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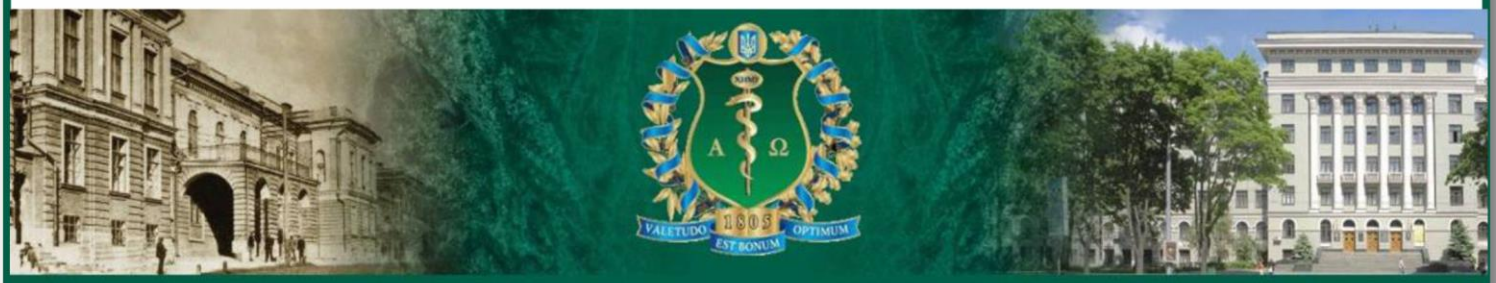

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HISTORY OF MEDICINE

Ağayev Elnur[1], Rusanov Constantin[2]

"WHITE RUSSIAN" DOCTORS IN CYPRUS: THE FATE OF SIX GRADUATES OF IMPERIAL KHARKOV UNIVERSITY

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Abstract: The article discusses the life of six physicians who graduated from the medical faculty of Kharkov University before 1917 and emigrated in 1918-1920 together with other refugees from the Bolsheviks to Cyprus, which became a British colony. Three of the physicians were unable to find work, and in 1922 the new authority moved them from the refugee camps on the island to Serbia (later Yugoslavia). But for the rest Cyprus became the second home. The names of former Kharkov doctors, who provided medical assistance to the Greek and Turkish communities on the island for many years, remained in the memory of grateful people. A surgeon Pavel Smitten was the most experienced of them. Before emigrating he worked in clinics of Kharkov University, in municipal and private hospitals, and he opened his own surgical and gynecological hospital. Smitten worked as a military doctor throughout Russian-Japanese War, World War I and Civil Wars. His experience, initiative and talent as a healthcare provider were fully demonstrated in Cyprus too. Here Smitten also had a private hospital and worked as the head of the city hospital for a long time. Almost 10 years he was the chief medical officer of a major American mining company, and was responsible for the health of the residents of the whole industrial region.

KeyWords: Cyprus; graduates of medical faculty; Kharkov University; Pavel Smitten; physicians; White emigration.

INTRODUCTION

The term "White Russians" was used by foreigners in regard to residents of the Russian Empire who had fled abroad from the Bolsheviks during the Civil War (1918-1922). These 2-3 million of people fleeing their homeland, had some influence on the history of the states, where they had to move to as refugees. Therefore, the topic of White Russians has its place in the historiography of these countries.

After the collapse of the USSR and the Soviet system in Eastern Europe, the interest of historians in this subject has increased markedly in connection with the discovery of new documentary sources and with the return of the historical rights of the White Russians. In 1919-1922 Turkey accepted about 200-250 000 refugees from Russia.

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The interest in this topic could be demonstrated by the books, published in Turkey in the post-Soviet period by such authors as Jak Deleon. Beyoğlu'nda Beyaz Ruslar. - Remzi kitabevi, İstanbul, 2003 [Jak Deleon. White Russians in Beyoglu. Remzi Publ., İstanbul, 2003]; Oya Dağlar Macar-Elçin Macar. Beyaz Rus Ordusu Türkiye'de. - Libra yayıncılık, İstanbul, 2010 [Oya Dağlar Macar-Elçin Macar. White Russian Army in Turkey. - Libra Publ., İstanbul, 2010]; Bülent Bakar. Esir Şehrin Misafirleri Beyaz Ruslar. - Tarihçi kitabevi, İstanbul, 2012 [Bülent Bakar. Guests of Captive City: White Russians. - Tarihçi Publishing İstanbul, 2012]; İstanbul'dan Geçen Ruslar, derleyen ve Rusçadan çeviren Orhan Uravelli. - Ümit yayıncılık, Ankara, 2005 [Russians of İstanbul, complied and transl. by Orhan Uravelli. - Ümit publ., Ankara, 2005]; Nikolay Rayevski. Gelibolu Günlüğü. Rus Gözüyle Gelibolu Zorunlu Bir Gurbetin Öyküsü, çeviren Aydın İbrahimov, Nesrin Bayraktar. - Ağaç yayınları, İstanbul, 2009 [Nikolay Rayevski. Gelibolu Dairy. Gelibolu from the perspective of Russian: A Story of Obligatory Abroad, transl. by Aydın İbrahimov, Nesrin Bayraktar. -

Ağaç publ., İstanbul, 2009]; Svetlana Uturgaui. Boğaz'daki Beyaz Ruslar: 1919-1929, çeviren Uğur Büke. - Tarihçi kitabevi, İstanbul, 2015 [Svetlana Uturgaui. White Russians of Bosphorus: 1919-1929, translated by Uğur Büke. - Tarihçi publ., İstanbul 2015]. But only recently historians of the White Russian emigration have focused on the so-called «stop in Cyprus». Thousands of refugees from Novorossiysk and Odessa, later from the Crimea (through Constantinople) arrived on this island by the sea in the spring of 1920, and in 1922 almost all of them left Cyprus. Only two major works consider this issue.

The first of them [1] was published in Cyprus, 2014 by Natalya Zykova (living there since 1993), a historian and the President of local Russian Orthodox Educational Centre. The character of her novel, Mikhail Boutchik (1868-1922), who graduated from the General Staff Academy and became a Lieutenant General, a corps commander, played a prominent role in the White Movement during the Civil War. M.M.Boutchik spent the last years of his life in Cyprus, died there and was buried at British military cemetery in the suburbs of Limassol (after 1923, the island de jure became a British colony, which has long since been de facto).

However, Zykov's book also briefly mentions the arrival, life facts and challenges concerning other White Russians in Cyprus.

The topic is much better presented in the book by E.Agayev, published on Cyprus in 2015 [2]. This work is based on the archives data from Russia, Ukraine, the UK, Turkey and Cyprus, newspaper advertisements and other literature. The author discusses the reasons for the refugees' arrival on the island and their number; their life in Cyprus – in the camp and later; their attempts to become employed; assistance to refugees from the Turkish and Greek Cypriot communities. The book [2] also tells about the departure of the greater part of White Russians from the island to the Balkans and their further life in other countries.

It happened because in 1922 the British government decided to evict the Russian refugees from the Cyprus, placing them under the custody of the League of Nations' Commissioner. In May-July 1922, many Russians were deported from Cyprus settling in Bulgaria and Serbia. Only a small part of them managed to find a permanent job on the island and remain in Cyprus. The life and work of some of these people, who became Russian Cypriots, can be traced in the sources until the mid-1960s [2, p.61-156].

As many as 1500-2000 refugees from Russia, who arrived on Cyprus between the dates of 22 March – 1 April, 1920 on the ships "Kherson" and "Anatoly Molchanov", were people of different social status, age, nationality and religion: officers and soldiers of the different regiments of the White army, officials, intellectuals and priests; Russians and Germans, Ukrainians and Poles, Jews and Armenians; Orthodox and Lutherans, Muslims and Jews; the elderly, women and children.

