, sciatica [4; 11–13].

Contraindications for use of the nonsteroidal anti-inflammatory drugs are:

- erosive and ulcerative lesions of the gastrointestinal tract, especially in the acute stage;
- pregnancy and breastfeeding;
- significant liver and kidney function disorders;
- cytopenia;
- increased sensitivity to the drug;
- the patient's profession that requires constant concentration of attention and precise coordination of movements [7].

Side effects of the nonsteroidal anti-inflammatory drugs are listed in *Table 1.*

NSAIDs are a group of drugs that are relatively dangerous in terms of side effects. The toxic effects of NSAIDs are caused by inhibition of COX-1 activity and disruption of prostaglandin synthesis in the gastrointestinal mucosa, kidneys, endothelium, and platelets.

The most frequent and dangerous side effects include gastrointestinal complications. Most often, NSAIDs cause symptoms of dyspepsia – heartburn, epigastric pain, nausea, vomiting, diarrhea, constipation, which occur with long-term use in 30–40% of patients and in 5–15% of cases are the reason for stopping treatment. The second most frequent manifestation of the toxic effect of NSAIDs on the digestive tract is gastropathy. The term "NSAID-gastropathy", which was introduced in 1986 by Roth S.H. means erosive-ulcerative gastrointestinal lesions on the background of taking NSAIDs. NSAID-gastropathies are characterized by some features: the appearance of ulcers associated with taking NSAIDs, acute multiple erosions or ulcers, localization of ulcers in the antral part of the stomach, little or asymptomatic course, frequent manifestations, disappearance after withdrawal of the drug. There are several factors that increase the risk of NSAID gastropathy. They include:

- age (over 60 years old);
- history of gastrointestinal pathology (especially peptic ulcers and gastric bleeding);
- taking high doses of NSAIDs (low doses taking of NSAIDs is linked to relative risk of NSAID gastropathy, high doses – the risk is tripled);
- simultaneous intake of several NSAIDs (risk doubles);
- simultaneous use with glucocorticoids (the risk increases 10 times);
- long-term use of NSAIDs (more than 3 months);
- taking NSAIDs with a long half-life and non-selective COX-2 (the most toxic – piroxicam, naproxen, indomethacin, the safest – meloxicam, nimesulide, celecoxib);
- therapy with anticoagulants and/or antiplatelet agents.

Other risk factors are the presence of rheumatoid arthritis, female gender, smoking, alcohol intake, helicobacter infection. They should be taken

Table 1. Frequency of occurrence and types of side effects of nonsteroidal anti-inflammatory drugs

Side effects	Frequency, %
Gastrointestinal	
Dyspepsia (poorly correlated with complications from the gastrointestinal tract)	>10
Erosions and ulcers (more often in the stomach)	1–5
Intestinal damage (possible cause of anemia)	1–5
Liver damage (usually a moderate increase in liver enzymes)	1–5
Esophageal damage	<1
Renal (more often caused by indomethacin)	
Glomerular filtration disorders	1–5
Increase in blood pressure	1–5
Papillary necrosis	<1
Interstitial nephritis	<1
Neurological	
Headaches (more often indomethacin)	1–5
Aseptic meningitis (ibuprofen, ketoprofen, flurbiprofen, naproxen)	<1
Dermal	
Itching, skin rash	<1
Hematological (most often – phenylbutazone, very rarely – indomethacin), including agranulocytosis	<1
Hypersensitivity (most often acetylsalicylic acid): asthma, urticaria, pneumonitis	<1
Others	
Ototoxicity (most often acetylsalicylic acid)	<1
Infertility in women	<1
Stomatitis, sialoadenitis, carditis, vasculitis, pancreatitis (more often phenylbutazone)	<1
Bronchospasm (COX-2 inhibitors cause less often than "standard" NSAIDs)	<1

into consideration before initiating NSAID therapy. Complications of NSAID-gastropathy include gastrointestinal bleeding and perforation.

It should be noted that the risk of ulcers directly depends on the dose and duration of NSAID treatment. To reduce the likelihood of ulceration, it is necessary to use the minimum effective dose of the drug for a short period of time. These recommendations are usually ignored. A clear relationship between symptomatic side effects, endoscopic ulcers, and severe complications is often lacking. In addition, in patients without symptomatic side effects, gastric ulceration during endoscopy is detected with the same frequency or even more often than in patients with these effects. Therefore, when choosing NSAIDs, the doctor should first of all pay attention to the risk factors of severe complications, and secondly to the subjective complaints of patients [1–15].

When symptoms of dyspepsia appear in patients with a low risk of developing damage to the digestive tract, first of all, it is necessary to cancel the NSAID, or reduce its dose (if possible), or replace the drug with another one with a better safety profile. It is a false statement that injectable and rectal forms of NSAIDs have a less damaging effect on the gastric mucosa. With rectal or parenteral use, the direct toxic effect of NSAIDs is excluded, while the synthesis of protective prostaglandins is disturbed by any method of administration of NSAIDs.

Proton pump inhibitors (PPIs) are the drugs of first choice in the treatment of NSAID gastropathies. The dose is selected individually. In patients with a high risk of cardiovascular complications and simultaneous NSAID gastropathy, the strategy of combining a non-selective NSAID (for example, diclofenac) and a PPI is more appropriate than replacing an NSAID with a highly selective one, which can increase the risk of thrombotic complications.

Although misoprostol (a synthetic analog of prostaglandin E1) is inferior in effectiveness to proton pump inhibitors, it can be considered the drug of choice for the prevention of the development of ulcers in patients receiving NSAIDs.

With long-term use of NSAIDs, 60–70% of patients may also develop asymptomatic enteropathy, which is accompanied by minor blood loss (1–10 ml daily) and protein loss, which leads to iron deficiency anemia and hypoalbuminemia. The mechanisms of enteropathy are the same as those of gastropathy. Much less often, NSAIDs cause damage to the large intestine – colonopathy. The spectrum of damage varies from colitis to perforations, bleeding, and complicated diverticulitis.

All NSAIDs can cause kidney complications. The starting point for renal dysfunction when using NSAIDs is inhibition of PG synthesis. PGs are modulators of renal vascular tone, excretion of electrolytes (sodium, potassium) and water. NSAIDs are characterized by the ability to cause rapid retention of sodium and water, a decrease in glomerular filtration and renal blood flow, hypertension, hyperkalemia, edema, and acute renal failure. In addition, interstitial nephritis, renal papillary necrosis, membranous nephropathy, glomerulonephritis with minimal changes may develop.

NSAIDs can also increase liver enzyme levels, but severe hepatotoxicity is rare. Hepatotoxic action of NSAIDs can, first of all, be manifested in chronic liver diseases. Also, the hepatotoxic effect of NSAIDs can be manifested by hepatogenic encephalopathy – Reye's syndrome, which is based on generalized mitochondrial damage in children with congenital defects of mitochondrial enzymes due to inhibition of oxidative phosphorylation and impaired β-oxidation of fatty acids. A rare, very dangerous emergency condition that occurs in children and male adolescents (more often at the age of 4–15 years) during the treatment of fever in viral diseases – more often influenza and other respiratory viral infections, less often measles, chicken pox, etc., with drugs that contain acetylsalicylic acid, which is characterized by rapidly progressive toxic encephalopathy and the development of fatty infiltration of the liver. Reye's syndrome is accompanied by hyperammonemia, increased activity of aminotransferases in blood serum (more than 3 times) with a normal level of bilirubin.

Side effects of NSAIDs from the hematopoietic system are manifested by thrombocytopenia, anemia, leukopenia.

Since NSAIDs are often prescribed to elderly and senile people with comorbidities (hypertension, coronary heart disease, and diabetes), special attention is paid to the cardiovascular safety of NSAIDs and, above all, COX-2 inhibitors (risk of cardiovascular events). If there is no increased likelihood of developing cardiovascular events, the introduction of NSAIDs with a favorable GI profile is recommended: etoricoxib, celecoxib, diclofenac, ibuprofen, and nimesulide. Ketorolac and ketoprofen are less acceptable in this situation. If the patient has a significant cardiovascular risk, selective COX-2 inhibitors, as well as diclo-

fenac and ibuprofen in high doses, are contraindicated. If the patient is already taking low-dose acetylsalicylic acid for secondary prevention of cardiovascular complications, naproxen is considered the best choice for concomitant use for a short period of time. Other side effects occur much less often and are determined by individual intolerance of one or another drug [7; 15; 16].

Quite often, NSAIDs are used with other drugs. At the same time, it is necessary to take into account the possibility of their interaction (*Table 2*).

When planning pharmacotherapy, it is advisable to consider the following:

1. The anti-inflammatory effect of NSAIDs directly depends on their affinity for COX, as well as on the level of acidity of the solution of the selected drug (information is provided in the instructions for use), which ensures concentration in the area of inflammation. The analgesic and antipyretic effect develops faster, the more neutral the pH of the NSAIDs solution. Such drugs penetrate the central nervous system faster and suppress the centers of pain sensitivity and thermoregulation.

2. The shorter the half-life, the weaker the enterohepatic circulation, the less risk of cumulation and unwanted drug interaction, and the safer the NSAIDs are [6].

It is necessary constantly remember that:

- patients with arterial hypertension or heart failure should be prescribed NSAIDs, which have the least effect on renal blood flow;
- it is necessary to strive for the appointment of minimum doses and short courses of NSAIDs for the elderly;
- when pregnant women take NSAIDs, there is often a delay in pregnancy and a slowdown in labor;
- in order to prevent the development of esophagitis, it is advisable not to lie down for 15 minutes after using NSAIDs;
- NSAIDs should be prescribed with particular caution to patients with bronchial asthma, erosive-ulcerative lesions of the gastrointestinal tract, tendency to bleeding, liver diseases, and impaired kidney function.

Conclusions

When using NSAIDs, certain rules of appointment and dosage must be followed. The most effective drug with the best tolerability should be selected for a specific patient. Before starting NSAID therapy, the patient's age, comorbidities, previous medical or surgical history, concomitant use of medications (including antiplatelet agents, anticoagulants, corticosteroids, ACE inhibitors, and selective serotonin reuptake inhibitors), H. pylori infection, and blood pressure monitoring should be considered. A drug new to the patient should be prescribed starting with the lowest dose followed by a further increase after 2–3 days. With long-term course prescription, NSAIDs are taken after meals. Also, taking NSAIDs can be synchronized with the maximum increase in symptoms of the disease. The simultaneous use of two or more NSAIDs is inadvisable due to the increased risk of side effects, a decrease in the concentration of drugs in the blood, and a decrease in the expected effect.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Table 2. Interaction of nonsteroidal anti-inflammatory drugs with other drugs

Drug	The result of the interaction	Recommendations
Indirect anticoagulants	Increased risk of gastrointestinal bleeding	Dynamic side effect monitoring
β-blockers	Decreased antihypertensive effect	Blood pressure control
Potassium-sparing diuretics (triamterene)	Decreased kidney function	Monitoring kidney function
Thiazide and loop diuretics	Reduction of natriuretic and antihypertensive effects of diuretics	The dose of diuretics can be adjusted
Other NSAIDs	Increased risk of NSAID-gastropathy	Dynamic side effect monitoring
ACE inhibitors	Decreased antihypertensive effect, increased risk of nephrotoxicity and hyperkalemia	Blood pressure control, monitoring kidney function, potassium level
Fluoroquinolones	Increased risk of seizures	Dynamic side effect monitoring

Data Transparency
The data can be requested from the authors.
Statement of Ethics
The authors have no ethical conflicts to disclosure.

Funding Sources
There are no external sources of funding.
Consent for publication
All authors give their consent to publication.

Received: 25 May 2023
Accepted: 26 Jun 2023

References

1. Abduieva FM, Bychkova OYu, Bondarenko IO, Burda IYu, Vlasenko OO, Yehorova A Yu, et al. Clinical pharmacology: Textbook for students and doctors. Gen. ed. Yabluchanskyi MI, Savchenko VM. Kharkiv: V.N. Karazin Kharkiv National University; 2011. 405 p. [In Ukrainian].

2. Haley RM, Recum HA. Localized and targeted delivery of NSAIDs for treatment of inflammation: A review. Experimental Biology and Medicine. 2019;244:433-44. DOI: 10.1177/1535370218787770. PMID: 29996674.

3. Kadusevicius E. Novel applications of NSAIDs: insight and future perspectives in cardiovascular, neurodegenerative, diabetes and cancer disease therapy. Int. J. Mol. Sci. 2021;22:6637. DOI: 10.3390/ijms22126637. PMID 34205719.

4. Clinical pharmacology and pharmacotherapy in rheumatology. Krasko MP, Kraidashenko OV, Kremzer OO, Krasko VV. 2nd ed., rev. and add. Zaporizhzhia; 2015. 317 p. [In Ukrainian].

5. R van Rensburg, Reuter H. An overview of analgesics: NSAIDs, paracetamol, and topical analgesics Part 1. South African Family Practice. 2019;61:sup1:4-10. DOI: 10.1080/20786190.2019.1610228.

6. Wheatley BM, Nappo KE, Christensen DL, Holman AM, Brooks DI, Potter BK. Effect of NSAIDs on bone healing rates: a meta-analysis. Journal of the American Academy of Orthopaedic Surgeons. 2019;27(7):330-6. DOI: 10.5435/JAAOS-D-17-00727. PMID: 30260913.

7. Compendium 2019 – medicinal products. Kyiv: Morion; 2019. 2870 p. Available at: https://compendium.com.ua/uk/handbooks-uk/compendium-uk/ [in Ukrainian].

8. Smith D, Wilkie R, Croft P, Parmar S, McBeth J. Pain and mortality: mechanisms for a relationship. Pain. 2018;159(6):1112-8. DOI: 10.1097/j.pain.0000000000001193. PMID: 29570110.

9. Pelletier R, Bourbonnais D, Higgins J, Mireault M, Harris PG, Danino MA. Pain interference may be an important link between pain severity, impairment, and self-reported disability in participants with wrist/hand pain. J Hand Ther. 2020;33(4):562-70.e1. DOI: 10.1016/j.jht.2019.06.001. PMID: 31481341.

10. Enthoven WTM, Roelofs PD, Koes BW. NSAIDs for chronic low back pain. JAMA. 2017;317(22):2327-8. DOI: 10.1001/jama.2017.4571. PMID: 28609520.

11. McMahon SB, Dargan P, Lanas A, Wiffen P. The burden of musculoskeletal pain and the role of topical non-steroidal anti-inflammatory drugs (NSAIDs) in its treatment. Ten underpinning statements from a global pain faculty. Current Medical Research and Opinion. 2021;37(2):287-92. DOI: 10.1080/03007995.2020.1847718. PMID: 33155849.

12. McHugh CG, Opare-Addo MB, Collins JE, Jones MH, Selzer F, Losina E, Katza JN. Treatment of the syndrome of knee pain and meniscal tear in middle-aged and older persons: A narrative review. Osteoarthr Cartil Open. 2022;4(3):100282. DOI: 10.1016/j.ocarto.2022.100282. PMID: 35991623.

13. Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage. 2019;27(11):1578-89. DOI: 10.1016/j.joca.2019.06.011. PMID: 31278997.

14. Ho KY, Cardosa MS, Chaiamnuay S, Hidayat R, Ho HQT, Kamil O, et al. Practice advisory on the appropriate use of NSAIDs in primary care. Journal of Pain Research. 2020;13:1925-39. DOI: 10.2147/JPR.S247781. PMID: 32821151.

15. Domper Arnal M-J, Hijos-Mallada G, Lanas A. Gastrointestinal and cardiovascular adverse events associated with NSAIDs. Expert Opinion on Drug Safety. 2022;21(3):373-84. DOI:10.1080/14740338.2021.1965988. PMID: 34376069.

16. Moore N. Coronary risks associated with diclofenac and other NSAIDs: an update. Drug Saf. 2020;43(4):301-18. DOI:10.1007/s40264-019-00900-8. PMID: 31916080.

Cite in Vancouver style as: Meretskyi VM, Meretska IV. Principles of effective use of non-steroidal anti-inflammatory drugs. Inter Collegas. 2023;10(1):20-6. https://doi.org/10.35339/ic.10.1.mer

MODELING THE CLINICAL PROFILE OF PATIENTS WITH HYPERTENSION AND ATRIAL FIBRILLATION BY SERUM NTpro-BNP LEVELS

Ivanov V.P., Zakrevska M.M.

National Pirogov Memorial Medical University, Vinnytsya, Vinnytsia, Ukraine

https://doi.org/10.35339/ic.10.1.ivz

ABSTRACT

Background. Hypertension and atrial fibrillation are a fairly common combination of heart pathology that occurs in the daily practice of a cardiologist. Associations of clinical laboratory and instrumental indicators with the levels of various biomarkers, in particular serum N-terminal fragment of brain natriuretic propeptide (NT-proBNP), are interesting and promising for scientific research and practical application.

The aim of the study was to simulate the clinical profiles of patients with hypertension and atrial fibrillation depending on the serum levels of NTpro-BNP.

Materials & Methods. 89 patients with stage II hypertension and various clinical forms of atrial fibrillation were included in the study. All patients underwent a general clinical examination, additional determination of NT-proBNP serum levels, and assessment of quality of life according to the Minnesota Living with Heart Failure Questionnaire (MLHFQ) for 2–3 days of hospital stay at against the background of selection of optimal therapy. Sequential statistical processing of the obtained data using Spearman's rank correlation analysis and multiple linear regression made it possible to create two clinical profiles of patients.

Results & conclusions. Thus, with a relatively high serum level of NTpro-BNP (≥810 ng/l), the following will be characteristic: hypertensive history >12 years; the presence of signs of left ventricular hypertrophy on the ECG according to the Sokolov-Lyon criteria; increase in the right atrium >36 mm and systolic pressure in the pulmonary artery >38 mm Hg according to Echocardiography; an increase in the average daily heart rate >110 per 1 min with Holter ECG monitoring; a decrease in the glomerular filtration rate <56 ml/min/1.73m^2 and an increase in the total MLHFQ score >27. The dominant markers of a relatively high level of NTpro-BNP were a decrease in quality of life, instrumental signs of hemodynamic overload of the right heart and clinically significant cardiorenal disorders. With a relatively low serum level of NTpro-BNP (≤220 ng/l), the following will be characteristic: hypertensive history anamnesis <8 years; lack of signs of the left ventricle hypertrophy on the ECG according to the Sokolov-Lyon criteria; the size of the right atrium <34 mm and/or the value of systolic pressure in the pulmonary artery <33 mm Hg according to Echocardiography; average daily heart rate with Holter ECG monitoring <92 per 1 minute; glomerular filtration rate >68 ml/min/1.73m^2 and the total MLHFQ score <21. The dominant markers of a relatively low level of NTpro-BNP were the absence of signs of left ventricular hypertrophy on the ECG and a balanced state of sympatho-adrenal activity by the nature of circadian regulation of heart rate.