The physicians and nurses made up a significant part of the refugees, with many wounded and sick. We identified eleven Russian doctors among those who arrived on Cyprus. Six of them graduated from medical faculty of Kharkov Imperial University, namely Pavel Smitten, Sergey Kozentsov, Aleksey Ivanov, Mkrtıch Arevshatyants, Boris Vroblevski, and Mark Freyman.

This article presents some data about the lives of these former Kharkov residents before fleeing from Russia, about their stay in Cyprus and for some of them – about the fate after the eviction from the island.

Pavel Nikolayevich Smitten (1876-1941) left the most significant trace in the history of Cyprus. He was born in the Transcaucasia: in Kutaisi according to one source [3], in Tiflis (now - Tbilisi) according to the other one [4], in a noble Orthodox family of a high rank judiciary official. In 1895 Pavel graduated from the 1st Tiflis City gymnasium and entered the medical faculty of Kharkov Imperial University [3]. In 1900 P.N.Smitten received the University diploma of a physician in surgery and women's diseases, and then continued to work in Kharkov. In 1901 he was admitted to the Kharkov Medical Society on the recommendation of the future famous surgeon N.P.Trinkler [4].

In Kharkov the young doctor worked for several years as the resident physician in a private hospital of Dr. Likhonosov (Fig. 1) with a polyclinic, maternity and ortho-

paedic departments, providing the latest methods of treatment and diagnosis, such as x-ray, phototherapy and electrotherapy hospital [5].


ГИРУРГИЧЕСКО-ГИНЕКОЛОГИЧЕСКАЯ ЛѢЧЕБНИЦА
съ поликлиникой, ортопедическимъ и родильнымъ отдѣленіями
Доктора Д. В. ЛИХОНОСОВА.
Харьковъ, Конторская улица, № 8. Телефонъ 1305.
Рентгографія, лѣченіе Рентгеновскими лучами, свѣтолѣченіе, электризація, массажъ и врачебная гимнастика.
Лѣчебница функціонируетъ круглый годъ. ✻ Постоянное дежурство врача.
Консультація по желанію больныхъ. ✻ Плата отъ трехъ руб. въ сутки.
Пріемъ стаціонарныхъ больныхъ и рожениць во всякое время, амбулаторныхъ отъ 1 час. до 3 час. дня.
Завѣдывающій лѣчебницей докторъ Д. В. Лихоносовъ.
Ординаторы лѣчебницы { Н. А. Скорупскій. Н. Н. Смиттенъ.

Fig.1 Advertisement

With the beginning of the Russo-Japanese War of 1904-1905, P.N.Smitten voluntarily went from Kharkov to the Far East with the sanitary train for 200 beds. The train staff included 5 doctors, 15 nurses, 30 sanitary assistants, pharmacist, and other officials [6].

In Kharkov P.N.Smitten twice began working at the University: prior to the departure to the Far East, as an assistant at the Faculty surgical clinic [7] and after the return, at the surgical clinical Department of the University, located in Kharkov Military hospital [8]. But both times not for too long.

In 1911 Pavel Smitten for some unknown reason (possibly for health state) left Kharkov and moved to Novorossiysk, to the Black Sea coast. Here Smitten opened a private surgical and gynecological hospital, located two blocks from the shore of the Tsemes Bay, on the corner of Camp and Quarantine streets [9, p. 162]. In his hospital, as a surgeon he used the experience of administration of modern treatment and diagnostic methods, received in Kharkov. At the same time P.N.Smitten began working as a resident surgeon in Novorossiysk city (municipal) hospital [10].

In just a few years Pavel Nikolaevich managed to get the city's great reputation as a surgeon. He did not publish articles in medical journals; Smitten reported about achievements in surgery to the authorities of Novorossiysk, and his notes were quoted on the national forum by another speaker [11, p. 107]:

“An outstanding surgeon, Dr. Smitten Recently, has recently arrived to Novorossiysk <...>, opened his surgical hospital, and received invitation to provide service in the city hospital. He began performing miracles of healing in Novorossiysk”. Smitten himself explained many of them by the city’s climate.

Here is what he says in one of his notes, which described the most complex and difficult cases he performed in Novorossiysk city hospital: “In this case, such a demonstrative one, I had a sense of the vast difference between conditions for operational manipulations in our climate (in Novorossiysk), in comparison with where I had to work earlier (in Kharkov). Never would I have dared to make such an operation at this stage of the disease somewhere in another place of Russia. This case, like the number of other similar ones, is very useful for me in the sense that in all my years of practice I have never seen such a rapid recovery of health and strength. The usual course in such cases is that the wound heals in a year or two, it is the total exhaustion and often entails amyloid degeneration of the internal organs, and it ends or death, or total disability for life. But in our case, complete healing of the wound occurred after 9 weeks and after 12 days the patient was shown to my colleagues. His youthful appearance and excellent overall condition leaves nothing to be desired, he is quite healthy and able-bodied.

This case is not the only one; the impression that I have learned over the years of my work in these climatic conditions, exceeds all expectations. I am absolutely entranced. I consider climatic conditions here to be appropriate for treatment of all types of tuberculosis of the bone, glandular, abdominal, and pulmonary, as well as to treat a variety of patients who suffer severe common infections and severe forms of general purulent infection of the blood”.

It should be noted that in those years some professors-physicians who spent summer at their cottages and villas in

the vicinity of Novorossiysk, highly estimated the city as a seaside resort. In favor of this opinion was the relatively warm and sunny climate of Novorossiysk, somewhat reminiscent of Egypt. The presence of the lake (estuary) with healing muds, extensive vineyards not far from this seaside city, opened up the possibility of treatment by solar and mud baths, sea bathing, and grape [9, p.150-153].

With the beginning of the World War I P.Smitten was mobilized; this was reported by the Novorossiysk press: "Our famous surgeon P.N.Smitten has been called up to the war theatre, and is in the Caucasian army now" [12].

As after the revolutions of 1917, the World War was changed by the Civil War in Russia, for the next 6 years Smitten had to repeatedly apply his experience of military field surgery obtained "on the hills of Manchuria". Returning to Novorossiysk from the Caucasian front, the surgeon entered the service in the Armed Forces of South Russia, commanded by General A.I.Denikin.

At the beginning of 1920 Denikin's army suffered a final defeat and retreated to Novorossiysk, where troops and civilian refugees were hurriedly evacuated by the sea to the Crimea, Georgia and Turkey. With the defeat of the White Russians, Pavel Smitten also managed to leave Novorossiysk.

In [13, p.251] this episode is described in the spirit of the legends surrounding later the name of the Russian doctor:

"Dr. Smitten was an <...> elderly Russian refugee <...>. During tzarist days he had studied in two or three of the best medical universities in Russia, then had entered practice at the Black Sea port of Novorossiysk. One person says that bandits once seized him and took him to the Caucasus Mountains, where he performed an emergency operation that saved their chief's life. In 1920, when Smitten was working in the field with the White Russian army, the bandit chief had an oppotunity to show his gratitude. A Bolshevik thrust cut the doctof off from Novorossiysk, where refugee ships were waiting. The only escape was through the high mountains behind the city. Smitten appealed to the bandits for help. They spirited him into the harbor along the dangerous, little known trails, and he caught the ship just it was sailing. On this ship he reached Cyprus <...>".

An American author [13] has insufficient understanding of Russian realities in those troubled years, so his text contains a lot of exaggeration (for example in relation to the number of universities) and is self-explanatory. A military doctor Smitten made his way to Novorossiysk with the thousands of other White Russians through the wooded mountains separating the city and the port from the Kuban plain. These mountains throughout the Civil War were rife with gangs of deserters, the so called "greens", hiding from mobilizations and living by looting. If the chieftain of one of the gangs, was obligated his life of Smitten's surgical arts, helped the doctor to move through the coastal Markotkh ridge to the port, where the ships were loaded with refugees. However, the reality was much simpler...

On April 1, 1920 Pavel Smitten, a former surgeon in the Armed Forces of South Russia, arrived to Famagusta with the ship "Anatoliy Molchanov" [14].