Keywords: *atrial fibrillation; N-terminal fragment of brain natriuretic propeptide; clinical profile of patients.*

Corresponding author:
Zakrevska Maryna Mykhailivna – Postgraduate Student of the Department of Internal medicine No.3 at National Pirogov Memorial Medical University, Vinnytsya, Vinnytsia.
Address: Ukraine, 21018, Vinnytsya, Pyrohova str., 56, National Pirogov Memorial Medical University.
E-mail: DrZakrevska@ukr.net

Introduction

Hypertension and atrial fibrillation (AF) is a fairly common combination of heart pathology that occurs in the daily practice of a cardiologist [1]. The practical interest in such an association of diseases is primarily related to the high prevalence of both pathological conditions in the European population, the close connection of diseases with the de-

velopment of various cardiovascular events, including fatal ones, as well as a significant decrease in the quality of life of patients [2; 3].

Associations of clinical laboratory and instrumental indicators with the levels of various biomarkers are interesting and promising for scientific research and practical application, which not only characterize the specificity and severity of systemic processes occurring in the cardiovascular system, but also can be used to predict the course of diseases and certain standardization of clinical profiles of patients. One such biomarker is the serum N-terminal fragment of brain natriuretic propeptide (NT-proBNP) [4; 5].

The aim of the study was to simulate the clinical profiles of patients with hypertension and atrial fibrillation depending on the serum level of NTpro-BNP.

Materials and Methods

The study was conducted in accordance with the main provisions of the Helsinki Declaration of the World Medical Association on the ethical principles of scientific medical research involving human subjects (2000) and the order of the Ministry of Health of Ukraine No.281 dated November 1, 2000. The research protocol was approved by the biomedical ethics commission of National Pirogov Memorial Medical University, Vinnytsya.

As part of an open observational randomized comparative study, 89 patients with stage II hypertension and various clinical forms of AF were examined. The average age in the studied contingent was (61.1±9.0) years. There were 39 men (43.8%) and 50 women (56.2%) in the study. All patients were examined and treated on the basis of the Municipal Institution of Vinnytsia Regional Clinical and Diagnostic Center for Cardiovascular Pathology during 2018–2021.

All patients underwent a general clinical examination in accordance with current international guidelines [3; 6; 7], additional determination of NT-proBNP serum levels and assessment of quality of life according to the MLHFQ (Minnesota Living with Heart Failure Questionnaire [8]) on day 2^{nd}–3^{rd} of hospital stay against the background selection of optimal therapy.

The levels of serum NT-proBNP were determined using the appropriate ELISA test systems (Critical Diagnostics, USA). The different levels of NT-proBNP and the selection of groups with a relatively low (RL, ≤220 ng/l), intermediate (Im, 221–809 ng/l) and relatively high (RH, ≥810 ng/l) levels were calculated by the method of variational statistics with determination of the median and interquartile range for the levels of biomarkers in the examined sample of patients (n=89). The RL level for this sample was defined as the value of the biomarker <25^{th} and RH – >75^{th} percentile, respectively. Instead, the Im level corresponded to the range of the indicator, which was between the 25^{th} and 75^{th} percentiles.

Statistical analysis was performed using Microsoft Excel (2016) and Statistica 12.0 (Statsoft, USA).

At the first stage of the analysis, in order to "filter" and select the most informative indicators, Spearman's rank correlation analysis was used between the actual biomarker serum levels (ng/l) and various clinical and instrumental indicators, as well as indicators of the quality of life according to the MLHFQ questionnaire.

Based on the results of the analysis, indicators that demonstrated statistically significant rank correlations ($p<0.05$) with the content of serum NT-proBNP were selected. These indicators were taken for the next analysis – multiple linear regression.

The serum level of NTpro-BNP was taken as the initial parameter of the multiple linear regression in points, where 1 point is RL, 2 points is Im, and 3 points is RH level, respectively.

When conducting a multiple regression analysis in order to determine the most informative combination of indicators, the procedure of stepwise inclusion of features ("Forward stepwise") was used. It allowed us to determine the combination with the largest coefficient of multiple regression – the coefficient of determination (R2). In addition, the beta coefficients (of the obtained parameters of the model, which demonstrate the nature and strength of the connection with the original parameter), the level of their statistical significance (p-value) and the strength of the influence of the parameters on the original parameter in points were determined. The latter was calculated as the ratio of the beta-coefficient of the parameter to the sum of the beta coefficients of all parameters of the model, multiplied by 100 and rounded to whole numbers.

To build a clinical profile of patients with different serum levels of NTpro-BNP we used two levels of the biomarker – RH and RL, which were previously determined for the examined sample of patients. In addition, threshold values of model parameters were calculated for each selected biomarker level, which made it possible to conduct a more detailed assessment of the clinical profile of patients. Threshold values of the parameters

were calculated as the values that determined the maximum informativeness (namely, the maximum value of the odds ratio of events – OR) in predicting separately RL and RH level of serum NTpro-BNP. For discrete values, the threshold values (in the case of a positive regression relationship) were taken as 0 points for RL and as 1 point for RH of the biomarker level, respectively.

Results and Discussion

Based on the results of Spearman's rank correlation analysis, those that demonstrated statistically significant rank correlations ($p<0.05$) with the NT-proBNP serum levels were selected from the wide variety of studied indicators (*Table 1*).

The indicators in *Table 1* were taken as the main parameters for multiple linear regression. The exceptions were the HM ECG indicators (HRday, HR24-hrs and CI – the ratio of day HR to night HR), which had the same clinical interpretation, so only the HRday indicator, which had the highest correlation coefficient, was taken for further regression analysis.

The results of multiple linear regression are shown in *Table 2*.

The rather high coefficient of multiple regression ($R^2=0.64$) with a significance level of $p=0.00002$ draws attention.

Therefore, analyzing the obtained data, it was observed that the model of the clinical profile of the patient based on the serum level of NTpro-BNP included 7 clinical and instrumental parameters, which revealed statistically significant regression relationships with the level of the biomarker ($p<0.05$):

1) duration of hypertensive medical history in years (beta=0.008; p=0.048);

2) the presence of signs of LV hypertrophy on the ECG according to the Sokolov-Lyon criteria (beta=0.106; p=0.008);

3–4) the size of RA in mm (beta=0.137; p=0.002) and STLa in mm Hg according to Echocardiography (beta=0.038; p=0.01);

5) HR_{day} per 1 minute according to the data of the HM ECG (beta=0.150; p<0.0001);

6) the value of GFR [ml/min/1.73m^2] (beta=-0.113; p=0.005);

7) the value of the total score according to the MLHFQ questionnaire (beta=0.193; p<0.0001).

Table 1. Statistically significant results of Spearman's rank correlation between various clinical and instrumental indicators and NTpro-BNP serum levels (ng/l)

Clinical and instrumental indicators	Spearman R	T(N-2)	P-value
Duration of hypertensive history, years	0.23	2.14	0.03
LV hypertrophy on ECG according to the Sokolov-Lyon criteria in points (1 point – yes, 0 – no)	0.32	3.10	0.002
FC according to NYHA	0.27	2.61	0.01
BMI, kg/m^2	-0.25	-2.42	0.02
RA according to EchoCG, mm	0.30	2.79	0.006
STLa according to EchoCG, mm Hg	0.29	2.75	0.007
Blockade of LAF of the LBB on ECG in points (1 point – yes, 0 – no)	0.24	2.22	0.02
HR_{day} according to HM ECG data, per 1 min	0.32	3.08	0.002
$HR_{24\text{-}hrs}$ according to HM ECG data, per 1 min	0.31	3.03	0.003
CI according to HM ECG data, um. unit	0.26	2.46	0.01
Daily number of VE according to HM ECG data	-0.27	-2.54	0.01
GFR, ml/min/1.73m^2	-0.28	-2.71	0.008
MLHFQ total score	0.41	4.56	<0.0001

Notes: LV – left ventricle; ECG – electrocardiography; HM – Holter monitoring; FC – functional class; BMI –body mass index; RA – right atrium size; EchoCG – echocardiography; STLa – systolic pressure in the pulmonary artery; LAF of the LBB – left anterior fascicle of the left bundle branch (His bundle); HRday and HR24-hrs are average daily and average 24-hours heart rate, respectively; CI – circadian index; VE – ventricular extrasystole; GFR – glomerular filtration rate; MLHFQ – Minnesota Living with Heart Failure Questionnaire.

Table 2. Results of multiple linear regression with the initial parameter of NTpro-BNP serum level in points

Model parameters	Beta-coefficient	P-value	Power of influence in points
Duration of hypertensive history, years	0.008	0.048	1
LV hypertrophy on ECG according to the Sokolov-Lyon criteria in points (1 point – yes, 0 – no)	0.106	0.008	14
RA according to EchoCG, mm	0.137	0.002	18
STLa according to EchoCG, mm Hg	0.038	0.01	5
HR_{day} according to HM ECG data, per 1 min	0.150	<0.0001	20
GFR, ml/min/1.73m^2	-0.113	0.005	15
MLHFQ total score	0.193	<0.0001	26

Notes:

Informativeness of the obtained model: coefficient of determination (multiple linear regression) – R^2=0.64; Fisher's actual test (F) = 56.73 at the appropriate level (df) = 3.16; level of significance (p) of the model = 0.00002; standard error of analysis according to the model (St. Error of estimate) = 0.04.

LV – left ventricle; ECG – electrocardiography; HM – Holter monitoring; RA – right atrium size; EchoCG – echocardiography; STLa – systolic pressure in the pulmonary artery; HRday – average daily heart rate; GFR – glomerular filtration rate; MLHFQ – Minnesota Living with Heart Failure Questionnaire.

Almost all indicators had a direct regression relationship with the serum level of NTpro-BNP (an increase in the serum level of the biomarker predicted an increase in the value of the indicator or a transition to a higher score), while only one parameter showed an inverse regression relationship with the level of the biomarker – the value of GFR [ml/min/1.73m^2]. The latter demonstrated that an increase in the serum level of NTpro-BNP predicted an actual decrease in the value of GFR and deterioration of the filtration function of the kidneys and vice versa.

The calculated influence of the parameters on the serum level of NTpro-BNP in points showed that the value of the total score according to the MLHFQ questionnaire (impact = 26 points), the average daily heart rate (20 points) and the size of the PP (18 points) had the greatest influence, in that time as the smallest – the value of STLa (5 points) and duration of hypertensive anamnesis (1 point). Such parameters as the value of GFR and the presence of LV hypertrophy on the ECG occupied an intermediate position – the impact was 15 and 14 points, respectively.

Thus, the analysis demonstrated that the level of quality of life, determined by the MLHFQ questionnaire adapted to patients with chronic heart failure, had the greatest impact on the serum level of NTpro-BNP; the nature of HRday regulation, which, first of all, reflected the activity of the sympatho-adrenal system and the nature of hemodynamic overload of the right heart, characterized by the echocardiogram size of RA. To a lesser extent, the effect on the biomarker level was found to be the nature of violations of the kidneys filtration function, which is a consequence of the cardiorenal continuum in patients with hypertension and is characterized by the value of GFR and the nature of structural damage to the LV myocardium, which is determined by signs of hypertrophy on the ECG (*Table 3*).

Analyzing the data in the Table 3, it was necessary to pay attention to the fact that the threshold values of the parameter determined for different serum levels of NTpro-BNP have different prognostic value in a priori prediction of different levels of the biomarker. For example, the duration of hypertensive history >12 years increases the a priori probability of RH level by 1.1 times, while history of <8 years – 1.6 times the probability of RL serum level of NTpro-BNP. The latter demonstrates that a short hypertensive history (<8 years) is more likely to predict the RL serum level of NTpro-BNP than a long hypertensive history (>12 years) – the RH level of the biomarker. Such logistics also apply to other parameters listed in the corresponding table.

Therefore based on the data we obtained, it should have been thought that in patients with hypertension and AF, regardless of its variant, in the

Table 3. Threshold values for parameters of the patient clinical profile model depending on the serum level of NTpro-BNP

Model parameters	Threshold values of parameters for different serum levels of NTpro-BNP	
	≥810 ng/l	**≤220 ng/l**
Duration of hypertensive history, years	>12 OR=15/14=1.1	<8 OR=18/11=1.6
LV hypertrophy on ECG according to the Sokolov-Lyon criteria in points (1 point – yes, 0 – no)	Yes OR=19/10=1.9	No OR=23/6=3.8
RA according to EchoCG, mm	>36 OR=21/8=2.6	<34 OR=17/12=1.4
STLa according to EchoCG, mm Hg	>38 OR=16/13=1.2	<33 OR=14/15=0.93
HR_{day} according to HM ECG data, per 1 min	>110 OR=18/11=1.6	<92 OR=20/9=2.2
GFR, ml/min/1.73m^2	<56 OR=20/9=2.2	>68 OR=16/13=1.2
MLHFQ total score	>27 OR=22/7=3.1	<21 OR=19/10=1.9

Notes: LV – left ventricle; ECG – electrocardiography; HM – Holter monitoring; RA – right atrium size; EchoCG – echocardiography; STLa – systolic pressure in the pulmonary artery; HRday – average daily heart rate; GFR – glomerular filtration rate; MLHFQ – Minnesota Living with Heart Failure Questionnaire.

case of a high serum level of NTpro-BNP (≥810 ng/l), the following clinical profile will be characteristic: hypertensive history >12 years; the presence of signs of LV hypertrophy on the ECG according to the Sokolov-Lyon criteria; increase in RA >36 mm and STLa >38 mm Hg according to Echocardiography; an increase in HR_{day} >110 per 1 min by HM ECG; a decrease in GFR <56 ml/min/1.73m^2 and an increase in the total score according to MLHFQ >27. The dominant markers of the NTpro-BNP serum level in these patients were a decrease in the quality of life, instrumental signs of hemodynamic overload of the right heart and clinically significant cardiorenal disorders.

In turn, in the case of low NTpro-BNP serum level (≤220 ng/l), the following clinical profile will be characteristic: hypertensive history <8 years; absence of signs of LV hypertrophy on ECG according to the Sokolov-Lyon criteria; the size of RA <34 mm and/or the size of STLa according to Echocardiography <33 mm Hg; HR_{day} by HM ECG <92 per 1 min; the value of GFR >68 ml/min/1.73m^2 and the total score according to MLHFQ <21. The dominant markers of RH of NTpro-BNP level in patients with hypertension and AF are the absence of signs of LV hypertrophy on the ECG (excludes the presence of significant structural lesions of the LV myocardium) and a balanced state of sympatho-adrenal activity by the nature of circadian heart rate regulation.

It is worth noting that the a priori clinical portrait of a patient with hypertension and AF and RL serum level of NTpro-BNP with a high probability implies, first of all, the absence of significant structural changes of the LV myocardium and signs of its hypertrophy on the ECG and not a high level of average HR_{day}.

Thus, in the absence of LV hypertrophy on the ECG, the chances of RL biomarker level are 3.3 times higher than when it is present, while at HR_{day} <92, it is 2.2 times higher compared to HR_{day} >92 per 1 min. In addition, the clinical portrait of a patient with hypertension and AF and RL serum level of NTpro-BNP implies a short history of hypertension (<8 years), no signs of hemodynamic overload of the right heart (RA <34 mm or/and STLa <33 mm Hg); absence of cardiorenal disorders (GFR >68 ml/min/1.73m^2) and mild deterioration of quality of life (total MLHFQ score <21).

Conclusions

1. Dominant markers of a relatively high level (≥810 ng/l) of serum N-terminal fragment of brain natriuretic propeptide in patients with hypertension and atrial fibrillation are a decrease in quality of life, instrumental signs of hemodynamic overload of the right heart, and clinically significant cardiorenal disorders.

2. The dominant markers of a relatively low level (≤220 ng/l) of serum N-terminal fragment of brain natriuretic propeptide in this contingent of patients are the absence of signs of left ventricular hypertrophy on the ECG and a balanced state of sympatho-adrenal activity by the nature of circadian regulation of heart rate.

In the future, it is planned to study an expanded range of biomarkers of cardiovascular disease and create a comprehensive clinical profile of the patient.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Funding Sources

There are no external sources of funding.

Consent for publication

All authors give their consent to publication.

Received: 14 May 2023
Accepted: 25 Jun 2023

References

1. Su L, Sun L, Xu L. Review on the prevalence, risk factors and disease Management of Hypertension among floating population in China during 1990–2016. Glob Health Res Policy. 2018;3:24. DOI: 10.1186/s41256-018-0076-9. PMID: 30123839.

2. Perry M, Kemmis BS, Downes N, Andrews N, Mackenzie S; Guideline Committee. Atrial fibrillation: diagnosis and management-summary of NICE guidance. BMJ. 2021;373:n1150. DOI: 10.1136/bmj.n1150. PMID: 34020968.

3. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020;75(6):1334-57. PMID: 32370572. DOI: 10.1161/HYPERTENSIONAHA.120.15026.

4. Xu L, Chen Y, Ji Y, Yang S. Influencing factors of NT-proBNP level inheart failure patients with different cardiacfunctions and correlation with prognosis. Exp Ther Med. 2018;15(6):5275-80. DOI: 10.3892/etm.2018.6114. PMID: 29904410.

5. Yoo J, Grewal P, Hotelling J, Papamanoli A, Cao K, Dhaliwal S, et al. Admission NT-proBNP and outcomes in patients without history of heart failure hospitalized with COVID-19. ESC Heart Fail. 2021;8(5):4278-87. DOI: 10.1002/ehf2.13548. PMID: 34346182.

6. McCormack T, Boffa RJ, Jones NR, Carville S, McManus RJ. The 2018 ESC/ESH hypert ension guideline and the 2019 NICE hypertension guideline, how and why they differ. Eur Heart J. 2019;40(42):3456-8. DOI: 10.1093/eurheartj/ehz681. PMID: 31589745.

7. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C, et al; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42(5):373-498. DOI: 10.1093/eurheartj/ehaa612. Erratum in: Eur Heart J. 2021;42(5):507. Erratum in: Eur Heart J. 2021;42(5):546-7. Erratum in: Eur Heart J. 2021;42(40):4194. PMID: 32860505.

8. Bilbao A, Escobar A, Garcia-Perez L, Navarro G, Quiros R. The Minnesota living with heart failure questionnaire: comparison of different factor structures. Health Qual Life Outcomes. 2016;14:23. DOI: 10.1186/s12955-016-0425-7. PMID: 26887590.

Cite in Vancouver style as: Ivanov VP, Zakrevska MM. Modeling the clinical profile of patients with hypertension and atrial fibrillation by serum NTpro-BNP levels. Inter Collegas. 2023;10(1):27-32. https://doi.org/10.35339/ic.10.1.ivz

VALEOLOGICAL RELATIONSHIP OF PHYSICAL WORKABILITY WITH HEALTH INDICATORS

Heera H.S.[1,2], Najar S.S.H.[1,3], Shevchenko A.S.[4,5], Lytvynenko O.Yu.[4]

[1]Donetsk National Medical University, Kropyvnytskyi, Ukraine
[2]Sri Manakula Vinayagar Medical College, Pondicherry, India
[3]Al-Azhar University, Gaza, Palestine
[4]Kharkiv National Medical University, Kharkiv, Ukraine
[5]Kharkiv Regional Institute of Public Health Services, Kharkiv, Ukraine

https://doi.org/10.35339/ic.10.1.hns

ABSTRACT

A theoretical study is written in the form of a short report on approaches to qualitative and quantitative assessment of health and physical performance. Physical, mental, social, sexual health, their relationship to physical performance, and measurability to assess and compare individual and population outcomes are discussed. Separate models of health quality assessment and its formation are noted. Philosophical systems of understanding health, psychological approaches to its study, pedagogical systems of formation are described. It was noted that the level of physical health of a person depends on his ability to maintain the balance of homeokinesis parameters. The significance of adaptation and dysadaptation processes is described. It is proposed to draw up a "vegetative passport" of a person with an indication of the vagosympathetic balance. Physical performance, which is often evaluated together with anthropometric data, aerobic and anaerobic endurance, neuromuscular coordination, flexibility, stress resistance, is taken into account when planning sports training and professional tasks with a difficult physical component. In ordinary life, it can be reduced due to the wide distribution of hypertension, coronary disease and smoking, and frequent vascular crises. Cardiorespiratory capacity (reserves) and exercise tolerance can be carefully determined using special functional tests. The relationship between physical capacity and health indicators determined in the study allows to objectively determine tolerance to physical exertion and compare capacity in the population and in different periods of a person's life.