Upon arrival of the ship, the incidence of typhus among the refugees exceeded the epidemic threshold, and Smitten with the others was placed in a quarantine camp in Famagusta. As in the camp, with a lack of medical means, issued by the British administration, and during his further life on Cyprus, the comprehensive set of surgical instruments, which Smitten brought from Novorossiysk, was very helpful to him [15, p.6].

When the quarantine period was over, Smitten registered his medical diploma of Kharkov Imperial University in Famagusta to obtain permission to work as a doctor in Cyprus [16]. He liked the island, and wanted to stay here, where the sea and the sun reminded Novorossiysk which he left forever.

Smitten went from Famagusta to Nicosia to get permission of local authorities to open a private hospital in this city. To do this, the surgeon had to walk several tens of kilometers; to preserve the neatness of his only clean pair of shoes, which he did not want to become older for his future uses, Smitten walked barefoot [13, p. 252]. The initiative of the "White Russian doctor" in Nicosia was supported by the all-Russian Zemstvo Union (ARZU) for aid

to sick and wounded soldiers. This public and political organization was created in Russia during the World War I. Financed mainly by government grants, it provided charitable assistance to the families of soldiers, and then to refugees; equipped hospitals and ambulance trains, stored medicines and underwear, trained nurses, etc. For some time ARZU continued to perform these functions also in emigration, including the help to refugees in Cyprus [2, p. 86-93].

The Smitten's surgical and gynecological hospital was opened in Nicosia by joint efforts in 1920. The well furnished hospital had 12 beds; some Russian refugees worked there as nurses and sanitary assistants. Pavel Smitten brought to hospital his disabled wife, his highly-skilled operating nurse, Miss Tripolitova, and a protégé, young Boris Vroblevsky (see below) [13, p.252]. The Smitten's private hospital in Nicosia was listed as a successful establishment in the ARZU report, among the entities opened with the Union's assistance [15, p.36].

The British administration and the Cyprus community became interested in this hospital, as well as in the owner, who "saved many lives with his extraordinary talent", and he was assigned to Nicosia municipal hospital in 1921 [17, 18]. Thus, Pavel Nikolaevich worked in two Nicosia medical institutions until 1930 [19], when he left municipal service and shifted his private hospital to Egypt, but soon returned to Cyprus. Then, on July 1931, Smitten was appointed a health officer of Cyprus Mines Corporation (CMC).

Smitten worked at CMC for a relatively short time, namely the last 10 years of his life. But in this decade he displayed his talent as a healthcare provider. The former Kharkov doctor showed his skills in the most adverse conditions quickly and cost-effectively solving complex health care challenges. In fact, Smitten became one of the heroes of the book [13] on CMC, a US company, founded in 1912, which after World War I opened a mine producing copper, sulfur and other minerals in the region of Lefke (see also article Feridun Kemal Feridun (2000). Lefke Kasabası'nın Tarihsel Boyutuna Bir Kesit: Kıbrıs Maden Şirketi (Cyprus Mines Corporation - CMC) ve Bugünkü Demografik Yapı [Feridun Kemal Feridun (2000). A Part of Historical Aspect from Lefke Town: Cyprus Mines Corporation - CMC and Existing Demographical Structure. Journal of Cyprus Studies. 16/17. 111-124]).

Thanks to the author [13], a famous American historian and writer David Sievert Lavender (Febr. 4, 1910 – Apr. 26, 2003), Pavel Smitten, the White Russian Cypriot, entered the history of the island as a legendary figure: "This old refugee doctor was almost a legend" [13, p. 251]. This sentence is a significant statement summarizing Smitten's life in Cyprus.

So let us take a closer look at his life. Two Smitten's appointments to positions in the CMC were mentioned in the issues of "The Cyprus Gazette" during this period. In January 1932 he was appointed the head of the hospital in Pendayia (now Yeşilyurt) near Morphou Gulf [20]. The second one was Smitten's assignment to Morphou Gulf Port Health Centre as a health officer [21]. His duty there was extended on 28 December, 1937 [22]. The last register in "The Cyrus Gazette" concerning Smitten's work in CMC was from the year 1940, and his name was not mentioned in the registers after that year [23].

The author of the book [13] has left us a vivid verbal portrait of Pavel Smitten and, more importantly, highlighted the fact that the surgeon had excellent taste in modern medical technology [13, p. 252]:

"Portly of figure, easily excited, with a sandy goatee to march his imperial courtliness, Smitten complitely enthralled the staff's wives. He was an accomplished chief and a lavish entertainer. He spoke Russian and French fluently; Turkish, Greek and English of most of his patients he mastered only indifferently. He often burst into strange conglomerations of sound <...>".

Smitten never let himself rusticate. He spent his vacations visiting hospitals on the Continent, especially those attached to industrial concerns. He brought back to Pendaiya the latest techniques in treating fractures, installed a laboratory and X-ray equipment, introduced physiotherapy.

But the focus of his activity was always centered on people and their needs. With his assistant Vroblevsky's help, Smitten formed "health and beauty" teams for staff's

wives, engaging them vigorously in callisthenics. Recognizing that health and morale were intertwined, he eagerly supported any party or sports events that would interest and bring together families from Skouriotissa, Xeros and Mavrovouni. Safety and first-aid programs received his full co-operation.

Every day (except Sunday) he visited hospitals that were established at each of the mine villages. Several hundred children from 7 schools in the mining area were given free treatment and drugs [13, p. 252-253].

Smitten considered the food to be a very important health factor. He became fanatical about diet, and thought the staff's families were too dependent on canned goods and by precept and exhortation made kitchen gardens stylish. He advocated and finally obtained the permission to open a restaurant in each mining village where single men could have at least one hot meal a day at a reasonable price. Vehemently, Smitten endeavored to persuade the village bakers to produce more nutritious bread by adding eggs, minerals, and chopped vegetables [13, p. 252].

Mainly due to Smitten's efforts, the company rented 100 acres of land and hired unemployed miners to grow potatoes and beans to sell through CMC canteens. It also imported wheat and barley, milled the grain at Morphou, baked the bread at Xeros and sold the loaves at low rates. Consumption averaged 764 loaves a day [13, p.274-275].

P. Smitten paid greatest attention to the healthy nutrition for children. He tried to reduce the cost of milk, important for their health and development [13, p. 274]. Smitten achieved that $13,000 was expended to build the plant where milk was produced of imported powder. This was to be distributed, either as whole or skim milk, first in schools and later to preschool children in nearby villages. Families who could pay were sold the milk at a rate of 2 shillings per month for a pint of milk a day. If it was proved beyond the family's means, and if the welfare department indicated so, the child received the milk for free.

To overcome the Cypriots' ingrained conservatism toward change, Smitten took groupes of school teachers, salaried Cypriot employees, and made a tour for their wives through the plant, gave them samples of milk and ice cream, then invited them to his home for a lecture on the nutritional value of the product. Government officials attended the opening ceremony at the plant, and for the first 20 days milk was passed out free to every child in school.

Inspite of the careful campaign, the program made a slow start. Many children soon grew tired of the new food; the other ones poorly tolerated the new food. Than someone thought that yoghurt, familiar throughout the Near East, might be more acceptable. This proved true, and in July the plant began the production of 200 half-pint pots of yoghurt per day in addition to milk and ice cream (Fig. 2). It was followed by a gradual increase in the consumption of milk.

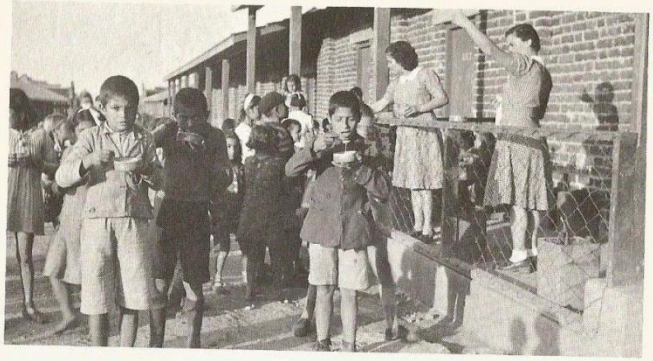

Photo: Cyprus Mines Corporation
The milk plant of the company's welfare department made yoghurt for distribution to school children.