Keywords: *models of health diagnosis, adaptation and maladaptation, homeokinesis, tolerance to physical exertion.*

The future of successful medicine largely depends on its preventive (valeological) direction. Relying only on the medical direction is hopeless. Therefore, it is rational to focus the efforts and resources of national health care systems on developing the adaptive potential of practically healthy people [1]. An important step in this direction should be a reassessment of the non-alternative attitude of the medical staff towards everyone who is in their field of vision as "healthy-sick". The quality and quantity of health can be evaluated from the philosophical position of "rehabilitation dualism", the balance of the work of systems and anti-systems [2; 3, p. 34]. A person's functional reserve determines both his resistance to adverse factors and the ability to adapt. And, according to M. Amosov, this reserve ("amount of health") can be measured [4]: *"The amount of health" can be defined as the sum of the "reserve capacities" of the main functional systems. In turn, these reserve capacities can be determined through the "reserve coefficient"*. Quantitative measurement of quality (qualimetry), based on the method of weighting coefficients expert determination, is used by the World Health Organization to determine the levers of public health regulation [5] and is the basis of many academic disciplines studying it [6]. There are also models that use the definition of "quantity of health", in particular, the model of "pre-nosological diagnosis" by Kaznacheev V.P.

Corresponding Author:
Saleh Najar – MD, PhD, Associate Professor,
Department of Rehabilitation and Sports Medicine,
Donetsk National Medical University.
Address: Korolenka str., 1, DNMU,
Kropyvnytskyi, 25005, Ukraine.
E-mail: dr.salehnajar@gmail.com

and Baevsky R.M. (1974), and the model of "diagnosis of health by direct indicators" by Apanasenko H.L. et al. (1985) [7].

The authors of the first model propose to carry out pre-hospital diagnosis based on the indicators of vegetative tone and tension of adaptation mechanisms, as well as to make a functional diagnosis that reflects 4 stages of approaching the disease: 1) satisfactory adaptation (eustress); 2) functional tension of adaptation mechanisms (sub-adaptation); 3) unsatisfactory adaptation; 4) disruption of adaptation mechanisms (dysadaptation). The vectorial nature of the changes in homeokinesis and adaptation mechanisms reflects the rehabilitation diagnosis, which takes into account the genotype and "vegetative passport" of the patient.

The model of "health diagnosis by direct indicators" focuses on the coincidence of biological age with the calendar age, biological function of survival, rehabilitation potential. Health assessment according to this model takes into account self-assessment of health, clinical and physiological indicators (vital lung capacity, body mass index, etc.), which are compared with the average values of these indicators at a certain calendar age for a specific population. According to the obtained result, the patient is assigned to one of the groups: I (from –15 to –9 years, *slowed aging*), II (from –8.9 to –3 years), III (from –2.9 to +2.9 years, *normal aging*), IV (from +3 to +8.9 years) and V (from +9 to +15 years, *accelerated aging*). The model operates with the concepts of "age-related destruction" and "health reserve", and also philosophically connects health with longevity due to the rate of aging.

Another important component of health is well-being, to which the WHO appeals in its definition of health [5]. To some extent, this well-being is characterized by positive emotions and satisfaction with one's life, social adaptability and resistance to psychosocial stress. This actually leads to the need to discuss mental adaptation and maladaptation. Psychological and sociocultural ideas about health are reduced to three models: *antique* (based on internal consistency), *adaptive* (in which the individual is adapted to the natural and social environment), and *anthropocentric* (in which all-round self-realization and the disclosure of the creative potential of the individual are important) [8]. They actually describe adaptation options.

It is also known [9] that mental maladaptation is a prerequisite for neurotic disorders. Mental well-being is closely related to mood balance, the ability to sleep normally, good physical well-being, energy, adaptation to stress, industriousness and sufficient social activity. Extreme degrees of mental maladjustment are self-destructive behavior, overwhelming tendency to violence and suicidal behavior. Other signs of maladaptation are reduced ability to perform economic, social, biological, emotional and intellectual tasks, deviant behavior. Certain non-pathological disorders of biological, psychological and behavioral adaptation harm the survival and reproduction of the species. Therefore, many health researchers place sexual health alongside mental, somatic, and social health [10, p. 20–30]. And to characterize mental, somatic, and social health, they offer the following list of signs: absence of complaints about well-being, moderate altruism, self-respect, self-sufficiency (autonomy), sense of self-worth, and the ability to love.

In academic psychology, cross-cultural, discursive, norm-centric, phenomenological, holistic, axiological, and integral approaches are used to study health [11]. A cross-cultural approach allows us to identify national influences on perceptions of normal health. The discursive approach examines the logic of constructing ideas about health, different health systems and individual health practices. Within the holistic approach, natural and scientific principles of analysis are complemented by humanitarian ones. The axiological approach consists in treating health as a universal human value. In the practice of valeological education, a competence approach is used [12]. Valeological competence is considered as the ability to lead a healthy lifestyle and practice safe behavior patterns. The key to good health is giving up bad habits, a balanced diet, sufficient physical activity, a rational regime of work and rest, avoiding injuries, environmental, radiological and toxicological risks, cooperation with the medical system (vaccination of infectious diseases, timely treatment of detected diseases, participation in screening examinations, for example, annual fluorography, etc.), psychohygiene (maintaining emotional balance), safe sex.

Within the framework of H.L. Apanasenko's theory (1985) the level of somatic health of a person determines the performance of aerobic metabolism. High productivity increases the body's resistance to various adverse factors (hypoxia, intoxication, blood loss, radiation, etc.). In turn, the high resistance of the body forms normoreactivity and eustress, which are also correlated with high rehabilitation potential and work capacity. Another

important basis of health is the vagosympathetic balance, which is determined by the density of receptors and their sensitivity (eutonia). Within the preventive paradigm of future medicine, it is appropriate to draw up a person's "vegetative passport", which should indicate the predominant reaction to external and internal influences – vagotony or sympathotony [7; 13].

Physical capacity, which is manifested in various forms of muscle activity, characterizes the physical "form" of a person or his ability to do physical work and sports. It is often equated with physical endurance. To assess physical performance, the ability to perform dynamic, static or mixed work is studied. Quantitative determination of physical capacity is necessary for drawing up a sport training plan, determining the volume of tasks for representatives of processions with a heavy physical component (military, rescuers, etc.). At the same time, both indicators of physical strength and endurance, as well as cardiometabolic parameters, are subject to measurement and improvement [14; 15]. Physical capacity is evaluated together with anthropometric data, aerobic and anaerobic endurance, neuromuscular coordination, flexibility, stress resistance. Various types of sports and professional activity require a higher minimum level of these indicators. In ordinary life, the intensity of physical exertion is not high, and such exertion has a pronounced aerobic nature, therefore, everyday work is limited by the oxygen transport system. But the high frequency of vascular crises, the spread of hypertension, coronary disease and smoking force us to pay attention to the cardiorespiratory capabilities (reserves) of every person in age after 40. The load tolerance threshold is determined by special functional tests [16–20]. The clinical signs of the threshold of tolerance include complaints of difficulty breathing, an attack of angina pectoris, pronounced fatigue, weakness, dizziness, acute pallor or cyanosis, coldness of the extremities, impaired coordination of movements. Threshold loads determine the limit of possibilities, so they should be tested in conditions where medical care can be provided to the patient.

Conclusions

The indicators of health and physical performance are closely related and measurable. The valeological connection of physical working capacity with health indicators allows objective determining tolerance to physical exertion and comparison of working capacity in the population and in different periods of a person's life.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Funding Sources

There are no external sources of funding.

Consent for publication

All authors give their consent to publication.

Received: 14 May 2023
Accepted: 24 Jun 2023

References

1. Adams ML, Katz DL, Shenson D. A healthy lifestyle composite measure: Significance and potential uses. Prev Med. 2016;84:41-7. DOI: 10.1016/j.ypmed.2015.12.005. PMID: 26724520.

2. Wade D. Why physical medicine, physical disability and physical rehabilitation? We should abandon Cartesian dualism. Clin Rehabil. 2006;20(3):185-90. DOI: 10.1191/0269215506cr952ed. PMID: 16634337.

3. Mykhaliuk YeL, Cherepok OO, Malakhova SM. Biological age and quantitative assessment of the level of physical health of a person. Tutorial. ZSMU; 2013. 137 p. Available at: https://is.gd/IDRLUz [in Ukrainian].

4. Health. In: Mykola Amosov. Outlook [Internet]. Available at: http://icfcst.kiev.ua/amosov/book/361 [accessed 14 Jun 2023]. [In Ukrainian].

5. Constitution of the World Health Organization. Adopted by the International Health Conference (New York, 19 Jun – 22 Jul 1946), signed on 22 Jul 1946 by the representatives of 61 States, entered into force on 7 Apr 1948. [Internet]. Available at: https://apps.who.int/gb/bd/PDF/bd47/EN/constitution-en.pdf [accessed 14 Jun 2023].

6. Shevchenko A. Qualimetric criteria for formation of valeological competence in the adaptive education system. Adaptive management: theory and practice. "Pedagogy" series. 2022;13(25):18p. DOI: 10.33296/2707-0255-13(25)-06.

7. Sokrut VM, Syniachenko OV, Sokrut OP, Mysula IR, Aleksieieva LA, Siabrenko HP, Popov VM. Physical, rehabilitation and sports medicine. 1st vol. Ed. Sokrut VM. Kramatorsk: Kashtan; 2019. 480 p. [In Ukrainian].

8. Tsarenko L. Models of health in the interpretation of personal experience. Herald of psychology and pedagogy. 2012;(9):17c. Available at: https://core.ac.uk/download/pdf/32305879.pdf [in Ukrainian].

9. Prorok N, Tsarenko L, Boiko S. Adaptation, maladaptation, adaptation disorders: issues of terminology. Grail of Science. 2021;(9):373-81. DOI: 10.36074/grail-of-science.22.10.2021.66 [in Ukrainian].

10. Kotsan IIa, Lozhkin HV, Mushkevych MI. Psychology of human health. Ed. Kotsan IY. Lutsk: RVV Vezha, Lesya Ukrainka Volyn National University; 2011. 430 p. Available at: https://core.ac.uk/download/pdf/323530716.pdf [in Ukrainian].

11. Tsarenko L. Ukrainian traditional models of health. Psychological Journal. 2015;1(2):100-13. DOI: 10.31108/1.2015.2.2.15 [in Ukrainian].

12. Shevchenko A. Adaptation of the educational achievement evaluation system to the educational competency approach. Oleksandr Dovzhenko Hlukhiv National Pedagogical University Bulletin. Series: Pedagogical Sciences. 2022;3(50)Pt1:194-203. DOI: 10.31376/2410-0897-2022-3-50-194-203.

13. Apanasenko GL. A book about health. Kyiv: Medknyga; 2007. 132 p. [In russian].

14. Holtermann A, Mathiassen SE, Straker L. Promoting health and physical capacity during productive work: the Goldilocks Principle. Scand J Work Environ Health. 2019;45(1):90-7. DOI: 10.5271/sjweh.3754. PMID: 30021029.

15. Feldpausch JE, Blok AL, Frederick EL, Coburn JW, Malek MH. The Evolution of the Physical Work Capacity at the Fatigue Threshold Test: Past, Present, and Future. J Strength Cond Res. 2021;35(12):3529-36. DOI: 10.1519/JSC.0000000000004124. PMID: 34570058.

16. Kelly JO, Kilbreath SL, Davis GM, Zeman B, Raymond J. Cardiorespiratory fitness and walking ability in subacute stroke patients. Arch Phys Med Rehabil. 2003;84(12):1780-5. DOI: 10.1016/s0003-9993(03)00376-9. PMID: 14669183.

17. Manttari A, Suni J, Sievanen H, Husu P, Vaha-Ypya H, Valkeinen H, et al. Six-minute walk test: a tool for predicting maximal aerobic power (VO_2 max) in healthy adults. Clin Physiol Funct Imaging. May 31, 2018. DOI: 10.1111/cpf.12525. PMID: 29851229.

18. Sorensen L, Honkalehto S, Kallinen M, Pekkonen M, Louhevaara V, Smolander J, Alen M. Are cardiorespiratory fitness and walking performance associated with self-reported quality of life and work ability? Int J Occup Med Environ Health. 2007;20(3):257-64. DOI: 10.2478/v10001-007-0023-3. PMID: 17932015.

19. Tammelin T, Nayha S, Rintamaki H, Zitting P. Occupational physical activity is related to physical fitness in young workers. Med Sci Sports Exerc. 2002 Jan;34(1):158-65. DOI: 10.1097/00005768-200201000-00024. PMID: 11782662.

20. Drain JR, Reilly TJ. Physical employment standards, physical training and musculoskeletal injury in physically demanding occupations. Work. 2019;63(4):495-508. DOI: 10.3233/WOR-192963. PMID: 31282465.

Cite in Vancouver style as: Heera HS, Najar SSH, Shevchenko AS, Lytvynenko OYu. Valeological relationship of physical workability with health indicators. Inter Collegas. 2023;10(1):33-6. https://doi.org/10.35339/ic.10.1.hns

SLEEP QUALITY IN MEDICAL STUDENTS AND ITS DIFFERENT EFFECTS

Almoghrabi B., Nestrenko V.G.

Kharkiv National Medical University, Kharkiv, Ukraine

https://doi.org/10.35339/ic.10.1.aln

ABSTRACT

Background. Sleep disorders is a distressing and disabling condition that affects many people, and can effect the quality of work and education of medical students. Sleep problems, which are accompanied by disruption of the circadian cycle in students, are partly solved by sports and psychological influences (sleep hygiene).

Purpose of the study was to assess the sleep quality during different years of study of medical university students.

Materials & Methods. First to final year students (114 male and 80 female) filled out questionnaires. Pittsburgh Sleep Quality Index (PSQI) questions were used in the form. Qualitative variables were represented as frequencies and percentages. Chi-square and was applied for statistical significance, and p-value <0.05 was considered. The students were divided according to their years of study into 3 groups. Group A for 1st- and 2nd-years, group B – for 3rd- and 4th-years, group C – for 5th- and 6th-years medical students.

Results. About half (47.42%) of the students rated their sleep as very bad, which, however, is less than in the literature (more than 60%). 57% of respondents had daytime dysfunction due to sleep disturbance. 60.31% of survey participants reported that they slept 5–7 hours every night. 20.1% regularly used sleeping pills at least once during the last month. Subjective sleep quality and sleep latency were directly related to the years of study, with p values 0.006 and 0.004.

Conclusion. Our findings show that sleep disruptions among medical students is significant. By calculating the mean score of PSQI we found that the score values increase respectively with the years of studies in the medical faculty explaining more sleep disturbances.

Keywords: *sleep disorders, Pittsburgh Sleep Quality Index, sleep hygiene*.

INTRODUCTION

Sleep problems are widespread and can have a negative impact on person's health and quality of life. While certain sleep problems are more difficult to cure than others, the majority are simply treatable with the right therapies [1]. The stress of the academic environment causes circadian cycle abnormalities in university students. Sports and extracurricular activities are linked to better sleep quality. The modern society is plagued with sleep disorders; almost one-third of individual's report experiencing some kind of sleeplessness [2].

Compared to non-medical students and the general community, medical students make up a demographic that is significantly more susceptible [3]. This is due to a variety of stress-inducing academic load, packed schedules, protracted study sessions, test stress, peer pressure, high parental expectations, and an intensely competitive atmosphere.

Based on previous studies we find that there is a higher prevalence of numerous somatic and/or psychiatric ailments, as well as social issues, is linked to sleep difficulties [4].

Some behavioral, physiological, and neurocognitive functions take place when we sleep; lack of sleep may disrupt these activities. Lack of sleep causes a number of negative effects, including drowsiness and diminished neurocognitive and psychomotor function [5].

The purpose of the current study was to assess and compare medical students' subjective sleep quality across the different periods of their training by utilizing the PSQI. This study was conducted trying to find a correlation between medical studies and the sleep quality. No contraindications were taken into consideration, trying to make the study more generalized and not limited.

Corresponding Author:
Almoghrabi Bachir – student
at Kharkiv National Medical University,
4, Nauky avenue, Kharkiv, 61022, Ukraine.
E-mail: balmohkhrabi.6f18@knmu.edu.ua

Material & Methods

The Pittsburgh Sleep Quality Index (PSQI) contains 19 items, which address sleep latency, usual bedtime and wake time, and sleep and nap quality [6].

This was a study involving medical undergraduates at Kharkiv National Medical University, located in the city of Kharkiv, Ukraine. First- to sixth-year students (n=194) participated. The data were collected from 30 January 2023 till 07 February 2023. All participants filled in an online Google form.

The PSQI is a legitimate and widely used analytic tool for determining sleep disorders, hence it is included in the study instrument. Each of its elements - subjective sleep quality, sleep latency, sleep length, habitual sleep efficiency, sleep disruptions, usage of sleeping pills, and daytime dysfunction- was examined independently. This instrument's range is 0 to 21 points, scores 5–9 signify poor sleep quality, and scores between > 9 of sleep disturbance. The sum of the seven component scores produces a global score.

Using Microsoft Excel, the information from the completed questionnaires was put into tables. One of the tables displayed the findings for the en tire sample and the others the results for each undergraduate class year. The participants were split into three groups: group A, which consisted of 1st- and 2nd-year students; group B, which consisted of 3rd- and 4th-year students; and group C, which consisted of fifth- and sixth-year students. Comparisons within and between groups as well as descriptions of the results for the entire sample were done.

The study was anonymous, with a total of 194 students who participated in the study; they were divided as follow. 83 first and second year, 47 third and fourth year, and 64 were in their last years of study. As for gender distribution, there was a remarkable proportion of males 114, and 80 females (*Table 1*).

Table 1. Sample distribution of the students that participated by group and gender

Sample characteristics		Students
Group	A	83
	B	47
	C	64
Gender	Male	114
	Female	80

The proportions of various answers as a function of each component were used for analysis. In the inductive analysis, the seven PSQI components were compared between groups using the chi-square test, and the global score was compared between groups. P values lower than 0.05 were regarded as significant.