Fig.2 Milk consumption

In Cyprus Smitten also showed himself well in the prevention of infectious diseases [13, p. 253-254]. Malaria was the biggest challenge, with incidence increasing and decreasing with the amount of rain each winter. Smitten carried out anti-malaria activities still more vigorously. The houses where the patients, ill with malaria lived were immediately sprayed. He experimented with the newest drugs and serums and kept elaborate records of the findings. Smitten lectured at village clubs, provided health education to school children through their teachers, prepared and distributed bulletins in three languages.

Persistently he importuned the government for help. The Cyprus authorities were sympathetic but handicapped by lack of funds. At last, in 1935, Smitten received an ally, when American owners of the CMC helped the Cyprus government arrange a survey by Dr. M.A.Barber of the Rockefeller Foundation. After the government began expanding its own program, Smitten was regularly called on as a consultant. In the minds of many people, Cyprus was disease-free largely due to his efforts.

Sanitation was another grave problem. Smitten's inspection teams checked regularly the slautherhouses, restaurants, and dwellings in the villages under the mine's jurisdiction. To overcome the workers' carelessness about rubbish, the CMC distributed large cans and arranged for garbage disposal. Unaccustomed to toilets, the families would not maintain private ones and had to be educated to use the communal latrines provided in each village. Great number of horses, mules, donkeys, etc. added to the undesirable condition, but continual attention brought progress: dysentery, the scourge of the village at Scouriotissa, was eliminated by the mid-1930-s.

The overcrowding attendant upon the mine's growth complicated Smitten's problems. In the second half of 1936 a serious ourbreak of spinal meningitis began in Cyprus. Itinerant workers evidently brought the disease to CMC's region from either Paphos or Famagusta, where the initial cases were reported in September.

During the following winter of 1936/37 there were a total of 829 reported cases throughout the island. A quarter of these (202 cases) were registered in the area surrounding the CMC's mines. Fatalities run as high as 30 percent. Fear swelled toward panic: when outbreak of influenza occurred in the early months of 1937, swarms of frightened people besieged Smitten's hospitals, thinking they had meningitis [13, p. 254].

Completely alarmed, the island's health authorities prepared the port of Xeros to quarantine. Such a step would have disrapted the entire shipping program and have dislocated the work of the European acid plants and smelters dependent upon the CMC's ore. However, Smitten and his allies convinced the authorities that adequate preventive steps could be taken without the quarantine.

Although the laboratory of the Pendayia hospital was not designed for such tests, Smitten managed to detect three different strains of the diseas, one of them particularly virulent. He sent this and all other relevant information immediately to Pennsylvania University, to expert on serums. Soon vaccines and antitoxines against meningitis were rushed by ship and air to Cyprus.

In such a way Pendayia hospital was prepared for patients' admission. Not only people working in the CMC but also all the residents of the area were also coming there. Foreseeing that it would be crowded, tents to shelter 150 patients were rented from the government. Meanwhile two buildings across the river from the Pendayia hospital were turned into isolation wards.

Some of the radical Greek newspapers used the outbreak to launch vituperative editorials about conditions in which the miners were "compelled" to live. But the statistics showed that only 37 of the 202 cases, treated in the CMC area during the winter of 1936-37, came from the company houses; the other 165 came from localities outside the mine's supervision. The island's director of medical services and the inspector of mines issued denials of the more irresponsible statements in the press, and gradually the attacks dwindled away.

Warm wheather brought respite from the disease. Experts predicted the recurrence with the onset of cold wheather the following winter. To combat the expexted attack, Smitten and the director of medical services elaborated a vaccination program whereby the CMC would treat 12,000 people in its area while the government had to inoculate 30,000 in other areas. Superstitution among the workers was certain to create resistance to the program. To remove any possible charge of compulsion, Smitten insisted on making a nominal charge of 1/3 shilling for 2 shots involved in the program. Thus reassured, hundreds of people came to the hospitals, each being tattooed to show the date and number of his injection. 8,306 people received treatment through the CMC, 6,412 being given both injections [13, p. 255].

These and other measures provided by Smitten, which

proved to be very effective, would have done an honor to an experienced epidemiologist. It is necessary, however, to remind that the organizer and leader of the impressive campaign was a representative of an entirely different medical speciality. As it turned out, the medical faculty of Kharkov University gave well-grounded knowledge on epidemiology and sanitation even to surgeons, helping in difficult life circumstances!

Smitten's activities against this spinal meningitis epidemic also caught the attention of British health team working on the island and reflected their observations in a published article:

"While visiting the villages, we saw that Dr. P. Smitten had already started to vaccinate the mine workers, their spouses and children, and he was working in the way to vaccinate as many people as possible. What Smitten had done should be remembered with gratitude" [24].

But this victory was the last for Pavel Smitten. Soon the World War II came to the Mediterranean Sea. The CMC began to experience serious difficulties with the export of its products and with the importation of food and other commodities. Many miners have lost their jobs. Food prices began to rise, including the price of milk. This is seriously violated Dr. Smitten's activity in health care.

Because of the import difficulties, only the most undernourished children could be helped. The ability of families to pay dropped sharply; in January, 1941 no charge was made to 521 of 597 children receiving a daily pint of milk or yoghurt.

But, of course, not only this disturbed former Kharkov doctor. The war was already close to Cyprus. In April 1941 Nazi blitzkrieg went by tank rink through Greece. The Germans appeared in Syria (formally French), very close to Cyprus. On May 20, 1941 Luftwaffe's paratroopers and gliders landed on the island of Crete and within 10 days defeated strong British and Greek troops. Who could be certain that their next leap will not be to Cyprus?

There is almost no doubt that the newspaper message about the success of the Nazi assault on Crete became the cause of Dr. Smitten's sudden death. Pavel Nikolaevich died suddenly of a heart attack as he set reading in his chair in the evening of May 23, 1941 [13, p. 278]

To be continued.

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PHARMACOLOGY

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THE BENEFITS OF THE COMBINED TOPICAL ADMINISTRATION OF KETOPROFEN AND GLUCOSAMINE HYDROCHLORIDE TO BACK PAIN TREATMENT

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Abstract: The article presents research data on analgesic activity of different samples of combinations with glucosamine and ketoprofen in topical dosage forms. The study showed significant analgesic activity (55.1%) of glucosamine hydrochloride 5.0% / ketoprofen 2.0% cream-gel combination with the indices significantly higher than in ketoprofen 2.5% cream-gel and glucosamine hydrochloride 2.5% / ketoprofen 2.0 % cream-gel. The findings showed that glucosamine hydrochloride 5.0% / ketoprofen 2.0% cream-gel combination offers challenge for further study and implementation into wide clinical practice, including for the treatment of spinal osteoarthritis and back pain.

KeyWords: glucosamine hydrochloride, ketoprofen, back pain, spinal osteoarthritis, cream-gel, analgesic activity.

INTRODUCTION

Spinal disorders include trauma, mechanical injury, spinal cord injury, inflammation, infection, and tumors. Low back pain, the most common spinal disorder, affects over 80.0% of patients at some point in their life, and from 4.0-33.0% of the population at any one time. Back pain is the most common cause of disability among young adults. Many factors, physical, psychological and occupational, contribute to the development of back pain. Spinal osteoarthritis is one of the common causes of back pain. Spinal osteoarthritis is the mechanical breakdown of the cartilage between the aligning facet joints in the back portion (posterior) of the spine that quite often leads to mechanically induced pain [8].

Osteophytes (small bony growths also known as bone spurs) form on facet joints and around vertebrae recompensing the lost stability of the joint. Gradually, the spine stiffens and loses flexibility. Osteophytes sometimes become large enough to cause narrowing of the spinal canal or foramen, irritating or entrapping nerves passing through them (spinal stenosis and foraminal stenosis).