The results for the three groups as well as the entire sample were evaluated for the seven PSQI components. In the entire sample, 47% of the participants rated their sleep as very or fairly bad, and 43.3% said they frequently took longer than 30 minutes to fall asleep. The average amount of sleep each night is 6 hours' 10 minutes. Inductive statistical results showed no significant differences among the three groups regarding subjective sleep quality or sleep latency (*Table 2*).

Table 2. Results of KNMU students answers on the form with PSQI questions represented by Group, and correlated P value for each question

	Group A n=83	Group B n=47	Group C n=64	Total. students	P*
Subjective sleep quality					
During the last month, how would you rate your sleep quality overall?					0.006
Very bad	8	5	16	29	
Fairly bad	22	23	18	63	
Fairly good	46	16	22	84	
Very good	7	3	8	18	

Table 2 continued on next page

	Group A n=83	Group B n=47	Group C n=64	Total. students	P*
Sleep latency					
During the last month, how long (in minutes) did it usually take you to fall asleep each night?					0.004
≤15 min	27	18	8	53	
16 to 30 min	30	8	19	57	
31 to 60 min	14	9	15	38	
>60 min	12	12	22	46	
Sleep duration					
During the last month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed)					0.3
<5 h	8	6	14	28	
5 to 6 h	18	11	18	47	
6 to 7 h	35	18	17	70	
>7 h	22	12	15	49	
Habitual sleep efficiency					
How often do you make a day time nap? (per week)					0.19
Rarely	67	41	47	155	
Usually	16	6	17	39	
Sleep disorders					
During the last month, how often did you have trouble sleeping because you wake up in the middle of the night or early morning?					0.22
Not during last month	21	20	19	60	
Less than once a month	23	7	10	40	
Once or twice a week	19	12	20	51	
Three or more times a week	20	8	15	43	
Use of sleeping medication					
During the last month, how often did you take medicine to help you sleep (prescription or "over the counter")?					0.49
Less than once a month	4	6	9	19	
Not during last month	70	38	47	155	
Once or twice a week	5	2	5	12	
Three or more times a week	4	1	3	8	
Daytime dysfunction					
During the last month, how much trouble was it for you to keep up enough enthusiasm to get things done?					0.14
No problem at all	6	11	10	27	
Only slight problem	30	9	17	56	
Somewhat of a problem	31	16	25	72	
A very big problem	16	11	12	39	

Table 2 presents the students' answers to the different 7 questions of their sleep quality, organized by groups and a total for each answer from all three groups, as well a calculated P value is present beside each question using the chi-square table. *Table 3* shows the calculated PSQI scores of each question and a total for each group.

The analysis by undergraduate class year revealed scores < 5 in 30.12% of first- second-years, 27.66% of third- fourth-years, 20.31% of fifth-sixth-years. Logistic regression, revealed no significant intergroup influence (p=0.64) (*Table 4*).

Nearly 47.42% of the students in our sample rated their sleep as fairly or very bad, which is a lower percentage than that seen in the literature, which found that medical students in particular had poor sleep in the proportions of 61.5% [10], specifically among medical students. 57% of the participants in the current research showed daytime dysfunction, reporting that they have problem to keep up enough enthusiasm to pass their day. Such indicators of daytime sleepiness among medical students are consistent with literature data: 31%; 42.1% and 63%.

Table 3. Mean global PSQI scores for each group

PSQI	1st	2nd	3rd	4th	5th	6th	7th	Total
A	1.37	1.13	1.15	1.15	1.46	0.31	1.02	7.59
B	1.64	1.32	1.23	1.23	1.17	0.28	0.79	7.66
C	1.66	1.8	1.48	1.48	1.48	0.44	0.86	9.2

Table 4. Chi-square table for the PSQI scores of different groups

SCORE PSQI	A	B	C	Grand Total	p
<5	30.12%	27.66%	20.31%	26.29%	0.64
5–9	34.94%	36.17%	34.38%	35.05%	
>9	34.94%	36.17%	45.31%	38.66%	

Discussion

Since it has an impact on their academic schedule and personal lives, medical students' sleep quality is a topic that has received much research on a global scale. Thus, evaluating the quality of your sleep using a tool that has been approved for usage and allows quantification, such as the PSQI [7] is crucial for tracking these students sleep health. By using this method, we discovered that several components of sleep quality were changed in our sample, with 26.29% of scores below 5, which denote considerable sleep quality degradation.

Adherence in this study was nearly 60%, which is in line with researches results of such a form of questionnaire (70%) [8]. In terms of participation by gender, we found a male predominance in effective participation in the study, which is also consistent for other studies that used this method with medical students, in which there was a predominance of males 54.7% [9].

As a result, group C students had more negative impacts on subjective sleep quality and daytime dysfunction than did students in the other groups, with group A and B students' daytime dysfunction indicating a tendency toward a significant difference (A vs C p = 0.03 and B vs C p=0.004). This can be explained by the fact that students go through during their last years of studies, which is characterized by an excessive number of academic activities and irregular daily routines. It should be underlined that studying medical program calls for a high level of commitment and selflessness, which indicates unhealthy lifestyle modifications, such as sleep deprivation and poor sleep hygiene practices.

The results for the sleep latency revealed that 43% of the participants' sleep latency was slightly altered, whereas the results for the sleep duration component showed that 60.31% of the participants reported sleeping 5–7 hours every night, which is comparable to the average of 5.8 hours of

participants [11], but different from the average of 6.48 hours reported by students at the Universidad Adventista del Plata [12].

Remarkably, 20.1% of the participants in the current study reported regularly using sleeping pills at least once during last month, but this number is convenient with the study of Saudi Arabian medical students, which found that 17% of medical students regularly used sleep aids. This finding highlights the need for early intervention programs that focus on bad lifestyle choices [13].

We found that 73.71% of the people in our sample had global PSQI values more than 5, which is higher than the 20.7% [14] reported in the literature.

We discovered that the mean global PSQI scores ranged from 7.59 to 9.2 in the various groups, which is also compatible with the values mentioned in another study (8.1) [15].

In summary, we investigated sleep quality among medical students at this medical school in the city of Kharkiv, Ukraine, and discovered impairments in some PSQI components. This suggests that further research should be conducted in other parts of the nation and the world to monitor the profile of such students and to promote the translation of findings into health promotion practices. Our findings are consistent with the research that shows a high frequency of sleep quality changes that is not considered a problem or condition but may have negative impacts.

We did not employ additional instruments, such as the Epworth Sleepiness Scale, which may have provided information on daytime sleep dysfunction, which was a limitation of the current study because the most significant findings were obtained for the sleep quality and daily dysfunction components. Additionally, given that students in group C reported more issues with subjective sleep quality and daytime functioning than did students in groups A and B.

Among the population of higher education students, there is a need for health promotion measures, such as suggestions of modifications to established health habits especially connected to excellent sleep hygiene. Such recommendations may be found in the literature and are aimed at the general public.

We conclude that students in all academic years of the undergraduate medical program had a significant prevalence of poor subjective sleep quality. First- and second-year students (group A) reported better sleep quality and less daytime dysfunction than students in other class years, according to comparisons throughout the course's various phases (groups B and C).

Conclusions

Our study shows that sleep disorder among medical students is significant. Subjective sleep quality and sleep latency were directly related to the years of study, with p values 0.006 and 0.004. By calculating the mean score of PSQI we found that the score values increase respectively with the years of studies in the medical faculty explaining more sleep disturbances.

DECLARATIONS:

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Consent for publication

All authors give their consent to publication.

Disclosure statement

The authors have no potential conflicts of interest to disclosure.

Funding sources

There are no external sources of funding.

References

1. Sleep disorders. The American Journal of Medicine. 2019;132(3):292-9. DOI: 10.1016/j.amjmed.2018.09.021. PMID: 30292731.

2. Benavente SB, Silva RM, Higashi AB, Guido Lde A, Costa AL. Influence of stress factors and socio-demographic characteristics on the sleep quality of nursing students Rev Esc Enferm USP. 2014;48(3):514-20. DOI: 10.1590/S0080-623420140000300018. PMID: 25076281. [In Portuguese].

3. Nojomi M, Ghalhe Bandi MF, Kaffashi S. Sleep pattern in medical students and residents. Arch Iran Med. 2009;12(6):542-9. PMID: 19877745.

4. Rocha LF, Guerra HL, Lima-Costa MFF. Prevalence of insomnia and associated socio-demographic factors in a Brazilian community: the Bambui study. Sleep Med. 2002;3:121-6. DOI: 10.1016/s1389-9457(01)00119-8. PMID: 14592230.

5. Harrison Y, Horne JA. The impact of sleep deprivation on decision making: a review. J Exp Psychol Appl. 2000;6:236-49. DOI: 10.1037//1076-898x.6.3.236. PMID: 11014055.

6. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213. DOI: 10.1016/0165-1781(89)90047-4. PMID: 2748771.

7. Bertolazi AN, Fagondes SC, Hoff LS, Dartora EG, Miozzo IC, de Barba ME, et al. Validation of the Brazilian Portuguese version of the Pittsburgh Sleep Quality Index. Sleep Med. 2011;12(1):70-? DOI: 10.1016/j.sleep.2010.04.020. PMID: 21145786.

8. Correa CC, Oliveira FK, Pizzamiglio DS, Ortolan EVP, Weber SAT. Sleep quality in medical students: a comparison across the various phases of the medical course. J Bras Pneumol. 2017;43(4):285-9. DOI: 10.1590/S1806-37562016000000178. PMID: 29365004.

9. Cardoso HC, Bueno FC, Mata JC, Alves AP, Jochims I, Vaz Filho IH, et al. Assessing quality of sleep in medical students [In Portuguese]. Rev Bras Educ Med. 2009;33(3):349-55. DOI: 10.1590/S0100-55022009000300005.

10. Rique GL, Fernandes Filho GM, Ferreira AD, de Sousa-Muñoz RL. Relationship between chronotype and quality of sleep in medical students at the Federal University of Paraiba, Brazil. Sleep Sci. 2014;7(2):96-102. DOI: 10.1016/j.slsci.2014.09.004. PMID: 26483910.

11. Alsaggaf MA, Wali SO, Merdad RA, Merdad LA. Sleep quantity, quality, and insomnia symptoms of medical students during clinical years. Relationship with stress and academic performance. Saudi Med J. 2016;37(2):173-82. DOI: 10.15537/smj.2016.2.14288. PMID: 26837401.

12. Fontana SA, Raimondi W, Rizzo ML. Quality of sleep and selective attention in university students: descriptive cross-sectional study [Article in Spanish]. Medwave. 2014;14(8):e6015. DOI: 10.5867/medwave.2014.08.6015. PMID: 25313650.

13. Al-Sayed AA, Al-Rashoudi AH, Al-Eisa AA, Addar AM, Al-Hargan AH, Al-Jerian AA, et al. Sedative Drug Use among King Saud University Medical Students: A Cross-Sectional Sampling Study. Depress Res Treat. DOI : 10.1155/2014/378738. PMID: 24551449.

14. Machado-Duque ME, Echeverri Chabur JE, Machado-Alba JE. Excessive Daytime Sleepiness, Poor Quality Sleep, and Low Academic Performance in Medical Students. Rev Colomb Psiquiatr. 2015;44(3):137-42. DOI: 10.1016/j.rcp.2015.04.002 PMID: 26578413. [In Spanish].

15. Waqas A, Khan S, Sharif W, Khalid U, Ali A. Association of academic stress with sleeping difficulties in medical students of a Pakistani medical school: a cross sectional survey. Peer J. 2015;3:e840. DOI: 10.7717/peerj.840. PMID: 25802809.

Received: 12 Apr 2023
Accepted: 25 Jun 2023

Cite in Vancouver style as: Almoghrabi B, Nestrenko VG. Sleep quality in medical students and its different effects. Inter Collegas. 2023;10(1):37-42. https://doi.org/10.35339/ic.10.1.aln

PHYSICO-CHEMICAL PROPERTIES OF THE ORAL FLUID AND THEIR IMPORTANCE IN ENSURING DENTAL HEALTH

Kotelban A.V.

Bukovinian State Medical University, Chernivtsi, Ukraine

https://doi.org/10.35339/ic.10.1.kot

ABSTRACT

Background. The incidence of dental caries is high regardless of age and region. In this regard, there is a need to study the risk factors for the development of caries, in particular, the physico-chemical properties of oral fluid as one of them.

Aim of the research was to study the physico-chemical properties of oral fluid in children with caries of different levels of intensity and in caries free children.

Materials & Methods. An examination of 6-year-old children living in Bukovina was conducted. The following observation groups were selected: Group I – 69 children suffering from caries, and Group II – 26 caries free children. The rate of saliva secretion, physicochemical properties of oral fluid were studied: pH, viscosity, buffer capacity. The probability of the results was statistically assessed.

Results. In children with different levels of caries intensity, the level of salivation differed: for children with a high level of intensity was characterized by a low level of salivation, and for children with a low level – a high level of salivation. The viscosity of saliva was increased in children with caries of varying intensity. The buffer capacity of saliva was low in children with low levels of caries and very low in children with high levels of caries. PH in children with medium and high intensity was below normal. The analysis of the results of the Test of enamel resistance depending on caries activity showed that in children with a low level of intensity of caries, the enamel was conditionally resistant, and under the conditions of medium and high levels of intensity – the average structural and functional resistance of the enamel and the average acid resistance of the teeth.

Conclusions. Thus, in children suffering from caries with different levels of intensity, there are changes in the quantitative and qualitative parameters of the oral fluid, which lead to disorders of the homeostasis of the oral cavity and deepening of the pathological process in the hard tissues of the teeth.

Keywords: *caries, children, buffer capacity, level of salivation, pH.*

INTRODUCTION

The literature indicates that dental well-being is fundamental in maintaining the health of children in general [1]. The condition of the organs of the oral cavity depends on the balance in the microbial landscape, trace element balance, composition and properties of the oral fluid [2–3]. The first changes in the structure of the enamel already begin when the acidity of the oral fluid decreases, its viscosity increases, saliva secretion decreases, and the concentration of the mineralizing component changes. In addition to the imbalance in the "enamel-saliva" system, more than 100 other factors lead to the development of caries [3–5]. They can be of different intensity and character, different variants of their interaction. A number of researchers assign a significant role to local risk factors for the development of dental diseases in children – thus, the specificity of dental plaque, local mechanisms of protection of the oral cavity, some quality indicators of oral fluid, the presence of bad habits [1–5].

The incidence of caries is high in hole world, in different parts of Ukraine in particular [2–6]. In this regard, there is a need to study the risk factors for the development of caries, in particular, the physico-chemical properties of oral fluid as one of them.

Corresponding author:
Kotelban Anastasiia – MD, PhD, Associate Professor, Department of Pediatric Dentistry, Bukovinian State Medical University, Chernivtsi, Ukraine.
Address: Ukraine, 58002, Chernivtsi, Teatralna Sq., 2.
E-mail: kotelban_anastasiia@bsmu.edu.ua

The aim of the study – to evaluate the physical and chemical properties of oral fluid in children and to determine their role in ensuring of dental health.

Materials and Methods

To solve the goal, we examined 95 children aged 6 years living in Bukovyna. The following observation groups were selected: Group I – 69 children suffering from caries with different levels of intensity, and Group II – 26 caries free children.

Visual assessment of the volume of saliva secretion was carried out by observing after drying the appearance of drops of saliva near the small salivary glands on the mucous membrane of the lower lip. The level of natural salivation was assessed as normal when a drop of saliva appeared within 1 minute, low – more than 1 minute, and high – less than 30 seconds. The viscosity of saliva was also determined visually: significantly increased if saliva foams, increased – saliva foams, there are bubbles, normal – saliva is transparent and watery. The collected saliva was used for pH-metry and determination of the buffer capacity [7].

The hydrogen index of oral fluid (pH) (before eating) was determined using litmus paper with a graduated color scale (5.6–8.0). An indicator piece of paper was dipped into the tubes with unstimulated saliva for 10 seconds. The obtained pH data were compared with a standard color scale: red – 5.0–5.9; yellow – 6.0–6.7 and green – 6.8–7.8.

The buffer capacity of saliva was determined using special strip systems. With a pipette, saliva was applied to 3 test fields and after 3 minutes the change in color from green to red was evaluated. If the sum of points was 10–12, then the indicators were evaluated as normal, 6–9 – low, and up to 5 – very low [7].

To determine the resistance of tooth enamel to caries, the enamel resistance test (TER) according to Okushko V.R. and Kosareva L.I. was used [7]. The degree of enamel staining was assessed by comparing it with a color polygraphic 10-point scale. In accordance with the color of enamel staining, the following levels of enamel resistance were distinguished:

- high caries resistance of enamel (1–3 points) – pale blue coloring;
- moderate resistance of enamel (4–5 points) – blue staining;
- reduced enamel resistance to caries (6–7 points) – blue staining;
- very low enamel caries resistance (8–10 points) – dark blue staining.

The degree of probability of the obtained results was statistically evaluated in the case of normality of the distribution of both samples using the Student-Fisher test, in other cases – the U-Wilkson test for independent samples and the T-Wilkson test for dependent samples. Statistically evaluated the probability of the obtained results in the case of normal distribution of both samples by Student-Fisher test, in other cases - U-Wilkson for independent samples and T-Wilkson test for dependent samples using the program "STATISTICA 6.1" ("StatSoft, Inc", USA).

Results and Discussion

Changes in the composition and structure of oral fluid during pathological processes of the oral cavity, in particular when the hard tissues of the teeth are affected by caries, are unquestionable. After all, not only the level of acid-salt balance – pH, but also its mechanical and physico-chemical properties changes.

The amount of secreted saliva is an extremely important indicator, because the effectiveness of local protective properties depends on its volume. We determined changes in the level of salivation in 6-year-old children with different levels of caries intensity of temporary teeth (*Table 1*).

The normal level of salivation prevailed in children with low and medium caries intensity (in 34.78% and 52.17% of cases, respectively). A low level of salivation was characteristic of children with medium (in 58.33% of the examined) and high caries intensity (in 54.54% of children). As for the high level of salivation, it was found in 52.17% of children with low intensity of caries and 12.50% of children with medium intensity of caries. Caries free children have a high level of salivation.

Qualitative analysis of saliva showed an increase in its viscosity even at a low level of caries intensity of temporary teeth in 52.17% of children (*Table 2*). Predominance of increased viscosity of saliva contributes to reduced cleaning of the oral cavity from food residues, microorganisms and their decay products and, as a result, to a decrease in the resistance of enamel to the action of cariesogenic factors.

The buffer capacity of saliva is a property of the oral fluid, thanks to which neutralization of acids and alkalis is ensured. This indicator is considered as a protective mechanism during the action of acids on the hard tissues of the teeth, that is, it increases the resistance of enamel to caries. Thus, at a low level of disease intensity, the buffer capacity

of saliva was assessed as normal (in 39.13%) and low (in 52.17%), with medium and high caries intensity as low (in 54.16% and in 31.81%%, respectively of those examined) and very low (in 33.33% and in 54.54%) (Table 3).

Under normal conditions, the pH of saliva is in the range of 6.4–7.3 [7]. The concentration of hydrogen ions affects the processes of mineralization and remineralization of enamel, microcirculation, activity of microflora, specific and nonspecific resistance of tissues of the oral cavity. Determination of the pH level of oral fluid in children showed that this value changes depending on the level of intensity of the disease. If at low intensity of caries no significant difference in the values of this indicator compared to dentally healthy children was found ([6.75±0.01] and [6.83±0.02], respectively), then at medium and high intensity of caries its value probably decreased and were (6.28±0.02) and (5.96±0.01) units (*Fig. 1*).

In order to evaluate caries resistance of tooth enamel, we used the TER test. The analysis of the results depending on the caries activity showed that in children with a low level of caries intensity, the TER test is (2.89±0.32) points, which is the extreme limit of the norm, and the enamel is assessed as conditionally resistant (Fig. 2). Under the conditions of an average level of caries intensity in children, the value of this indicator is equal to (4.02±0.43) points, and under the conditions of a high level – (5.07±0.24) points. The obtained data indicate the average structural and functional resistance of the enamel and the average acid resistance of the teeth.

Table 1. The level of saliva secretion in children of observation groups depending on the level of dental caries intensity

Level of saliva secretion	Level of dental caries intensity						Caries free children (n=26)	
	low (n=23)		middle (n=24)		high (n=22)			
	%	abs.	%	abs.	%	abs.	%	abs.
normal	34.78	8	29.17	7	22.72	5	11.54	3
low	13.04	3	58.33	14	54.54	12	-	-
high	52.17	12	12.50	3	22.72	5	88.46	23

Table 2. Salivary viscosity in children of observation groups depending on the level of dental caries intensity

Salivary viscosity	Level of dental caries intensity						Caries free children (n=26)	
	low (n=23)		middle (n=24)		high (n=22)			
	%	abs.	%	abs.	%	abs.	%	abs.
normal	34.78	8	29.17	7	22.72	5	76.92	20
increased	52.17	12	58.33	14	54.54	12	23.08	6
very high	13.04	3	12.50	3	22.72	5	-	-

Table 3. The buffer capacity of saliva in children of observation groups depending on the level of dental caries intensity

Buffer capacity	Level of dental caries intensity						Caries free children (n=26)	
	low (n=23)		middle (n=24)		high (n=22)			
	%	abs.	%	abs.	%	abs.	%	abs.
normal	39.13	9	12.50	3	13.63	3	76.92	20
low	52.17	12	54.16	13	31.81	7	23.07	6
very low	8.69	2	33.33	8	54.54	12	-	-

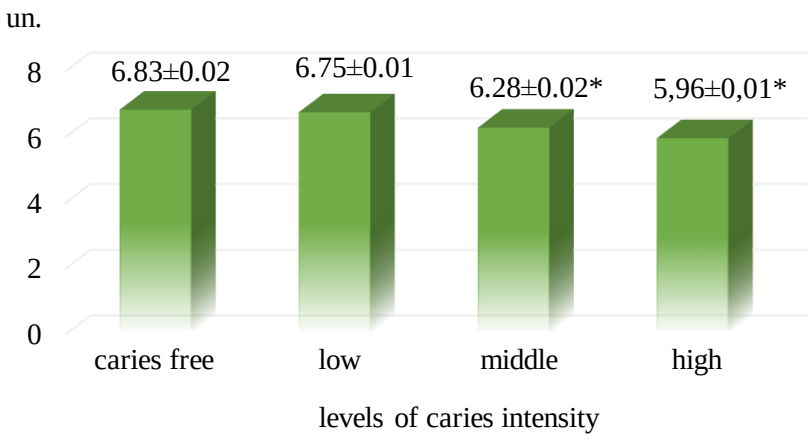

Fig. 1. PH of saliva in children of observation groups depending on the intensity level of dental caries.

Note: * – the difference between the indicators of caries free children and children with caries is significant ($p<0.05$).

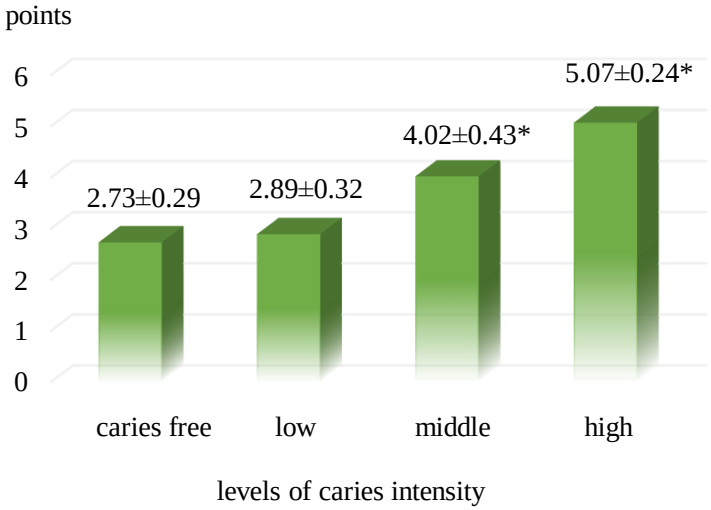

Fig. 2. The results of the TER test in children depending on the intensity level of dental caries.

Note: * – the difference between the indicators of caries free children and children with caries is significant ($p<0.05$).

Conclusions

Therefore, in children suffering from caries with different levels of caries intensity, a decrease in the level of functional reactions is observed. Changes in the quantitative and qualitative properties of oral fluid, a decrease in the level of salivation, a shift in the active reaction of oral fluid in the direction of increased acidity lead to a violation of the homeostasis of the oral cavity, reducing the level of protective reactions of the oral cavity and deepening the pathological process in the hard tissues of the teeth.

DECLARATIONS:

Disclosure Statement

The author has no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The author has no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the author.

Funding Sources

There are no external sources of funding.

Received: 23 Apr 2023
Accepted: 25 Jun 2023

References

1. Klitynska OV, Stishkovskyy AV, Hasiuk NV. Analysis of the effect of stress level in children 6–7 years of age permanently living in conditions of biogeochemical deficiency of fluorine and iodine on caries incidence rates. Bukovinian Medical Herald. 2020;2(94):46-51. DOI: 10.24061/2413-0737.XXIV.2.94.2020.42 [in Ukrainian].
2. Godovanets OI, Kotelban AV, Grinkevich LG, Romanyuk DG. Factors that cause caries among children. Current state of question. Medicine Today and Tomorrow. 2019;85(4):111-20. DOI: 10.35339/msz.2019.85.04.16 [in Ukrainian].
3. Chukhrai NL, Bezvushko EV, Savchyn SV, Sementsiv KhH, Shpotiuk OO. Features of the course of temporary dental caries in children with Epstein-Barr viral infection. Bukovinian Medical Herald. 2020;3(95):157-64. Available at: http://e-bmv.bsmu.edu.ua/article/view/2413-0737.XXIV.3.95.2020.87/216790 [in Ukrainian].
4. Lynge Pedersen AM, Belstrom D. The role of natural salivary defences in maintaining a healthy oral microbiota. J Dent. 2019;80:3-12. DOI: 10.1016/j.jdent.2018.08.010. PMID: 30696553.
5. Narepekha O, Lisak T. Structural and functional enamel resistance (TER-test) in children who are studying in boarding school. Ukrainian dental almanac. 2015;6:56-8. Available at: https://dental-almanac.org/index.php/journal/article/download/95/95/ [in Ukrainian].
6. Oral health surveys basic methods, 5th ed. Geneva: World Health Organization; 2013. 132 p. Available at: https://apps.who.int/iris/bitstream/handle/10665/97035/9789241548649_eng.pdf
7. Kaskova LF, Amosova LI, Kulay OO. Prevention of dental diseases: textbook. Lviv: PP "Magnolia 2006", 2019. 404 p.

Cite in Vancouver style as: Kotelban AV. Physico-chemical properties of the oral fluid and their importance in ensuring dental health. Inter Collegas. 2023;10(1):43-7. https://doi.org/10.35339/ic.10.1.kot

CONTEMPORARY TYPOLOGY OF STRESS-ASSOCIATED DISORDERS IN VOLUNTEERS RESIDING IN THE FRONTLINE REGIONS

Zelenska K.O.

Kharkiv National Medical University, Kharkiv, Ukraine

https://doi.org/10.35339/ic.10.1.zel

ABSTRACT

Background. A volunteer is a person who voluntarily joins socially oriented non-profit activities, carried out by providing free assistance in various areas of the population's life. Volunteering is usually associated with the specifics of contact with human losses and suffering, and in the event of an armed conflict, it can be accompanied by additional psychological, physical and emotional stress. During armed conflicts, volunteers are faced with a significant change in the rhythm of life for a large number of the country's population, and in some cases, a risk to the life of the volunteer himself. In general, volunteering is characterized as highly stressful.

Aim of the study wis to analyze of the clinical picture of stress-related disorders in volunteers living in the front-line regions.

Materials & Methods. In the course of work, a comprehensive clinical-psychopathological and pathopsychological examination of 76 patients suffering from stress-related disorders and living in the front-line regions was conducted.

Results & Conclusions. The study involved the patients of both genders (40 women and 36 men), aged 25–65. The clinical structure of stress-related disorders in the examined patients was represented by post-traumatic stress disorder; adjustment disorders, anxiety disorders. The nosological structure of anxiety disorders is represented by episodic paroxysmal anxiety and generalized anxiety disorder. According to the results of the psychodiagnostic study based on the traumatic stress expressiveness scale, 63.1% of the examined men and 66.8% of the women have a partial manifestation, 36.9% and 33.2% of the examined, respectively, a full manifestation of stress disorder. In 55.6% of the examined men and 57.1% of the women, the presence of an extremely high level was noted, in 33.4% and 41.1% of the examined, respectively, an increased level of social frustration, which is due to the specificity of the psychotraumatic situation. Based on the data obtained during the research, a comprehensive personalized system was developed for the correction of stress-related disorders in the examined volunteers.

Conclusions. It can be concluded that the clinical structure of stress-related disorders in the examined volunteers is represented by post-traumatic stress disorder, adjustment disorders, anxiety disorders.

Keywords: *anxiety, depression, stress disorders, stress*.

INTRODUCTION

As a result of the full-scale invasion, the population of Ukraine is in a multifactorial stressful state, the extreme forms of which are stress-related disorders. As on August 2022, the Ministry of Health of Ukraine provided information that more than 15 million people in Ukraine will need psychiatric or psychological help. Unfortunately, at the moment, according to the number of appeals from Ukrainians, this indicator may increase. For example, a study of mental health in Sumatra showed an increase in psychiatric illnesses after the tsunami compared to the pre-tsunami situation. However, the provision of aid was continuous and all those who needed it could receive it, especially since with a certain frequency these natural disasters occur in this region [1].

One of the most important social and medical issues of our society is the study of specificity, typology, and clinical structure of post-stress disor-

Corresponding author:
Zelenska Kateryna – M.D., Ph.D., Associate Professor of the Department of Psychiatry, Narcology, Medical Psychology and Social Work,
Kharkiv National Medical University.
Address: Ukraine, 61022, Kharkiv, Nauki Ave., 4.
E-mail: zelenskaya135@gmail.com

ders in persons who have survived combat operations, also development of a pathogenetically based and personalized program for its correction and rehabilitation of patients [2–4].

Today, the volunteer movement in Ukraine is talked about with admiration in many countries of the world, calling this phenomenon unique. After all, in an extremely difficult period, it is this movement that unites society, is included in the processes of providing for the army and immigrants, creates an effective structure of groups of people ready to take on the solution of the most urgent and painful problems of the state [5–8].

A volunteer is a person who voluntarily, based on his own convictions, joins socially oriented non-profit activities, which is carried out by providing free assistance. Volunteering is associated with the specifics of contact with human suffering and loss, in the case of an armed conflict, it is accompanied by additional physical, psychological and emotional stress, a significant change in the rhythm of life, and in some cases – a risk to life. All this generally characterizes volunteer activity as stressful, which is a risk factor for the development of stress-related disorders [8–10].

Undoubtedly, one of the most significant social and medical issues of today is the study of specifics of clinical structure, development of the latest directions for diagnosis, therapy of stress-related disorders, and rehabilitation of persons affected by a full-scale invasion [11; 12].

The foregoing determined relevance of our study. The **aim of the study** was to analyze of the clinical picture of stress-related disorders in volunteers living in the front-line regions.

Materials & Methods

In the course of our work, in compliance with the principles of bioethics and deontology all persons who participated in the study signed an informed consent. A comprehensive clinical-psychopathological and pathopsychological examination was conducted in 76 subjects with stress-related disorders of both sexes (40 women and 36 men), aged 25–65 years, who were engaged in volunteer activities, living in the front-line regions. Mathematical and statistical processing of the study results was performed using specialized software packages (Statistica 6.0, MS Excel, USA).

Results & Discussion

In relation to the data obtained during the work, the clinical structure of stress-related disorders in the examined patients was presented: post-traumatic stress disorder – 21.1% of men and 19.6% of women; adjustment disorders – 43.2% and 42.8% of the examined, respectively, anxiety disorders – 33.7% of men and 35.6% of women.

With post-traumatic stress disorder, the following were observed: a depressed background of mood, an affect of longing (51.1% of men and 59.8% of women), obsessive memories of life-threatening situations (39.3% and 28.6% of the examined, respectively), sleep disorders in the form of nightmares (41.8% of men and 44.8% of women), flashback effects (44.9% and 40.9%, respectively), intemperance of affect, dysphoria (43.7% of men and 38.7 % of women), a feeling of internal tension with the inability to relax (66.5% of men and 70.1% of women), efforts to avoid memories and conversations related to combat mental trauma (41.1% and 40.9%, respectively), a feeling of alienation and distance from other people (68.8% of men and 56.9% of women). At the same time, according to the Clinical administered Posttraumatic Stress Disorder (PTSD) Scale [13], the condition of the patients corresponded to the condition of clinically expressed manifestations of PTSD.

The clinical structure of PTSD was represented by anxious (33.8% of men and 51.4% of women), dysphoric (46.3% and 19.5%, respectively) and somatoform (19.9% of men and 9.1% of women) variants of psychopathologic symptoms.

For adjustment disorders, the following were typical: depressive symptoms (48.6% of men and 66.4% of women), groundless anxiety, feelings of internal tension (71.1% and 75.2%, respectively), various fears and apprehensions (33.5 % and 36.5%, respectively), anhedonia (39.8% of men and 40.3% of women), apathy (36.6% and 33.9%, respectively), sleep disorders (44.1% and 46.3% in accordance).

The nosological structure of adjustment disorders was mainly represented by a prolonged anxious depressive reaction (96.8% of men and 97.1% of women).

Anxiety disorders were manifested by unmotivated, persistent, constant anxiety (43.2% of men and 51.1% of women) or unpredictable attacks of severe anxiety (47.8% and 49.9%, respectively), unmotivated bad premonitions (51.6% of men and 55.3% of women), unjustified anxiety (69.2% and 70.3%, respectively), insomnia (43.2% of men and 44.8% of women), psychogenic suffocation (69.2% and 73.1%, respectively), tachycardia (81.1% of men and 85.1% of women).

The nosological structure of anxiety disorders is represented by episodic paroxysmal anxiety

(56.5% of men and 49.8% of women) and generalized anxiety disorder (43.5% and 50.0% of the examined, respectively).

As evidenced by the results of a psychodiagnostic study based on the Expressiveness Scale of Traumatic Stress (by Kotenev O.I., 1996) [14], 63.1% of the examined men and 66.8% of the women have a partial manifestation, 36.9% and 33.2% of the examined, respectively, have a full manifestation of stress disorder.

In 55.6% of the examined men and 57.1% of the women, the presence of an extremely high level of social frustration was noted, and in 33.4% and 41.1% of the examined, was noticed an increased level of social frustration, which is due to the specificity of the psychotraumatic situation. Social frustration is most often manifested by the following signs: disorganization of consciousness and activity in a state of hopelessness, loss of future prospects. All of this is a factor that significantly affects the social adaptation of patients with stress-related disorders.

According to Kukihara H. et al., Matsumoto K. et al. [15; 16], after the earthquake and tsunami in Japan with the subsequent radiation threat, the number of PTSD and depression of various degrees increased. In our opinion, a disaster of this scale can be compared to the impact of war on mental health. But in our study, there was not only an increase in PTSD, but also an increase in adjustment disorders and anxiety disorders. Persons who permanently live in the Kharkiv region participated in our study. Since most of the region's patients seek help from state institutions, it can be said that the obtained results demonstrate the real state of the problem. Not many of those who sought help with this problem agreed to participate in our study.

Based on the data obtained during the research, a comprehensive personalized system was developed for the correction of stress-related disorders in the examined volunteers.

Conclusions

It can be concluded that the clinical structure of stress-related disorders in the examined volunteers living in the front-line regions is represented by: post-traumatic stress disorder, adjustment disorders, anxiety disorders.

DECLARATIONS

Disclosure statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Funding Sources

There are no external sources of funding.

Consent for publication

All authors give their consent to publication.

Received: 26 Feb 2023
Accepted: 23 Jun 2023

References

1. Frankenberg E, Friedman J, Gillespie T, Ingwersen N, Pynoos R, Rifai IU, at al. Mental health in Sumatra after the tsunami. Am J Public Health. 2008;98(9):1671-7. DOI: 10.2105/AJPH.2007.120915. PMID: 18633091.

2. Kilpatrick DG, Resnick HS, Milanak ME, Miller MW. National estimates of exposure to traumatic events and PTSD prevalence using DSM–4 and DSM–5 criteria. Journal of Traumatic Stress. 2013;26(5):537-47. DOI: 10.1002/jts.21848. PMID: 24151000.

3. Khaustova OO. Anxiety-depressive disorders in the conditions of war distress in Ukraine. Health of Ukraine 2022;4:22-4. Available at: http://surl.li/lpfjo [in Ukrainian].

4. Markova MV. Poststresova psihologichna dezadaptaciya: zakonomirnosti rozvitku i specifika klinichnih proyaviv dezadaptivnih staniv u okremih specifichnih grup naselennya, vrazlivih do diyi makrosocialnogo stresu [Post-stress psychological maladaptation: patterns of development and specificity of clinical manifestations of maladaptive states in certain specific population groups vulnerable to macrosocial stress]. Kharkiv: Printing House "Madrid"; 2019. 492 p. [In Ukrainian].

5. Chaban OS, Khaustova OO. Medical and psychological consequences of war distress in Ukraine: what do we expect and what should be taken into account when providing medical aid? Ukrainian medical journal. 2022;4(150):11p. DOI: 10.32471/umj.1680-3051.150.232297. [In Ukrainian].

6. Law of Ukraine No.2849-IX on 13 Dec 2011 "On Volunteering", valid on 20 Jun 2023. Verkhovna Rada (Parliament) of Ukraine. Legislation of Ukraine. Available at: https://zakon.rada.gov.ua/laws/show/3236-17#Text [In Ukrainian].

7. Markova MV, Glagolych SYu. State of the psycho-emotional sphere of volunteers whose activity is connected with assistance to the military in the area of armed actions. Psychiatry, Neurology and Medical Psychology. 2018;1(9):93-100. Available at: http://surl.li/lpgga [In Ukrainian].