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Stenosis, while related to osteoarthritis, is a separate medical condition. Osteoarthritis can also be confused with degenerative disk disease, a gradual deterioration of disks between the vertebrae, but is considered to be a separate medical condition [1].

Therefore, effective treatment of back pain requires not only administration of analgesic drugs (analgesics and NSAIDs), but also drugs with chondroprotective effect. The most efficient method involves administration of combinations of the above drugs, including topical dosage forms.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of our study was to investigate the analgesic properties for the perspective of combined use of NSAIDs and chondroprotector glucosamine (GA) hydrochloride, at different doses in the dosage form of a cream-gel.

2.2 Subjects & Methods

The study of analgesic properties of different topical combinations with GA hydrochloride and ketoprofen was conducted under the conditions of induced pain reaction [3, 5]. The study involved a model of inflammatory hyperalgesia in rats [5], in which the intensity of pain was

measured by Randall-Selitto method [6]. Assessment comprised Analgesy-meter Ugo Basile 37215 (Ugo Basile, Italy) [2, 4], which gives a possibility to provide a very accurate determination of threshold pain sensitivity (THPS) by changing the mechanical pressure on the limb of the animal. The trial was conducted on 70 white nonlinear rats of both sexes, with the body mass of 150-180 g. We also evaluated topical drugs of ketoprofen in 2.5% and 2.0% concentrations and combinations of ketoprofen in 2.5% concentration and glucosamine hydrochloride in 2.5%, 5.0% and 10.0% concentration. At the beginning of the trial the rats were subjected to the procedure of determining initial indicators THPS using Analgesy-meter Ugo Basile 37215 by stimulating pain reaction on the right rear paw [2, 4]. Then, at least in 30 minutes, inflammatory hyperalgesia on the right rear paw of animals was reproduced by subplantar injection of 0.1 ml of 1.0% λ-carrageenan solution («Sigma», USA) into the paw [3, 5]. In 2 hours after injection we conducted a single application of the gels under investigation (except for the control pathology group) on the right rear paw through the skin in equivalent therapeutic doses of 50 mg (or 25 mg /cm2).

The study drugs were applied onto the area of the paw below the ankle joint of approximately 2×2 cm, with careful rubbing excluding the possibility of topical medical forms leaking from the skin of animals. THPS was determined in 3 hours after carrageenan administration for all the animals [6]. Further analgesic properties were evaluated according to analgesic activity (AA) and the ability of investigated drugs to reduce the degree of hyperalgesia in the animals [3, 5]. Thus, AA was calculated in terms of increasing the THPS in animals compared to the control pathology group and expressed as a percentage by Formula 1:

$$AA = \frac{\Delta THPSc - \Delta THPSr}{\Delta THPSc} \times 100\%$$

AA – analgesic activity%
ΔTHPSr – the percentage difference in the levels of pain sensitivity in a group of experimental animals before and after inflammatory hyperalgesia and application of the drug under investigation;
ΔTHPSc – the percentage difference in the levels of pain sensitivity in the control pathology group before and after inflammatory hyperalgesia.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The findings of the trial are presented in Table 1 and show a significant induction of pain in animals following the development of inflammatory hyperalgesia, as evidenced by the probable THPS decline in control pathology group by 2.9 times (Table 1).

Table 1.

The study of the analgesic activity of different combinations of glucosamine hydrochloride and ketoprofen in topical dosage forms (n = 60)

Conditions of the trial	THPS, conv. units.		Δ THPS, %	AA, %
	Initial indices	One hour after application of the drug		
Control pathology group	217.1 ±12.3	73.8 ±5.5	66.1 ±1.2	–
Control pathology group + ketoprofen 2.5 % cream-gel	233.0 ±16.8	149.4 ±10.7	35.8 ±2.2[1]	45.8 ±2.7
Control pathology group + ketoprofen 2.0% cream-gel	230.0 ±17.3	142.0 ±9.7	38.2 ±2.2[1]	42.2 ±3.3
Control pathology group +GA hydrochloride 2.5 % / ketoprofen 2.0 % cream-gel	234.0 ±16.7	150.3 ±12.2	35.6 ±2.0[1]	46.1 ±3.1
Control pathology group + GA hydrochloride 5.0 % / ketoprofen 2.0% cream-gel	235.0 ±23.2	166.0 ±18.5	29.6 ±2.0[1,2,3,4]	55.1 ±2.9 [2,3,4]
Control pathology group + GA hydrochloride 10.0 % / ketoprofen 2.0 % cream-gel	239.0 ±22.0	173.0 ±19.3	28.6 ±2.2[1,2,3,4]	56.8 ±3.3 [2,3,4]

Notes:
1. – p <0.05 relative to the control pathology group;
2. – p <0.05 relative to animals treated with 2.5% ketoprofen cream-gel;
3. – p <0.05 relative to animals treated with 2.0% ketoprofen cream-gel;
4. – p <0.05 relative to animals treated with GA hydrochloride 2.5% / 2.0% ketoprofen cream-gel;
5. n – total number of animals in the study.

Administration of ketoprofen 2.5% cream-gel showed a decrease in THPS by 1.6 times as compared to the initial indices and the percentage was significantly lower than in the control pathology group. Analgesic activity of this drug amounted to 45.8 ± 2.7%. NSAID-treated group was found to have a range of side effects, becoming more severe with an increase in dosage. To obtain the optimal dose NSAIDs were used in combination with ketoprofen cream-gel 2.0%. Its THPS indicator was 1.6 times lower than in the initial findings, the percentage was not significantly different from the previous drug, but higher than the THPS indicator in the control pathology group. Its AA was 42.2 ± 3.3%, which was not significantly different from the AA of ketoprofen 2.5% gel. According to the scientific literature, R. J. Tallarida provided evidence that combined use of NSAIDs and chondroprotectors caused analgesic synergism of NSAIDs properties and allowed to reduce the dosage of NSAIDs without disrupting the pharmacological effectiveness [7]. Our study design involved pharmaceutical combinations in cream-gel form which contained ketoprofen in 2.0% concentrations, GA hydrochloride in 2.5%, 5.0% and 10.0% concentrations. Another objective was to assess the effectiveness of GA hydrochloride 2.5% / ketoprofen 2.0% cream-gel combination. Its THPS decreased by 1.6 times, and AA was 46.1 ± 3.1%, which was on the level of 2.5% ketoprofen cream-gel. We also investigated the potential of GA hydrochloride 5.0% / ketoprofen 2.0% cream-gel combination. Its THPS, which decreased only by 1.4 times according to the initial indices and the AA was 55.1 ± 2.9%. The data exceeded all previous values and demonstrated the positive impact of glucosamine on the analgesic properties of NSAIDs.

Furthermore, we determined the effectiveness of GA hydrochloride 10.0% / ketoprofen 2.0% cream-gel combination. Its THPS decreased by 1.3 times as compared to the initial indices and the AA was 56.8 ± 3.3%. The results of latter combination in the percentage ratio by AA and THPS indices did not significantly differ from the abovementioned combination, although GA hydrochloride concentration was 2 times higher.

Taking the above into account, it is advisable to choose GA hydrochloride 5.0% / ketoprofen 2.0% cream-gel combination for further research, as it showed a higher AA indicator, which was 55.1%, that was significantly higher than the indices of the two other objects. Though the research indices of GA hydrochloride 5.0% / ketoprofen 2.0% cream-gel combination were lower than the latter object of the study, this difference was not significant and was only 1.0% for THPS and 1.7% for AA.

4 CONCLUSIONS

1. Spinal osteoarthritis is one of the common causes of back pain. Efficient treatment of spinal osteoarthritis requires the usage of combination of NSAIDs and chondroprotectors in different dosage forms.