8. Korniyevskij OA, Goryelov DM. Ukrayinskij volonterskij ruh u konteksti svitovogo dosvidu [Ukrainian volunteer movement in the context of world experience]. Strategichni prioriteti [Strategic priorities]. 2015;1:95-100. Available at: http://nbuv.gov.ua/UJRN/spa_2015_1_16 [in Ukrainian].

9. Lazos GP. Osoblivosti emocijnih staniv volonteriv – psihologiv/psihoterapevtiv u stosunkah z postrazhdalimi [Peculiarities of emotional states of volunteer psychologists/psychotherapists in relationships with victims]. Osoblivosti stosunkiv "psihoterapevt – kliyent" u suchasnomu sociokulturnomu seredovishi: monografiya. [Peculiarities of the "psychotherapist-client" relationship in the modern socio-cultural environment: monograph] Ed. Kisarchuk ZG. K. Kyiv: Publishing House "Slovo"; 2017. 225 p. [In Ukrainian].

10. Glagolych SY. Clinical and social features of maladaptive states among volunteers, whose work is related to the support of military men in ATO zone. Psychiatry, neurology and medical psychology. 2016;3(2(6)):69-76. Available at: http://nbuv.gov.ua/UJRN/psyneur_2016_3_2_12 [in Ukrainian].

11. Semyhina T, Pavlenko I, Ovsiannikova Y, Teslenko O. Protection of mental health in conditions of war. Translation from English: Combat And Operational Behavioral Health Office of The Surgeon General United States Army Falls Church, Virginia Borden Institute Fort Detrick, Maryland; 2011. In two volumes, volume 1. Kyiv: "Nash format"; 2017. 568 p. [in Ukrainian].

12. Voloshin PV, Maruta NO. Socialno-stresovi rozladi (klinika, diagnostika, profilaktika) [Social stress disorders (clinic, diagnosis, prevention)]. Kharkiv: IE "Strokov DV"; 2016. 335 p. Available at: http://surl.li/lpgni [In Ukrainian].

13. Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, Charney DS, Keane TM. The Development of a Clinician-Administered PTSD Scale. Journal of Traumatic Stress. 1995;8(1):75-90. DOI: 10.1007/bf02105408. PMID: 7712061.

14. Ahaiev NA, Kokun OM, Pishko IO, Lozinska NS, Ostapchuk VV, Tkachenko VV. Collection of methods for diagnosing negative mental states of military personnel: Methodical manual. Kyiv.: NDTs HP ZSU; 2016. 234 p. [In Ukrainian].

15. Kukihara H, Yamawaki N, Uchiyama K, Arai S, Horikawa E. Trauma, depression, and resilience of earthquake/tsunami/nuclear disaster survivors of Hirono, Fukushima, Japan. Psychiatry Clin Neurosci. 2014;68(7):524-33. DOI: 10.1111/pcn.12159. PMID: 24444298.

16. Matsumoto K, Sakuma A, Ueda I, Nagao A, Takahashi Y. Psychological trauma after the Great East Japan Earthquake. Psychiatry Clin Neurosci. 2016;70(8):318-31. DOI: 10.1111/pcn.12403. PMID: 27192947.

Cite in Vancouver style as: Zelenska K.O. Contemporary typology of stress-associated disorders in volunteers residing in the frontline regions. Inter Collegas. 2023;10(1):48-51. https://doi.org/10.35339/ic.10.1.zel

PRESENT-DAY FEATURES OF MALADJUSTMENT STATES IN ENGLISH MEDIUM STUDENTS

Vasylieva O.V.

Kharkiv National Medical University, Kharkiv, Ukraine

https://doi.org/10.35339/ic.10.1.vas

ABSTRACT

Background. During studying, international students require integration into a new linguistic and socio-cultural environment, an unusual climate, large volumes of rather complex new information, new forms and methods of educational process organization, emerging problems outside the educational process, separation from relatives and friends, all this inevitably causes students have new emotional experiences and mental states.

The aim of the research was to study the modern features of the states of psychological maladjustment of international medical English medium (EM) students.

Materials & Methods. 372 international year 1-6 EM students of Kharkiv National Medical University (223 men and 149 women) with an average age of (19±3) years were examined. All the examinees were divided into three groups: Group 1 – 194 students from India; Group 2 – 96 students from other Asian countries (Pakistan, Lebanon, and Syria); Group 3 – 82 students from African countries (Sudan, Tunisia, Morocco, Egypt, Namibia, and Israel).

Results & Conclusions. The conducted psychodiagnostic study showed that students with a high and moderate level of maladjustment have clinical manifestations of anxiety according to Hamilton Anxiety and Depression Rating Scales (29.8% of students of Group 1, 30.1% of Group 2, 29.9% of Group 3) and subclinical manifestations of anxiety (36.2%; 39.5% and 41.1% of students, respectively). Clinical manifestations of depression were typical for 12.4% of students of Group 1, 14.2% of students of Group 2, and 13.4% of students of Group 3; subclinical manifestations of depression – for 21.1%, 19.6% and 19.9%, respectively. The analysis of the expressiveness of the manifestations of hypotensive states allowed distinguishing asthenodepressive (23.1% of the examined Group 1, 15.8% of Group 2 and 25.6% of Group 3), hypersthenic (29.9%; 29.8% and 22.2% of the examinees, respectively), anxious (25.5% of the students of Group 1, 18.9% – of Group 2, 31.1% – of Group 3) and dysphoric (21.5%; 35.5% and 21.1%, respectively) syndromes.

Keywords: *maladaptation, international students of higher education, anxiety, depression*.

INTRODUCTION

Instruction of international students improves not only the image of a higher education institution, but also the image of Ukraine in the international arena. In the age of mass society globalization, process of adaptation of higher education applicants is becoming increasingly relevant. The most vulnerable category among them should be attributed to higher medical education applicants who came to study from abroad [1; 2].

Corresponding author:
Vasylieva Oksana – Candidate of Medical Sciences, Associate Professor, Department of the Physiology, Kharkiv National Medical University.
Address: Ukraine, 61022, Kharkiv, Nauki Ave., 4.
E-mail: oksana_vasylieva@i.ua

International students are citizens of other countries, thus not only studying problems, but also adaptation and social factors of adaptation of their lives in Ukraine, come to the fore.

After enrolling in a higher education institution, an international student finds himself in new social and psychophysiological conditions, exactly during this period the physiological process of adaptation should work, which is included in the majority of international students [3; 4].

During studying, international students face the need to integrate into a new socio-cultural and linguistic environment, an unusual climate, new methods and forms of organization of education, large volumes of fairly complex information, problems of extracurricular activities, separation from relatives and friends. All this inevitably

causes them new emotional experiences and mental states [5; 6].

A large number of international students with different mentalities, differences in national and cultural traditions, different levels of general training and English proficiency level, definitely, require a special approach in conducting educational work with them in medical universities [7–9].

Development of maladjustment states in students during professional training is the main psychological, medical and socio-economic problem, which adversely affects the effectiveness of the future professional activity of medical students. According to the literature, the prevalence of maladaptive disorders in the student population ranges from 5.8% to 61.35%. It leads to reduction in work capacity, deterioration of educational adaptation and academic success, as well as student's quality of life [10; 11].

The forced change of the lifestyle in the conditions of full-scale combat invasion and online studying increases restlessness, feelings of loneliness, leads to exhaustion and even to the development of signs of anxiety and depression among the international students. Development of maladjustment states in students in modern Ukrainian realities is a priority psychological, medical and socio-economic problem, which in the future may negatively affect the effectiveness of the professional activities of international students.

The aim of the research was to study the modern features of the states of psychological maladjustment of the international medical English medium (EM) students.

Materials and Methods

To solve the set goal, in compliance with the principles of bioethics and deontology, a comprehensive survey was conducted on 372 international year 1–6 EM students of Kharkiv National Medical University (223 males and 149 females) with an average age of (19±3) years.

All surveyed students were divided into 3 groups: Group 1 – 194 students from India; Group 2 – 96 students from other Asian countries (Pakistan, Lebanon, and Syria); Group 3 – 82 students from African countries (Sudan, Tunisia, Morocco, Egypt, Namibia, and Israel).

The following psychodiagnostic methods were used in the study: the Spielberger-Khanin Scale (State-Trait Anxiety Inventory, STAI) [12], Hamilton Anxiety and Depression Rating Scales [13; 14], the Symptom Check List-90-Revised (SCL-90-R) Scale [15], scale of nervous and mental tension according to Nemchin T.A. [16]. Mathematical and statistical processing of the study findings was performed using specialized software packages (Statistica 6.0, MS Excel, USA).

Results and discussion

All students who participated in the study were divided into the following groups by maladaptation: "high level", "pronounced level", "moderate level", "insignificant level", "no signs of psychological maladaptation". These groups were formed based on the data of clinical history, clinical-psychopathological and psychodiagnostic methods. Table shows the distribution of students into groups by manifestations of maladaptation. The criteria for maladaptation that became the basis during division into groups were relative cultural and social deprivation, insufficient preparedness for self-regulation processes, low degree of psychological readiness for mastering the profession, loss of the usual social group (social environment).

During the research, certain regularity was revealed: the international students with a higher level of maladjustment did not consider it necessary to receive psychological or medical help and could even neglect it.

The conducted psychodiagnostic study showed that for students with a high and moderate level of maladjustment: 29.8% of students from Group 1, 30.1% subjects from Group 2 and 29.9% from Group 3 had clinical manifestations of anxiety (according to Hamilton Anxiety and Depression Rating Scales); 36.2%, 39.5% and 41.1% of students, respectively, had subclinical manifestations of anxiety. Clinical manifestations of depression were typical for 12.4% of students of Group 1, 14.2% of students of Group 2, and 13.4%

Table. Distribution of students depending on the manifestations of maladaptation.

	Group 1	Group 2	Group 3
high level	2.1%	1.3%	2.9%
pronounced level	6.1%	11.5%	12.6%
moderate level	25.1%	26.2%	31.3%
insignificant level	31.5%	33.9%	35.1%
not show signs of psychological maladaptation	35.2%	27.1%	18.1%

of students of Group 3; subclinical manifestations of depression for 21.1%, 19.6% and 19.9%, respectively.

Results of the students' reactive and personal anxiety assessment (according to the Spielberger-Khanin Scale with maladjustment conditions showed that 44.4% of students of Group 1, 46.2% of the students of Group 2, and 45.4% of Group 3 had anxiety disorders of a low degree; in 32.5%, 35.6% and 36.1% of the examined respondents, anxiety disorders of moderate degree; 23.1% of students from Group 1, 17.2% of students from Group 2 and 18.5% of students from Group 3 had anxiety disorders of a high degree of expressiveness.

The markers of maladjustment states according to the Symptom Check List-90-Revised (SCL-90-R) Scale in the examined students were high levels of anxiety (54.2% of the examined in Group 1, 55.2% in Group 2 and 56.1% in Group 3), depression (31.5%, 28.5% and 32.2%, respectively) and somatization (29.2% of examined in Group 1, 31.1% in Group 2 and 32.2% of Group 3).

The analysis of scale of nervous and mental tension according to Nemchin T.A. (neuropsychological tension level in the structure of maladjustment states among international students) demonstrated the predominance of intensive (moderate) tension in students of Group 1 and Group 2 (37.2% and 37.4%, respectively) and extensive (excessive) tension (38.1%) among students of Group 3 (38.1%).

The analysis of manifestations expressiveness of maladaptive states made it possible to distinguish it by following variants: asthenodepressive (23.1% of the examined in Group 1, 15.8% in Group 2 and 25.6% of the subjects examined in Group 3), hypersthenic (29.9%, 29.8%, 22 .2% of examinees, respectively), anxious (25.5% of students from Group 1, 18.9% of Group 2, and 31.1% of Group 3) and dysphoric (21.5%, 35.5%, and 21.1%, respectively) syndromes.

Asthenodepressive syndrome manifested clinically by a decrease in mood during the day, indifference to oneself, own future, prolonged inactivity, decelerated thinking, motor retardation; as well as reduction in self-esteem and self-confidence, self-blame, lack of/or decreased interest in studying, focusing on the state of physical health were revealed.

Hypersthenic syndrome had the following clinical signs: a constant feeling of fatigue, which was aggravated by mental or physical exertion; excessive irritability and increased sensitivity in response to external influences of normal intensity; hypersensitivity; episodic lacrimal reactions; superficial sleep with frequent awakenings.

Manifestations of the anxious syndrome were feeling of agitation, unmotivated anxiety, nervousness, irritability and impatience, negative excitement and restlessness, difficulty in concentration, sleep disorders, early awakenings, frequent nightmares, poor appetite or overeating, fussiness, inquietude.

Dysphoric syndrome manifested by bright and stormy emotional reactions that did not differ in the depth of feelings, unmotivated irritability, offensiveness, theatrical behavior directed at the immediate environment, mannerism, lively facial reactions, and affective reactions varying in intensity and duration.

Dragichi G.L. and Kazan A.M. described the anxiety problems of students who also work during their studies [17]. Their study emphasizes the fact that the students have a higher level of anxiety during testing and exams time if there are manifestations of maladaptation and emotional burnout. According to our study, significant increase in anxiety in students from groups with high manifestations of maladaptation was also noticed.

Conclusions

The study established that a high level of psychological maladjustment is observed in 2.1% of students of Group 1, 1.3% of students of Group 2 and 2.9% of students of Group 3; pronounced level in 6.1%, 11.5% and 12.6%, respectively; moderate level of maladjustment in 25.1% of students of Group 1, 26.2% of Group 2 and 31.3% of students of Group 3; insignificant level in 31.5%, 33.9% and 35.1% of students, respectively. 35.2% of students in Group 1, 27.1% of students in Group 2, and 18.1% of students in Group 3 did not show any signs of psychological maladaptation. The data obtained during the study regarding the psychodiagnostic manifestations of maladaptive states in the students determines direction of correction and prevention methods of maladjustment disorders among international students.

DECLARATIONS

Disclosure statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Funding Sources
There are no external sources of funding.

Consent for publication
All authors give their consent to publication.

Received: 27 Feb 2023
Accepted: 24 Jun 2023

References

1. Zorach IA, Lipka O. Adjustment to higher education among students with mental health disorders. Higher education research & development. 2022;42(1):1-17. DOI: 10.1080/07294360.2022.2052815.

2. Sinyavskaya NYa. Determining the personality type of medical students as an adaptation potential for future physicians. 2022;34(1):213-33. Available at: https://is.gd/gW67wc [In Ukrainian].

3. Voronenko IuV, Fysun YuI. Actual problems of the development of the system of training foreign students in higher medical (pharmaceutical) educational institutions of Ukraine. Proceedings of the All-Ukrainian conference "Problems of studying foreign students in medical higher educational institutions of Ukraine". (Ukraine, Ternopil, 19–20 Apr 2002). Ternopil: "Medical Education"; 2002. P. 14. [in Ukrainian].

4. Kozhyna AM, Markova MV, Grinevich YG, Zelenskaya EA. The problem of the undergraduate students of universities III–IV accreditation levels. Archives of psychiatry. 2011:17(4(67)):32-5. Available at: http://nbuv.gov.ua/UJRN/apsuh_2011_17_4_9 [in Ukrainian].

5. Kozhyna GM, Zelenska KO, Gajchuk LM, Khaustov MM, Zelenska GM. A medical-psychological view of the problem of adaptation of English-speaking junior year students to educational activities. English-language education at KhNMU: current state, problems and prospects: materials of the LI educational and methodological conference (Ukraine, Kharkiv, 31 Jan 2018). P. 54-6. Available at: https://repo.knmu.edu.ua/handle/123456789/19673 [in Ukrainian].

6. Sinaiko VM, Khaustov MM. Comprehensive assessment of the dynamics of mental disadaptation of students at a medical higher educational institution. Archive of Psychiatry. 2018;24(4(95)):212-5. Available at: http://nbuv.gov.ua/UJRN/apsuh_2018_24_4_11 [in Ukrainian].

7. Vashkite I, Khaustov M. Features of the clinical picture of depressive disorders of different registers in university students. Inter Collegas. 2019;2(6):112-9. DOI: 10.35339/ic.6.2.112-119.

8. Babatina SI. Peculiarities of time perception and experience of students on the stage of adaptation and identification. Science and education. 2013;7:120-5. Available at: https://is.gd/I2MPKB [in Ukrainian].

9. Hritsuk OV. Students' emotional states as metacognitive formation. Science and education. 2014;6:30-4. Available at: http://nbuv.gov.ua/UJRN/NiO_2014_6_8 [in Ukrainian].

10. Pereira MA, Barbosa MA, de Rezende JC, Damiano RF. Medical student stress: an elective course as a possibility of help. BMC Res. Notes. 2015;8:430. DOI: 10.1186/s13104-015-1399-y. PMID: 26358029.

11. Marakushyn D, Vasylieva O, Sinaiko V. KhNMU is a leader in choosing foreigners for higher medical education. Proceedings of the II International Education Forum "Best Educational Practices: Ukraine, Europe, World" (Ukraine, Kyiv, 2021). Kyiv: Association for Promotion of Education and Science Globalization SPACETIME; 2021. P. 148-50. Available at: https://repo.knmu.edu.ua/handle/123456789/29002

12. Spielberger CD. Manual for the State-Trait Anxiety Inventory (STAI). PaloAlto, CA. 1983: 78 p. Available at: http://surl.li/luixh

13. Consulting Psychologists Press. Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol. 1959;32:50-5. DOI: 10.1111/j.2044-8341.1959.tb00467.x. PMID: 13638508.

14. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23:56-62. DOI: 10.1136/jnnp.23.1.56. PMID: 14399272.

15. Derogatis LR, Savitz KL. The SCL–90–R and Brief Symptom Inventory (BSI) in primary care. P. 297-334. In: Maruish ME (ed.). Handbook of psychological assessment in primary care settings. USA: Lawrence Erlbaum Associates Publishers; 2000. DOI: 10.4324/9781315827346.

16. Nemchin TA. States of nervous and mental stress. USSR: LU; 1983. 167 p.

17. Draghici GL, Cazan AM. Burnout and Maladjustment Among Employed Students. Front Psychol. 2022;22(13):825588. DOI: 10.3389/fpsyg.2022.825588. PMID: 35529564.

Cite in Vancouver style as: Vasylieva O.V. Present-day features of maladjustment states in English medium students. Inter Collegas. 2023;10(1):52-5. https://doi.org/10.35339/ic.10.1.vas

GENDER PECULIARITIES OF BLOOD PRESSURE CHANGES IN PATIENTS WITH ARTERIAL HYPERTENSION AND DIFFERENT BIORHYTHMS

Novak-Mazepa Kh.O., Marushchak M.I.

I. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine

https://doi.org/10.35339/ic.10.1.nmm

ABSTRACT

Background. It is known that the risk of cardiovascular diseases, especially in conditions of increased rhythm of life, psycho-emotional stress, social cataclysms, is associated with various biorhythms, therefore, the study of the influence of various factors on the course of hypertension, taking into account the patient's chronotype, remains relevant.

Aim of the study was to analyze the level of blood pressure in patients with arterial hypertension with different chronotypes of the female and male genders.

Materials & Methods. The study included 42 patients with diagnosed essential arterial hypertension who were receiving inpatient treatment. The inclusion criterion was patients with arterial hypertension of the 2nd degree. Measurements of Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) (mmHg) were performed using the Korotkoff method. To study the chronotype, we used the validated questionnaire "Composite Scale of Morningness" and scales from official available sources.

Results & Conclusions. Arterial hypertension was diagnosed in 33.33% of patients with the evening chronotype, 7.17% with the morning chronotype, and 59.53% with the intermediate chronotype. Taking into account gender, female patients with evening and morning chronotypes and male patients with an intermediate chronotype predominated. Patients with evening chronotype compared to patients with intermediate and morning chronotypes had significantly higher Body Mass Index (BMI) (by 62.69% and 40.33%), disease duration (by 42.68% and 6.23%) and SBP (by 8.21% and 12.21%), respectively. At the same time, BMI in patients with arterial hypertension with an evening chronotype was as close as possible to obesity. The obtained results can be used in the practical work of nurses for the prevention of arterial hypertension by adjusting the duration of sleep and wakefulness and the diet.

Keywords: *chronotype, gender, age, body mass index, relationships.*

INTRODUCTION

In modern conditions, the increase in the rhythm of life, psycho-emotional stress, and social cataclysms have led to an increase in the prevalence of somatic diseases in society, including cardiovascular pathologies, which are affected by the natural biorhythms inherent in humans. There is a limited number of researchings among the adult population of Ukraine that study chronotype in relation to cardiovascular diseases and their risk factors. Therefore, the study of relationships between blood pressure (BP) and chronotype is relevant.

Corresponding author:
Mariya Marushchak – M.D., Ph.D., D.Sci., Professor,
Department of Functional and Laboratory Diagnostics,
I. Horbachevsky Ternopil National Medical University.
Address: Ukraine, 46001, Ternopil, Maidan Voli, 1.
E-mail: marushchak@tdmu.edu.ua

Arterial hypertension, or high blood pressure, is a key risk factor for stroke, coronary heart disease, other cardiovascular diseases and chronic kidney disease worldwide [1; 2]. Arterial hypertension is the cause of more than 10 million deaths worldwide every year [2]. In recent years, the prevalence of hypertension has decreased and its treatment and control have improved significantly in some high-income countries such as Canada, South Korea, Germany, and Chile [3]. At the same time, both the prevalence and the absolute burden of hypertension are increasing in low- and middle-income countries, which makes it a target risk factor for non-communicable diseases [4; 5]. According to the estimates of the World Health Organization, 34.8% of the adult population of Ukraine, which is about 10.8 million people, have arterial hypertension and only 66.4% of them know about their diagnosis [6]. The high stage of hypertension

is caused by the lifestyle of Ukrainians, including smoking, excessive alcohol consumption, excess dietary salt, obesity, and lack of physical activity [7]. Armitage also notes [8] the lack of research on possible secondary causes of hypertension in 12.7% of Ukrainians aged 18–29 and 20.4% of people aged 30–40, as a result of which significant kidney disorders, vascular and endocrine pathologies may remain undetected.

The cardiovascular system, being part of a larger biological system that expresses the interaction between internal and external factors, such as light and dark cycles, feeding and fasting, exercise and rest [9; 10], is also involved in these processes. BP rhythm is one of the most common circadian rhythms in the cardiovascular system [11]. Thus, blood pressure has a characteristic diurnal fluctuation [11], characterized by a morning increase that persists throughout the day, and the lowest level at night [12]. Randler and Engelke note that men and women generally differ in their chronotype, with men more evening-oriented than women [13]. A number of researchers note that individuals with an evening chronotype have more health problems, including psychological, neurological, and gastrointestinal diseases, and higher mortality compared to individuals with a morning chronotype [14; 15]. Current epidemiological evidence also links evening chronotypes with cardiovascular disease and cardiometabolic risk factors, in particular, a higher risk of overweight and obesity, as well as type 2 diabetes mellitus [16; 17]. Roenneberg and Merrow proposed a hypothesis according to which individuals with an evening chronotype have a high risk of cardiovascular diseases associated with a chronic mismatch between the internal physiological time and the external time of work and social activities [18].

The aim of the study is to establish the association of blood pressure with different chronotypes in female and male patients with arterial hypertension.

Materials and Methods

The study included 42 patients diagnosed with stage 2 essential arterial hypertension who were receiving inpatient treatment at the "Torchyn District Hospital of the Torchyn Village Council" during 2021.

Criteria for inclusion in the study: patients with arterial hypertension of the 2nd degree. Exclusion criteria from the study: chronic diseases in the acute stage, unstable heart diseases, oncology, drug and alcohol addiction.

The recommendations of the European Society of Cardiology, the European Society of Hypertension (2018 ESC/ESH Guidelines for the management of arterial hypertension) [19] and the unified clinical protocol of primary, emergency and secondary (specialized) medical care "Arterial hypertension" (2012) were used to diagnose arterial hypertension (AH) [20]. According to the criteria of the European Society of Cardiology and the European Society of Hypertension, patients with the 2nd degree hypertension with systolic blood pressure (SBP) of 160–179 and/or diastolic blood pressure (DBP) of 100–109 were included in the study. SBP and DBP (mmHg) were determined by the Korotkoff method twice between 10:00 and 10:30 using a sphygmomanometer.

The body mass index (BMI) was interpreted according to the recommendations of the World Health Organization, in particular, a normal weight in the range of 20.0–24.9 kg/m^2; overweight (preobesity) – 25.0–29.9 kg/m^2; class 1 obesity – 30.0–34.9 kg/m^2; class 2 obesity – 35.0–39.9 kg/m^2 and class 3 obesity >40 kg/m^2 [21].

To study the chronotype, we used the validated questionnaire "Composite Scale of Morningness" and scales scales for evaluating the questionnaire from official available sources. The content and essence of the statements are completely preserved in the Ukrainian version of the questionnaire [22]. The internal consistency of the scales of the "Composite Scale of Morningness" questionnaire was checked using the Cronbach's α method, which was α=0.85 and testified to the high quality of the questionnaire. The results were evaluated as follows: 22 points and below – evening chronotype, 42 points and above – morning chronotype, and 23–42 points – intermediate chronotype.

The performed study is a single-moment case-control study. The study protocol included screening of patients to determine compliance with inclusion and exclusion criteria; carrying out determinations; patient survey; statistical analysis of the obtained data. All patients were informed about the purpose of the clinical study and gave written informed consent for their participation in it. The confidentiality of information about the patient's identity and state of health was preserved. The patient's informed consent form, the patient's examination card, as well as all stages of the dissertation research were approved by the bioethics commission of I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine.

Quantitative characteristics of the studied indices were described in the form of M (Mean) ± SD (Standard Deviation) in accordance with the Shapiro-Wilk and Lilliefors normality criteria; frequency characteristics were described as an absolute value (n) and a percentage (%). To establish the influence of the factor on the studied characteristic, frequency tables were used with the determination of the two-sided Fisher's exact test. At the level of reliability $p<0.05$, there is an influence of the factor on this feature.

Results and Discussion

Among patients with hypertension included in the study, there were almost equal numbers of men and women. When dividing patients according to the results of the "Composite Scale of Morningness" questionnaire, 14 patients with an evening chronotype were found, which accounted for 33.33% of all patients, 3 patients with morning and 25 patients with intermediate chronotypes, which accounted for 7.14% and 59.53%, respectively.

Analysis of the clinical characteristics of patients with arterial hypertension showed a number of differences. Thus, when dividing patients by gender, a significantly higher BMI was found in women than in men by 23.03%, which corresponded to excess body weight (*Table 1*). At the same time, age, SBP, DBP and the duration of the disease did not differ statistically significantly in the gender aspect.

Chronotype refers to a person's circadian inclination, when to wake up and be active, and when to sleep. Early chronotype (morning type, extended sleep phase) and late chronotype (evening type, delayed sleep phase) are two extreme types of chronotypes. Comparison of the data of patients with arterial hypertension depending on the chronotype showed a number of differences, in particular, the lowest values of indices were found in patients with an intermediate chronotype. Thus, compared to patients with an evening chronotype, BMI (by 62.69%), disease duration (by 42.68%) and systolic blood pressure (by 8.21%) were significantly lower in patients with an intermediate chronotype (*Table 2*). At the same time, the duration of the disease and the level of systolic and diastolic blood pressure in patients with a morning chronotype were significantly lower in accordance with similar indices in patients with an evening chronotype, by 40.33%, 6.23% and 12.21%.

Table 1. Clinical characteristics of patients with arterial hypertension in the gender aspect

Answers	Male patients (n=22)	Female patients (n=20)	Total (n=42)
Age (years)	58.27±3.99	57.80±3.83	58.05±3.88
Body mass index	26.36±8.17	32.43±7.81*	29.25±8.48
Systolic BP	155.91±8.68	160.75±6.93	158.21±8.18
Diastolic BP	99.77±7.63	98.00±5.94	98.93±6.86
Disease duration	7.27±2.05	7.75±2.05	7.50±1.76

Notes: * – statistically significant difference between patients of different genders, p=0.016.

Table 2. Clinical characteristics of patients with arterial hypertension depending on the chronotype

Answers	Evening chronotype (n=14)	Morning chronotype (n=3)	Intermediate chronotype (n=25)
Age (years)	60.36±4.58	57.00±1.73	56.88±3.0
Body mass index	39.11±3.63	26.67±4.73*	24.04±5.29&
Systolic BP	166.43±4.57	156.67±7.64*	153.80±6.17&
Diastolic BP	102.86±5.08	9.67±2.89*	97.60±6.94
Disease duration	9.36±1.45	6.67±2.08*	6.56±0.87&

Notes: * – a statistically significant difference between patients with an evening and morning chronotype; # – a statistically significant difference between patients with morning and intermediate chronotypes; & – a statistically significant difference between patients with evening and intermediate chronotypes.

The research results showed that no gender differences were found within one chronotype, while a number of differences were found in individuals of the same gender with different chronotypes (*Table 3*). Thus, in men with hypertension with an evening chronotype, BMI (by 66.09%), SBP (by 8.5%) and disease duration (by 35.34%) were significantly higher compared to similar indices with an intermediate chronotype. A similar trend was established for higher indices in patients with the evening, in relation to the morning chronotype. It is worth noting that the investigated indices in patients with hypertension with intermediate and morning chronotypes did not differ statistically significantly.

The next stage of the study was a comparison of the studied indices in female and male patients with arterial hypertension depending on the chronotype, since a number of studies have shown that men are more likely to show an evening or late chronotype than women [27; 28]. In general, the circadian rhythm is controlled by the hypothalamus, and is determined by the body's nutrition cycles, temperature rhythms, blood signals, and the external photoperiod. Circadian physiology is associated with the body's state of alertness, metabolism, endocrine functions, and cardiovascular activity and plays a central role in endocrine rhythms, behavioral characteristics, and sleep-wake cycles [29]. Chronotype is defined as a person's preferred time of sleep and wakefulness ranging from early or "morning" type to late or "evening" type and intermediate type in between [30]. The ratio of sleep time to wakefulness depends partly on genetics. However, the genetic predispositions underlying the chronotype are multifactorial, as they are also modulated by age, gender, work schedule, personality, sunshine time, and light exposure [31]. In addition, sleep time is determined both by endogenous circadian rhythms that regulate sleep-wakefulness, and by sociocultural factors that influence behavior [32].

Table 3. Clinical characteristics of patients with arterial hypertension with different chronotypes in the gender aspect

Indices	Evening		Intermediate		Morning
	Men (n=5)	Women (n=9)	Men (n=17)	Women (n=8)	Women (n=3)
Age (years)	62.40±3.85	59.22±4.76	57.00±3.14	56.63±3.07	57.00±1.73
Body mass index	38.50±4.36	39.44±3.40	23.18±6.00$^{\&}$	25.88±2.80$^{\&}$	26.67±4.73$^{\#}$
Systolic BP (mmHg)	166.00±5.48	166.67±4.33	152.65±6.64$^{\&}$	156.25±4.43$^{\&}$	156.67±7.64$^{\#}$
Diastolic BP (mmHg)	105.00±7.07	101.7±3.54	98.53±7.86	95.63±4.17	91.67±2.89
Disease duration (years)	9.00±1.41	9.56±1.51	6.65±0.86$^{\&}$	6.38±0.92$^{\&}$	6.67±2.08$^{\#}$

Notes: * – a statistically significant difference between patients of different genders; # – a statistically significant difference between patients of the same gender with morning and evening chronotypes; & – a statistically significant difference between patients with evening and intermediate chronotypes.

When comparing the obtained results with other scientific data, characteristic features of patients with hypertension were established. Thus, taking into account gender, the vast majority of female patients with evening and morning chronotypes and the vast majority of men with an intermediate chronotype were found. According to the results of Kobayashi Frisk et al., morning types were characteristic mainly of women [23]. It is also worth noting that BMI in patients with hypertension with an evening chronotype was as close as possible to obesity. The obtained results coincide with other scientific data, which indicate a higher BMI in patients with an evening chronotype, in relation to the morning type [23], which the authors associate with less physical activity of individuals with an evening chronotype. This is consistent with the results of other studies [24–26].

The results obtained regarding higher SBP and BMI in patients with hypertension in men with an evening chronotype are comparable to the data of other studies, which claim that people with an evening chronotype have a worse cardiovascular system than those with other chronotypes, with

a higher risk of hypertension [33], lower levels of high-density lipoprotein cholesterol [25], and higher rates of mortality from cardiovascular diseases [34]. According to Kobayashi Frisk, there is no consensus as to why individuals with an evening chronotype are less active and more likely to suffer from cardiovascular diseases than those with a morning chronotype, and this is probably due to many factors [23]. However, studies have shown that adequate blood pressure control reduces the risk of major cardiovascular events, including stroke, coronary heart disease, and cardiovascular death [14].

Studies of biological markers have shown that healthy women had a phase advance in melatonin peak time and core body temperature compared to men [28]. According to an American nationwide study that assessed chronotype based on bedtime, wake time, and the Munich Chronotype Questionnaire, men were more likely to have a late chronotype than women [35]. The conducted study showed the vast majority of women with hypertension of the evening and morning chronotypes, while men predominated with the intermediate chronotype. The obtained results may be related to age, in particular, the leveling of the role of reproductive hormones, which are closely related to the evening type in young men and the morning type in pre-menopausal women [35; 36]. It was also found that BMI increases significantly with age and with index of composite scale of morningness, with evening chronotypes gaining weight faster than morning chronotypes [37].

Summing up, it can be stated that the level of blood pressure in patients with hypertension is influenced by the chronotype, gender, and the duration of the disease.

Conclusion

In patients with arterial hypertension, the relationship between blood pressure and different chronotypes was established, in particular, SBP indices are significantly higher in the evening chronotype compared to the data of patients with intermediate and morning chronotypes. Similarly, the body mass index and disease duration were higher in patients with arterial hypertension with an evening chronotype. When taking into account gender characteristics, it was found that among patients with evening and morning chronotypes women predominated, among patients with an intermediate chronotype – men.

Within one chronotype, no gender differences were found, while men with hypertension with an evening chronotype significantly had higher BMI (by 66.09 %), SBP (by 8.5 %) and disease duration (by 35.34 %) compared to similar indices at intermediate chronotype. A similar trend was established regarding significantly higher indices in patients with evening, in relation to the morning chronotype.

In the future, it is planned to analyze the relationship between blood pressure and components of the metabolic syndrome in patients with arterial hypertension.

ACKNOWLEDGEMENTS

The authors express their gratitude to the academic administration of I. Horbachevsky Ternopil National Medical University for the opportunity to conduct this study as part of the scientific research work of the university.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

Funding Sources

There are no external sources of funding.

Consent for publication

All authors give their consent to publication.

Received: 20 May 2023
Accepted: 22 Jun 2023

References

1. Mackenzie IS, Rogers A, Poulter NR, Williams B, Brown MJ, Webb DJ, et al. Cardiovascular outcomes in adults with hypertension with evening versus morning dosing of usual antihypertensives in the UK (TIME study): a prospective, randomised, open-label, blinded-endpoint clinical trial. Lancet. 2022;400(10361):1417-25. DOI: 10.1016/S0140-6736(22)01786-X. PMID: 36240838.

2. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396(10258):1223-49. DOI: 10.1016/S0140-6736(20)30752-2. PMID: 33069327.

3. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet. 2021;398(10304):957-80. DOI: 10.1016/S0140-6736(21)01330-1. PMID: 34450083.

4. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020;16(4):223-37. DOI: 10.1038/s41581-019-0244-2. PMID: 32024986.

5. Nguyen TN, Chow CK. Global and national high blood pressure burden and control. Lancet. 2021;398(10304):932-3. DOI: 10.1016/S0140-6736(21)01688-3. PMID: 34450082.

6. Ukraine: Hypertension fact sheet, 2019. World Health Organization; 2021 [Internet]. Available at: https://cdn.who.int/media/docs/default-source/country-profiles/hypertension/ukr_en.pdf [accessed 03 May 2023].

7. STEPS prevalence of noncommunicable disease risk factors in Ukraine, 2019. World Health Organization; 2020 [Internet]. Available at: https://apps.who.int/iris/bitstream/handle/10665/336642/WHO-EURO-2020-1468-41218-56060-eng.pdf [accessed 03 May 2023].

8. Armitage R. The realities of hypertension management in Ukraine. BJGP Life, 13 Jun 2022 [Internet]. Available at: https://bjgplife.com/the-realities-of-hypertension-management-in-ukraine/ [accessed 03 May 2023]

9. Manoogian ENC, Panda S. Circadian rhythms, time-restricted feeding, and healthy aging. Ageing Res Rev. 2017;39:59-67. DOI: 10.1016/j.arr.2016.12.006. PMID: 28017879.

10. Ayyar VS, Sukumaran S. Circadian rhythms: influence on physiology, pharmacology, and therapeutic interventions. J Pharmacokinet Pharmacodyn. 2021;48(3):321-38. DOI: 10.1007/s10928-021-09751-2. PMID: 33797011

11. Thosar SS, Butler MP, Shea SA. Role of the circadian system in cardiovascular disease. J Clin Invest. 2018;128(6):2157-67. DOI: 10.1172/JCI80590, PMID: 29856365.

112. Vondrasek JD, Alkahtani SA, Al-Hudaib AA, Habib SS, Al-Masri AA, Grosicki GJ, Flatt AA. Heart Rate Variability and Chronotype in Young Adult Men. Healthcare (Basel). 2022;10(12):2465. DOI: 10.3390/healthcare10122465. PMID: 36553989.

13. Ujma PP, Horvath CG, Bodizs R. Daily rhythms, light exposure and social jetlag correlate with demographic characteristics and health in a nationally representative survey. Sci Rep. 2023;13(1):12287. DOI: 10.1038/s41598-023-39011-x. PMID: 37516741.

14. Knutson KL, von Schantz M. Associations between chronotype, morbidity and mortality in the UK Biobank cohort. Chronobiol Int. 2018;35(8):1045-53. DOI: 10.1080/07420528.2018.1454458. PMID: 29642757.

15. Nimitphong H, Mahattanapreut A, Chailurkit LO, Saetung S, Siwasaranond N, Sumritsopak R, et al. More evening preference is positively associated with systemic inflammation in prediabetes and type 2 diabetes patients. Sci Rep. 2018;8(1):15882. DOI: 10.1038/s41598-018-34045-y. PMID: 30367094.