2. The study showed that GA hydrochloride 5.0% / ketoprofen 2.0% cream-gel combination had a distinct analgesic activity (55.1%) as compared to ketoprofen 2.5% cream-gel (45.8%) and GA hydrochloride 2.5% / ketoprofen 2.0% cream-gel (46.1%). GA hydrochloride 5.0% / ketoprofen 2.0% cream-gel combination is perspective offers the challenge for further study and wide

implementation into clinical practice, including for the treatment of spinal osteoarthritis and back pain.

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CARDIOLOGY

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AORTIC STENOSIS IN 93 Y.O. FEMALE (case report)

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Abstract: The increase in life expectancy of patients contributes to development of new technology for treatments of patients with comorbidities of advanced age. Transcatheter aortic-valve implantation has been suggested as a less invasive treatment for high-risk patients with aortic stenosis.

KeyWords: aortic stenosis, transcatheter aortic-valve implantation

INTRODUCTION

Aortic stenosis (AS) has become the most frequent type of ventricular heart disease (VHD) in Europe and North America. It primarily presents as calcific AS in adults of advanced age (2–7% of the population over 65 years) [1, 2]. The primary treatment for severe aortic stenosis is aortic valve replacement surgery. The 3-year survival in patients with symptomatic aortic stenosis who undergo surgery is 87%; in those who do not have surgery, it is 21% (P <0.001) [3].

AS with a valve area 1.0 cm2 is considered severe, critical AS is most likely with a valve area 0.8cm2 [4].

CASE STUDY

A 93-year old women with a stress reaction on death of the husband. In anamnesis are the iron deficiency anemia, sigmodivertikulosis, colonic angiodysplasia (2014), cholecystectomy, appendectomy, chronic renal failure, presented with, paroxysmal atrial fibrillation (under Rivaroxaban therapy), symptomatic aortic (valve) stenosis, arterial hypertension, osteoporosis.

Physical examination:

Anthropometry - 156 cm, 65 kg. BP - 150/60 mm Hg. Loud systolic murmurs were heard in point 2 with right carotid radiating. Weak vesicular breathing was heard in the basal area; basal pleural effusions were noticed. The abdomen was soft, not resistant; the patient denied any tenderness. Discreet lower leg edema was present. She also denied chest pain, shortness of breath. She reported exercise dyspnea.

Chest X-ray demonstrated chronic signs of congestion and low angle effusions on both sides, sclerosis of the aorta without the evidence of infiltration. Laboratory data are presented in Table 1.

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Table 1.

Results of laboratory investigation of the female patient with aortic stenosis

Complete blood count	14.06. 2016	17.06. 2016	Unit	References
White blood cells	10.93	10.63	G./L	3.60-10.50
Platelets	565	503	G./L	160-370
Red Blood Cells	3.49	4.19	T/L	3.85-5.20
HGB (Hb, hemoglobin)	7.1	8.6	g/dl	11.8-15.8
HCT (hematocrit)	23.7	28.8	%	35-45%
NEUT%	77.8	72.3	%	50.0-70.0
LYM%	11.5	153.	%	20.0-44.0
Hypochromic Ery.	53.1	41.5	%	0-.2.5%
Kreatinin	1.56	1.37	mg/dl	0.51-0.95
GFR	28.38	33.21	mL/min/1.7 m^2	>90
BUN	32	22	mg/dl	8-23
Uric Acid	8.3	8.8	mg/dl	2.4-5.7
Na	140	138	mmol/L	136-145
K	4.8	4.4	mmol/L	3.5-4.6
Chlorid	101	102	mmol/L	3.5-4.6
Iron	16		µg/dL	33-193
Transferrin	2.45		g/l	2.0-3.6
Transferrin saturation	4.63		%	16.0-45.00
Ferritin	14		µg/L	15-150
Vitamin B12	341.7		Pg/mL	197-771.0
CRP	9.4		mg/l	0.0-5.0
ESR 1h	57		mm	0-45
Calcium	2.29	2.37	mmol/L	2.05-2.40
CK	38		U/L	20-180
Troponin T- hs	32.69		ng/L	0.0-14.0
ALAT (GPT)	27		U/L	0-35.0
Gamma-GT	39		U/L	0-40
Alk.Phosphatase (AP)	71		U/L	35-105
Bilirubin	0.27		mg/dL	0.00-1.20
LDH	317		U/L	0-250
Glucose	148		mg/dL	50-100
Cholesterol	126		mg/dL	150-200
HDL-cholesterol	22		mg/dL	>65
LDL-cholesterol	--		mg/dL	60-130
Chol./HDL-Ch.-ratio	5.7		-	0-3.6
Trigleceride	198		mg/dL	50-150
Total proteins	65		g/L	66-87
TSH (hormone)	2.50		µU/ml	0.27-4.20
Hemostasis				
aPTT	48.5	28.6	sek	26.0-38.0
INR	1.84	--	---	1.07

ECG revealed sinus rhythm, HR was 74 bpm. left axis, left ventricular hypertrophy, AV-Block I, T- neg.: I, II, V5-6 (Repolarization problem) (fig.1).

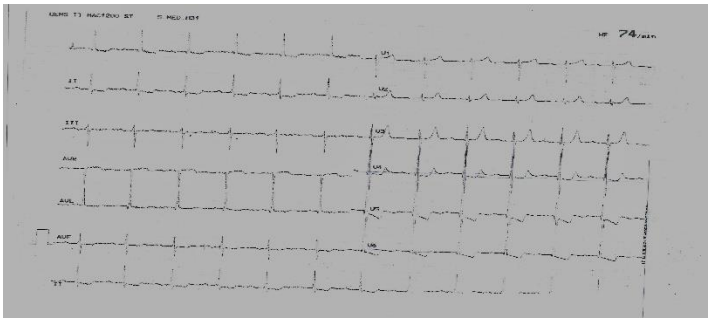

Fig. 1. ECG

Echocardiography demonstrated a normal borderline, normal Left Ventricular Ejection Fraction LVEF(EF 54%); Mitral Insufficiency grade II; Severe Aortic Stenosis, max. gradient 105 mm Hg, mean AV Pg 62 mm Hg., AVA V max/ VTI 0.8 cm 2, pulmonary hypertension 65 mm. Hg. (fig.2). Conclusively aortic stenosis together with mitral insufficiency and pulmonary hypertension were diagnosed.

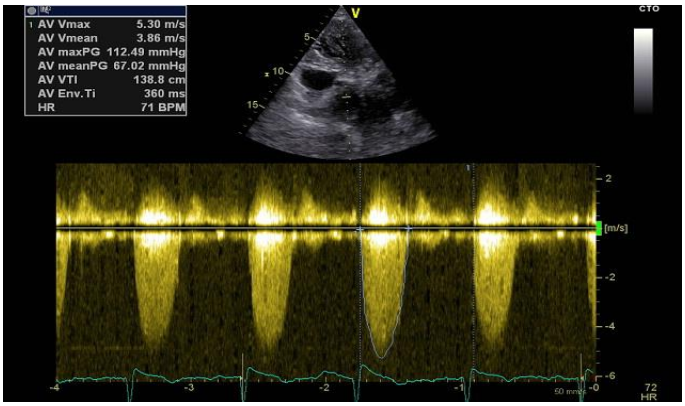

Fig. 2. Aortic valve velocity and pressure gradient.

Coronary angiography revealed coronary l-vessel stenosis with focal (about 70 %) proximal left arteria descending (LAD) stenosis.

The patient was diagnosed:

I35.0 - Aortic (valve) stenosis, valve area 0.8 cm^2

I25.1 - Atherosclerotic heart disease. Focal stenosis proximal LAD.

I34.0 - Mitral (valve) insufficiency.

I13.1 - Hypertensive heart and renal disease with renal

failure

I48. - Paroxysmal atrial fibrillation

I50.0 - Congestive heart failure

E14 - Diabetes mellitus

N18.9 - Chronic renal failure

D50 -Iron deficiency anemia.

K57 - Sigmodivertikulosis.

K55 - Angiodysplasia of the colon.

Treatment:

1. Oral rehydration therapy according standard protocol under the control of kidney function.

2. The earlier treatment was continued:

- Actonel 35 mg vis Calcimagnon 1 weekly
- Pantoloc 40 mg in the morning (1/0/0)
- Lexotanil 3 mg in the evening (0/0/1)
- Rasilez (aliskeren) / HCT 300 /12.5 mg in the morning (1/0/0)
- Concor 5 mg (2.5 mg twice per day) (1/2/0/1/2)
- Furon 40 mg (20 mg twice per day) (1/2/1/2/ 0)
- Digimerc 0.07 mg (0.035 in the morning) (1/2/0/0)
- Zanidic (lercanidipine) 10mg per day (0/1/0),
- Xarelto 15 mg per day (1/0/0) (under current International Normalized Ratio (INR) and glomerular filtration rate (GFR)
- Metformin 850 mg twice per day (1/0/1)

3. The erythrocyte concentrate infusion was successfully prescribed for treatment hypochromic microcytic anemia (no side effects with appropriate rise of Hb level).

4. Oral iron therapy for approximately 1 month, after a reassessment of the iron status. GIT examination was recommended one month after the discharge from hospital (iron therapy should be stopped for 10 days before it).

5. Transcatheter aortic valve implantation (TAVI) was considered.

Discussion

Aortic valve replacement (AVR) is the definitive therapy for severe AS. In contemporary series, operative mortality of isolated AVR for AS is 1–3% in patients younger than 70 years and 4–8% in selected older adults [1,4 - 13].

Surgery has been shown to prolong and improve quality of life, even in selected patients over 80 years of age [10 – 13].

Contraindications for transcatheter aortic valve implantation can be absolute, clinical and relative.

Absolute contraindications include:

- Absence of a ‘heart team’ and no cardiac surgery on the site
- Appropriateness of TAVI, as an alternative to AVR, not confirmed by a ‘heart team’

Clinical contraindications comprise:

- Estimated life expectancy <1 year
- Thrombus in the left ventricle
- Active endocarditis
- Elevated risk of coronary ostium obstruction (asymmetric valve calcification, short distance between annulus and coronary ostium, small aortic sinuses)
- Plaques with mobile thrombi in the ascending aorta, or arch
- For transfemoral/subclavian approach: inadequate vascular access (vessel size, calcification, tortuosity)

Relative contraindications are:

- Bicuspid or non-calcified valves
- Untreated coronary artery disease requiring revascularization
- Haemodynamic instability
- LVEF<20%
- For transapical approach: severe pulmonary disease, LV apex not accessible.

In patients with high surgical risk, TAVI has been shown to be feasible (procedural success rates 90%) using transfemoral, transapical or, less commonly, subclavian or direct trans-aortic access [13,14 – 22].

4 CONCLUSIONS

The Considering the patient's clinical condition: Severe aortic valve stenosis, the absence of decompensation of the cardiovascular and respiratory systems- patient is need of replacement surgery Trans catheter implantation of the aortic valve.

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PEDIATRICS

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DETECTION OF PSYCHOLOGICAL CHARACTERISTICS IN CHILDREN WITH CHRONIC GASTROINTESTINAL DISEASES USING MOS-SF-36 QUESTIONNAIRE

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Abstract: the article describes the main approaches in the study of psychological characteristics in children with chronic gastroenterological diseases according to MOS SF-36 questionnaire.

KeyWords: children, MOS-SF-36 questionnaire, chronic gastrointestinal diseases.

INTRODUCTION

The World Health Organization defines Quality of Life as the individuals' perception of their position in life within the framework of culture and value systems they live in and in relation to their goals, expectations, standards and concerns [1].

Any disease affects both physical and psychological conditions, changing emotional reactions, place and role in everyday life. It is very important to get a complete picture of the disease impact on the most important humans' functions when studying the nature of the disease. Identification of the exact type of abnormality and the level of severity is essential for right planning, treatment and rehabilitation. Physicians often assess only physical, laboratory and instrumental data describing only the physical condition of the patient. The majority of doctors are not interested in the information on individual psychological and social problems that have emerged due to the disease [2, 3].

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In recent years, evaluation of quality of life (QOL) has become an important new methodological approach to assess the results of medical interventions in clinical and epidemiological studies in the countries with high levels of medicine, because the traditional criteria of effectiveness of medical measures, reflecting changes in the physical condition, do not give the full picture not only of the physical but also psychological and social condition of the patient. QOL research methodology enhances capabilities of standardization of treatment, provides individual monitoring with the evaluation of early and long-term results of treatment, develop predictive models of disease course and outcome in the practice of health care [4, 5].

In other words, it is a new an integral approach to complex evaluation of the patient's health, that is based on the set of objective medical data and subjective evaluation of the patient.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

As the quality of life depends on the health status of children with chronic gastroenterological diseases, the purpose of the work was to study physical and psychological presentation in children with

gastroenterological disorders according to MOS SF-36 questionnaire.

2.2 Subjects & Methods

Quality of life was assessed in 66 patients aged from 2 to 17 years (of them, 32 girls (48.5%) and 34 boys (51.5%) with diseases of the digestive system. The average age of the patients was 11.3 ± 4.1 years. The survey respondents were treated at gastroenterology department of Kharkiv Regional Children's Clinical Hospital within the period from 2015 to 2016. The control group consisted of 47 age- and gender matched healthy children (students of Merefa gymnasium No. 1). The average age was 12.1 ± 3.2 years; boys - 25 (48.1%) and girls - 22 (51.9%).

The examined children with gastrointestinal diseases were diagnosed with chronic gastritis (42.4%), biliary dyskinesis (15.2%), pancreatopathy (12.1%), duodenal ulcer (9.1%).

The quality of life was assessed with the help of the questionnaire. Patients or their parents completed questionnaires, and then its individual parts were analyzed with special scales or summary index.

The Short Form Health Survey (MOS SF-36) is one of the most common methods for evaluating the quality of life related to health. The questionnaire Medical Outcome Study- SF-36 consists of 36 questions forming the eight scaled scores, which are the weighted sums of the questions in their section: vitality (VT), physical functioning (PF), bodily pain (BP), general health perceptions (GH), physical role functioning (PR), emotional role functioning (RE), social role functioning (SF), mental health (MH).

The questionnaire assesses two components of health: physical and psychological. Each scale is directly transformed into a 0-100 scale on the assumption that each question carries equal weight. The higher the score the less the disability, i.e. a score of zero is equivalent to maximum disability and a score of 100 is equivalent to absence of a disability.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The survey patients with gastrointestinal abnormalities and children without digestive disorders gave answers, describing the quality of life. The survey results are presented in Table 1.

Table 1.

Quality of life in children with gastrointestinal diseases

	PF	RP	BP	GH	VT	SF	RE	MH
The main group N=66	76.7 ±6.4	71.2 ±4.9	69.1 ±5.3	56.3 ±6.4	64.4 ±4.4	68.9 ±6.4	70.7 ±3.3	64.7 ±7.6
The control group N=47	93.6 ±5.6	97.4 ±7.1	87.2 ±8.6	70.4 ±8.8	66.3 ±2.8	83.4 ±2.1	88.7 ±2.2	78.3 ±9.5
p	p< 0.05	p< 0.05	p< 0.05	p< 0.05	p< 0.05	p< 0.05	p< 0.05	p< 0.05

Exacerbation of chronic gastrointestinal diseases causes pain, which is reflected in the reduction of bodily pain indices from 87.2 ± 8.6 to 69.1 ± 5.3. It is worth mentioning a decrease in the indices of physical activity from 93.6 ± 5.6 to 76.7 ± 6.4. significantly worsening emotional role functioning from 88.7 ± 2.2 to 70.7 ± 3.3. The ability to perform social responsibilities also reduced from 83.4 ± 2.1 to 68.9 ± 6.4. There has been a decrease from 70.4 ± 8.8 to 56.3 ± 6.4 on the general health scale. Physical condition also significantly declined from 97.4 ± 7.1 to 71.2 ± 4.9.