16. Patterson F, Malone SK, Grandner MA, Lozano A, Perkett M, Hanlon A. Interactive effects of sleep duration and morning/evening preference on cardiovascular risk factors. Eur J Public Health. 2018;28(1):155-61. DOI: 10.1093/eurpub/ckx029. PMID: 28371850.

17. Makarem N, Paul J, Giardina EV, Liao M, Aggarwal B. Evening chronotype is associated with poor cardiovascular health and adverse health behaviors in a diverse population of women. Chronobiol Int. 2020;37(5):673-85. DOI: 10.1080/07420528.2020.1732403. PMID: 32126839.

18. Roenneberg T, Merrow M. The Circadian Clock and Human Health. Curr Biol. 2016;26(10):R432-43. DOI: 10.1016/j.cub.2016.04.011. PMID: 27218855.

19. Arterial hypertension. Unified clinical protocol of primary, emergency and secondary (specialized) medical care, approved by Order of the Ministry of Health of Ukraine No.384 on 24 May 2012. State Expert Center of the Ministry of Health of Ukraine; 2012. Available at: https://www.dec.gov.ua/wp-content/uploads/2019/11/384_2012ykpmd_ag.pdf

20. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39(33):3021-104. DOI: 10.1093/eurheartj/ehy339. PMID: 30165516.

21. Body Mass Index: Considerations for Practitioners. USA: CDC [Internet]. Available at: https://www.cdc.gov/obesity/downloads/bmiforpactitioners.pdf [accessed 10 Jun 2023].

22. Senyk O, Jankowski KS, Cholii S. Ukrainian versions of the Composite Scale of Morningness and Munich Chronotype Questionnaire. Biological Rhythm Research. 2022;53(6):878-96. DOI: 10.1080/09291016.2020.1788807.

23. Kobayashi Frisk M, Hedner J, Grote L, Ekblom O, Arvidsson D, Bergstrom G, et al. Eveningness is associated with sedentary behavior and increased 10-year risk of cardiovascular disease: the SCAPIS pilot cohort. Sci Rep. 2022;12(1):8203. DOI: 10.1038/s41598-022-12267-5. PMID: 35581309.

24. Suh S, Yang HC, Kim N, Yu JH, Choi S, Yun CH, Shin C. Chronotype Differences in Health Behaviors and Health-Related Quality of Life: A Population-Based Study Among Aged and Older Adults. Behav Sleep Med. 2017;15(5):361-76. DOI: 10.1080/15402002.2016.1141768. PMID: 27148632.

25. Kuula L, Lipsanen J, Partonen T, Kauramaki J, Halonen R, Pesonen AK. Endogenous circadian temperature rhythms relate to adolescents' daytime physical activity. Front Physiol. 2022;13:947184. DOI: 10.3389/fphys.2022.947184. PMID: 36160868.

26. Ferri GM, Cavone D, Intranuovo G, Macinagrossa L. Healthy Diet and Reduction of Chronic Disease Risks of Night Shift Workers. Curr Med Chem. 2019;26(19):3521-41. DOI: 10.2174/0929867324666170720160632. PMID: 28730970.

27. Randler C, Engelke J. Gender differences in chronotype diminish with age: a meta-analysis based on morningness/chronotype questionnaires. Chronobiol Int. 2019;36(7):888-905. DOI:10.1080/07420528.2019.1585867.

28. Boivin DB, Shechter A, Boudreau P, Begum EA, Ng Ying-Kin NM. Diurnal and circadian variation of sleep and alertness in men vs. naturally cycling women. Proc Natl Acad Sci U S A. 2016;113(39):10980-5. DOI: 10.1073/pnas.1524484113. PMID: 27621470.

29. Bhar D, Bagepally BS, Rakesh B. Association between chronotype and cardio-vascular disease risk factors: A systematic review and meta-analysis. Clin Epidemiol Glob Health. 2022;16:101108. DOI: 10.1016/j.cegh.2022.101108.

30. Maghsoudipour M, Allison MA, Patel SR, Talavera GA, Daviglus M, Zee PC, et al. Associations of chronotype and sleep patterns with metabolic syndrome in the Hispanic community health study/study of Latinos. Chronobiol Int. 2022;39(8):1087-99. DOI: 10.1080/07420528.2022.2069030. PMID: 35509113.

31. Martinez-Nicolas A, Martinez-Madrid MJ, Almaida-Pagan PF, Bonmati-Carrion MA, Madrid JA, Rol MA. Assessing Chronotypes by Ambulatory Circadian Monitoring. Front Physiol. 2019;10:1396. DOI: 10.3389/fphys.2019.01396. PMID: 31824327.

32. Knutson KL, Wu D, Patel SR, Loredo JS, Redline S, Cai J, et al. Association Between Sleep Timing, Obesity, Diabetes: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Cohort Study. Sleep. 2017;40(4):zsx014. DOI: 10.1093/sleep/zsx014. PMID: 28329091.

33. Yang L, Luo Y, He L, Yin J, Li T, Liu S, et al. Shift Work and the Risk of Cardiometabolic Multimorbidity Among Patients With Hypertension: A Prospective Cohort Study of UK Biobank. J Am Heart Assoc. 2022;11(17):e025936. DOI: 10.1161/JAHA.122.025936. PMID: 36036170.

34. Douma LG, Gumz ML. Circadian clock-mediated regulation of blood pressure. Free Radic Biol Med. 2018 May 1;119:108-14. DOI: 10.1016/j.freeradbiomed.2017.11.024. PMID: 29198725.

35. Blood Pressure Lowering Treatment Trialists' Collaboration. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. Lancet. 2021;397(10285):1625-36. DOI: 10.1016/S0140-6736(21)00590-0. PMID: 33933205.

36. Michels KA, Mendola P, Schliep KC, Yeung EH, Ye A, Dunietz GL, et al. The influences of sleep duration, chronotype, and nightwork on the ovarian cycle. Chronobiol Int. 2020;37(2):260-71. DOI: 10.1080/07420528.2019.1694938. PMID: 31778080.

37. Bloom MJ, Jost SR, Keating DP, Lang ASID, Mankin NV, Mast ZW, et al. The influence of chronotype on the body mass index of U.S. college students. Sleep Sci. 2022;15(Spec 2):314-7. DOI: 10.5935/1984-0063.20200130. PMID: 35371401.

Cite in Vancouver style as: Novak-Mazepa KhO, Marushchak MI. Gender peculiarities of blood pressure changes in patients with arterial hypertension and different biorhythms. Inter Collegas. 2023;10(1):56-62. https://doi.org/10.35339/ic.10.1.nmm

FORMATION OF SCIENTIFIC POTENTIAL IN INSTITUTIONS OF HIGHER MEDICAL EDUCATION

Mykytenko A.O.

Poltava State Medical University, Poltava, Ukraine

https://doi.org/10.35339/ic.10.1.myk

ABSTRACT

Background. The progressive development of humanity is impossible without the development of science and the introduction of innovative technologies that fundamentally change the forms of human life in all areas and in medicine in particular. Scientific discoveries are the driving force of progress, which determines the prospects of the socio-economic development of the country and its status at the world level. The formation of scientific potential is an internal task of every country, and in accordance with the development strategies of the medical sphere of our country, higher educational institutions should pay considerable attention to the training of highly qualified specialists who can potentially replenish the number of scientific personnel of Ukraine.

The aim of the study was to analyze the possibility and necessity of creating a selective component: research work for students of the II (Master's) level studying in the specialty 222 "Medicine".

Materials & Methods. Scientific literature, educational programs and normative documents of higher medical education of Ukraine were studied. Bibliosemantic method and system analysis method were used.

Results. Ukraine is part of the European educational space and the scientific field in particular. In order to improve the training of students of the II (Master's) level, it is necessary to create conditions for the individual development trajectory of the student, which will improve their adaptability to changes in the conditions of the labor market. Introduction of new optional components to improve the special and general competencies of a specialist in the medical field increases the competitiveness of the student and improves the quality of higher medical education.

Conclusions. The author of the article, after analyzing the literary data and relying on his own experience, concludes that the introduction of a new selective component: research work will improve the level of knowledge of those seeking education regarding the use of modern research results in the work of a practical doctor, will introduce the career of a scientist and allow more effective preparation and selection of persons for the third educational and scientific level of training of Doctors of Philosophy.

Keywords: *research work, selective component, intellectual potential, medicine.*

INTRODUCTION

An important condition for national strength is the development of culture and science. In view of the current events in Ukraine, it may seem that the development of these areas is out of time, but it is culture and science that are the fundamental forces in the formation of national identity. Science in Ukraine is a field that has never received enough attention from the state. As a result, this led to a decrease in the prestige of the scientific field, an outflow of young and promising personnel [1]. It is indisputable that the development of humanity is not possible without the development of science and advanced technologies, which for many centuries in a row have fundamentally changed the forms of human life in all fields and in medicine in particular. At all times, the results of scientific research have become the driving force of progress, and this process is relentless, constantly changing, just like scientific research itself [2].

Today, the whole world has entered the Fourth Industrial Revolution (Industry 4.0). Thanks to technology, the boundaries between the material,

Corresponding author:
Mykytenko Andrii – PhD, Department of Biological and Bioorganic Chemistry,
Poltava State Medical University.
Address: Ukraine, 36011, Poltava, Shevchenko str., 23.
E-mail: mykytenkoandrej18@gmail.com

digital and biological worlds are blurring. The spectrum of achievements of technological progress is extremely wide, and now the task is to master and implement them in various spheres of human activity [1]. Modern technologies bring more and more new opportunities to our lives.

Research work of students of medical institutions of higher education is the most important aspect of the formation of the personality of a future scientist and highly qualified specialist, serves as a powerful means of high-quality personnel selection for the training of young scientists, the preservation and restoration of scientific schools and the formation of a scientific outlook among future doctors of practical medicine. Among the main directions of the implementation of the Concept of the Development of Higher Medical Education in Ukraine is the creation of conditions in higher educational institutions for attracting talented young people to scientific activities [3].

Unfortunately, domestic realities of conducting fundamental scientific research in medicine allow us to state that during the years of independence, there was a gradual loss of scientific potential, especially young scientists who prefer career growth in foreign companies or investment projects with foreign capital. Budget financing of priority areas of fundamental scientific research in medicine today is not able to ensure the implementation of their tasks, the revival and the rise of national academic medical science [2]. In order to receive funding for the implementation of scientific projects from non-budgetary (grants, foundations) institutions, it is necessary to have a sufficient level that would meet the requirements of competitions.

Starting from the first year, students can work in student research groups, first at fundamental departments, and then at clinical departments. Thus, they actually get their first experience in conducting scientific research. As they participate in a scientific experiment or clinical research, students may discover a lack in their knowledge regarding the methodology of scientific research, international standards and algorithms for recording intellectual property and other aspects of the realization of scientific potential. Usually, a scientific supervisor and self-education help to find answers to questions. Therefore, it is important to consider the possibility of creating a selective component: research work as part of educational professional program (EPP) "Medicine" with the aim of improving the training of highly qualified specialists in the medical field, who can potentially continue their studies at the third level of higher education.

The aim of the study is to analyze the possibility and necessity of creating a selective component: research work for students of the II (Master's) level studying in the specialty 222 "Medicine".

Materials and Methods

We studied scientific literature, educational programs and normative documents of higher medical education. Bibliosemantic method and system analysis method were used.

Results and Discussion

According to the Strategy for the Development of Medical Education in Ukraine for 2018–2028 [4] and the Development Strategy of the National Academy of Medical Sciences of Ukraine for the period until 2030 [5], the main pathway for implementation of the tasks and goals of these documents is the training of highly qualified scientific medical personnel on the basis of higher educational institutions. To ensure the sustainable development of personnel potential for medical science it is necessary to give the opportunity to students to master the principles of scientific research and methodological tools for their implementation at a high professional level.

An important argument for the need for a selective component: research work for education seekers is a requirement in the industry standard for obtaining the "Master of Medicine" degree, namely writing of qualifying work as a form of attestation. Qualifying work, as stated in the industry standard, must demonstrate the ability of the student to solve problems of a research and/or innovative nature in the field of medicine and health care. It should not contain academic plagiarism, falsification and fabrication. The qualification work must be published on the official website of the institution of higher education or its structural subdivision or in the repository of the higher education institution [6].

The main goal of the educational and professional program "Medicine" is the formation of specialized conceptual knowledge based on modern scientific achievements in the field of health care, which will ensure the academic training of highly professional specialists with the formation and acquisition by them of general and special competences of a doctor for further professional activity; make them able to solve complex problems in atypical situations or new environments, capable of research and innovative activities; capable of conducting studies with a high degree of autonomy at the next level of higher education; will form their capacity for effective activity in the

globalized information society, based on their worldview and social position [7].

In the educational and professional program "Medicine" of the second level of higher education of the Poltava State Medical University, which corresponds to the educational qualification "Master of Medicine", it is also stated that its feature is "an unique combination of classical university education, which ensures the formation of a worldview, the development of thinking, the unique abilities of an individual with the acquisition of full-fledged professional competences; with practice in educational and scientific treatment centers of the university; experience of surgical, cardiology and gastroenterology schools of Poltava State Medical University; with ensuring a close connection of the training of medical specialists with science, the latest technologies, and clinical practice. Progress in the field of fundamental and applied medical research and the implementation of their results in practice dictates the need to train medical specialists at the university with the use of innovative technologies as a component of the educational program of training of medical education applicants."

Thus, in order for students to acquire integrated competence, namely, the ability to solve complex problems, including research and innovation in the field of medicine, as well as special competencies, such as: the ability to develop and implement scientific and applied projects in the field of health care in compliance with ethical principles when working with patients, their relatives, laboratory animals and compliance with professional and academic integrity, bearing responsibility for the reliability of the obtained scientific results, it is necessary to create a selective component: research work. In general, such a component is needed to study the basic elements of scientific research, namely: the structure of the scientific project, intellectual property copyrights and the methodology of implementation and analysis of the obtained results, as well as the use of scientific metric databases for self-education and scientific research.

Based on the issues of the need for such a discipline, the main goal of the selective component "research work" can be: acquiring knowledge about the design of scientific research, its planning and application forms for participation in grant and fund competitions, copyright protection forms and its use, types of scientific articles and reports and features of their writing, rules and principles of scientific ethics and their legislative regulation in Ukraine and abroad, rules for writing qualification papers. Training should be conducted in the 3rd or 4th course at the request of the student and should be extended only to the circle of persons interested in conducting scientific research, based on an approximate estimate of no more than 20% of the total number of persons studying in the corresponding course. Successful completion of the assessment of the selective component “research work” must be taken into account in the recommendation for the student's research work by the academic council of the university.

The projected program of such a selective component must necessarily include the following topics: scientific search using modern software tools and electronic libraries; development, planning and design of basic and clinical research (main differences, mandatory elements); mathematical processing of results, choice of statistical methods, proof of research; copyright and protection of intellectual property rights; writing articles, their types, and working with magazine editors; the structure of the qualification work, legal requirements, the process of defense of the qualification work; forms of publication of scientific results, presentation and public defense of scientific research; ethical and moral code of the scientist, integrity in scientific research and their legal regulation; work with scientometric databases Scopus and Web of Science, use of social networks for scientists; familiarization with scientific schools of Poltava State Medical University and the results of their activities; perspectives of the Ukrainian scientist.

The standard of higher education of the second (Master’s) level, field of knowledge 22 "Health care", specialty 222 "Medicine" determines a minimum of 36 ECTS credits of the educational and scientific program must be provided to ensure the scientific and research component [6].

The prospects and advantages of the implementation of the selective component: research work for the student and the university are as follows: formation of education seekers' understanding of what a Ukrainian scientist does, his everyday life and prospects, will allow more effective preparation and selection of persons for the third educational and scientific level of training of Doctors of Philosophy; will increase the efficiency of student scientific groups as a whole and, in particular, improve the quality of writing scientific papers and articles; will increase the competitiveness of education seekers at the domestic and international level.

Conclusions

Taking into account the presence of a social demand among education seekers to improve knowledge about the use of modern research results in the work of a practical doctor and familiarization with the career of a scientist. It is also necessary to consider the opportunity prescribed in the industry standards of higher education and the perspective value of the new educational component for the university in general. It is advisable to ensure the opportunity for those seeking education to choose the path of a successful Ukrainian scientist. Prospects for further research. Analyze the results of the implementation of the selective component "research work" for students of 3rd–4th years of education within 5 years.

DECLARATIONS:

Disclosure Statement

The author have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The author have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

Funding Sources

There are no external sources of funding.

Consent for publication

Author give their consent to publication.

Received: 12 May 2023
Accepted: 22 Jun 2023

References

1. Medical science in Ukraine: real state, problems, prospects. Ukrainian medical journal. 2022;4:19-23. DOI: 10.32471/umj.1680-3051.150.233338. [In Ukrainian].

2. Tsimbalyuk VI, Antipkin YG, Bazika DA, Bogdanova LO, Kovzun OI, Malyshevska EM, et al. Status and prospects of fundamental research development in scientific institutions of the National Academy of Medical Sciences of Ukraine [Internet]. NAMSU, 16 Dec 2019. Available at: http://amnu.gov.ua/ctan-ta-perspektyvy-rozvytku-fundamentalnyh-doslidzhen-u-naukovyh-ustanovah-naczionalnoyi-akademiyi-medychnyh-nauk-ukrayiny/ [accessed 20 Jun 2023]. [In Ukrainian].

3. Mykytenko AO, Omelchenko OY. The role of the student's research work in the training of medical personnel. South Ukrainian Medical Scientific Journal. 2021;28:45-7. [In Ukrainian].

4. Order of the Cabinet of Ministers of Ukraine No.95-p on 27 Feb 2019 "On the approval of the Strategy for the development of medical education in Ukraine". Verkhovna Rada (Parliament) of Ukraine. Legislation of Ukraine. Valid on 20 Jun 2023. Available at: https://is.gd/hELJ7N [in Ukrainian].

5. Development strategy of the National Academy of Medical Sciences of Ukraine for the period until 2030 [Internet]. NAMSU, 04 Jul 2022. Available at: http://amnu.gov.ua/strategiya-rozvytku-naczionalnoyi-akademiyi-medychnyh-nauk-ukrayiny-na-period-do-2030-roku/ [accessed 20 Jun 2023]. [In Ukrainian].

6. The standard of higher education in the specialty 222 Medicine for the second (Master's) level of higher education, approved by order of the Ministry of Education of Ukraine No.1197 on 8 Nov 2021, valid on 20 Jun 2023. Ministry of Education and Science of Ukraine. Available at: https://is.gd/WWsBw9 [in Ukrainian].

7. Educational and professional program Medicine of the second (Master's) level of higher education, specialty 222 "Medicine", fields of knowledge 22 "Health care". Poltava: Poltava State Medical University; 2022. 35 p. [In Ukrainian].

Cite in Vancouver style as: Mykytenko AO. Formation of scientific potential in institutions of higher medical education. Inter Collegas. 2023;10(1):63-6. https://doi.org/10.35339/ic.10.1.myk