The received data due to the fact that the 12-duodenum synthesizes regulatory peptides to support not only the digestive tract but also participating in neuroregulation (for which it was called "pituitary gland" of the gastrointestinal tract); also the results showed systematic changes of

the microorganisms in local gastroduodenal lesions. Thus, there is the tendency to deterioration in each indicator of the quality of life: physical and psychological health scales.

4 CONCLUSIONS

The quality of life in children with gastroduodenal pathology is lower than in healthy children; it is mostly associated with a decrease in physical component. The most significant violations of life quality were observed in patients in role-functioning due to the physical component (RP) that is lowered ability of their daily social responsibilities. The study also showed a reduction in such indices as bodily pain (BP) due to exacerbation of diseases of the digestive system; general health (GH) reduction triggered by gastroduodenal abnormalities affecting the general condition of the patient and potentiating other organs and systems diseases. The psychological component of health also suffers mainly due to the emotional role functioning (RE). Thus, the quality of life in children with gastroenterological diseases is reduced both by physical and psychological component.

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PEDIATRICS

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CONGENITAL ACUTE MEGAKARYOCYTIC LEUKEMIA IN NEWBORNS (case report)

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Abstract: Acute megakaryocytic leukemia (AMKL) or acute myeloid leukemia (AML-M7) is a type of pediatric AML accounting for 3-10% of primary childhood AML and 50% of the AML in children with Down's syndrome. Median age of presentation is 6 years (ranging from neonatal period to 16 years). The onset of the disease can be similar to septicemia and congenital infections. Predominantly AMKL has a rapid deterioration that leads to death caused by hemorrhage and infections despite of intensive therapeutic measures. A case of congenital AMKL with manifestation in the neonatal period and without any features of Down's syndrome is presented.

KeyWords: Congenital megakaryocytic leukemia, newborn

A male infant was born from the 5th pregnancy, second premature delivery at gestational age of 32 weeks. This pregnancy was preceded by 3 spontaneous abortions at gestational age less than 12 weeks. Pregnancy proceeded against the background of threatened miscarriage at 28 weeks of gestation, premature rupture of membranes and chronic pyelonephritis in the mother at the stage of remission. X-ray examination of the mother's chest was performed at gestational age of 8-10 weeks. The child's father works at a car service station. Fetal respiratory distress syndrome was prevented by 24 mg of dexamethasone. The infant had a low birth weight of 2240 g, body length of 44 cm, chest circumference of 28 cm and head circumference of 30 cm. These parameters exceeded standard ones for this gestational age. Apgar score was 3-4 points.

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At birth the newborn had a severe condition due to respiratory disorders and neurological deficits on the background of the immaturity of organs and systems as a result of prematurity. Therefore, he was administered resuscitation measures which included sanation of upper airways, prolonged mask lung ventilation twice for 40 seconds, further non-invasive lung ventilation for 30 minutes, gastric probe administration, correction of hypovolemia, water and electrolyte balance and blood gases.

Since the first hours of life the child had severe pathological neurological symptoms (the child was lethargic, did not cry, his reflexes were depressed, with signs of hypersensitivity and muscle dystonia). On the 2nd day of life he developed signs of hemorrhagic syndrome, namely flow of blood from the gastric tube and ecchymosis on the limbs, with manifestations of hepatolienal syndrome. In spite of the therapy, the respiratory disorders grew acute. Blood tests showed anemia, leukopenia, thrombocytosis, distinct myeloid irritation due to promyelocytosis and basophilia. With dynamic management of the infant thrombocytosis increased from 600×109 to 1300×109 and reticulocytes decreased to 1%; leukopenia persisted to 2.5×109.

Differential diagnosis with congenital sepsis, hepatitis, the presence of TORCH-infections was conducted.

However, taking into account the follow-up findings, persisting respiratory disorders, intensification of neurological symptoms, hemorrhagic and hepatolienal syndromes and paraclinical data (thrombocytosis, hyporegeneratoric normochromic anemia, leukopenia, distinct myeloid irritation) suggested hemoblastosis, namely congenital myeloid leukemia (M7 type). Nevertheless, the severity of the condition did not allow to render total oncohematological examination, including myelogram.

The treatment included respiratory support, antibiotic therapy, detoxification, hemostatic therapy and resuscitation. However, with time the infant's condition progressively worsened. The infant died at the age of 9 days due to progressive multiple organ failure.

Postmortem examination showed leukemic infiltrates in the internal organs. The liver and spleen were found to have diffuse proliferation of leukemic cells and hyperthrombocytosis. Besides, examination revealed large venous thrombosis of the hepatic vessels and the spleen with infarction-like haemorrhages in these organs. In addition a large amount of similar cellular infiltrates was found in the lungs, brain and meninges. Microscopic study detected abnormal platelets and large cells (25-40 microns), with a large nuclear-cytoplasmic ratio (i.e., large nucleus) and a relatively poor, variably basophilic cytoplasm. The nuclear chromatin of the large cells was dense and homogeneous. Immunohistochemical studies confirmed that these cells belonged to megakaryoblasts.

The cause of death was determined as multiple organ dysfunction syndrome. The diagnosis of congenital megakaryocytic leukemia was confirmed.

DISCUSSION

This case was characterized by the development of hemoblastosis (myeloid leukemia M7) in a newborn with adverse premorbid background, presenting since the first days of life as severe respiratory and neurologic disorders, hemorrhagic and hepatolienal syndromes, changes in clinical blood tests, such as thrombocytosis, anemia and leukopenia. Diagnosis was extremely difficult due to the low incidence of the disease, especially in infants, and also difficulties in providing the diagnosis by oncohematological approach.

Congenital leukemia is a term including the cases presenting with clinical and hematologic syndromes in the first days of life. Leukemia in children of the first months of life is a very rare disease. According to Bajwa RP, Skinner R, Windebank KP, Reid MM. (2004), the incidence of congenital leukemia is 4.3 - 8.6 per million livebirths [2]. AML-M7 or AMKL is a very rare type of AML, which is about 1% of all cases of leukemia in children, with the incidence rate of 0.5 cases per million per year [1].

Primary thrombocytosis is a clonal myeloproliferative disorder with an estimated annual incidence of about 2 cases per million of adult population [3] and 0.09 cases per million of children [4, 5].

Literature review revealed a few descriptions of manifestation of congenital leukemia in the neonatal period. The youngest case of congenital myeloid leukemia not associated with Down’s syndrome has been described at the age of 1 day [6], and congenital megakaryocytic leukemia without Down’s syndrome has been described at the age of 17 days [1]. Another case of AMKL has been reported in a newborn at the age of 4 weeks and the infant was found to have only infiltration in the liver [7].

An increase in the incidence of congenital leukemia in infants was shown to be 2 times higher in mothers exposed to X-rays for diagnostic purposes [8].

At the same time healthy children are born from mothers who have leukemia. This fact excludes transplacental transmission of leukemia. Studies showed that maternal part of the placenta contained leukemic cells with their absence in the fetal part [9].

Risk factors for congenital leukemia are mother's age exceeding 35 years, fetal death in past history, macrosomia, cancer in family history and immunodeficiency states [10, 11].

Clinical criteria of congenital leukemia include anemic syndrome, haemorrhagic syndrome, intoxication syndrome, proliferative syndrome, neuroleukemia [12].

Such clinical signs as toxicity, bacterial, fungal or protozoal infection, fever, hemorrhagic syndrome (associated with both thrombocytopenia and intravascular thrombosis due to thrombocytosis), jaundice, leukemic infiltration, hepatosplenomegaly, neurological symptoms, testicular enlargement in boys should be considered as clinical manifestations of leukemia in neonates.

Clinical "masks" of acute leukemia include patients with sepsis, pneumonia, purulent skin lesions, congenital hepatitis, patients with hepatolienal syndrome of unknown origin, congenital syphilis, children with low birth weight. The greatest challenge is to make the differential diagnosis between leukemia and sepsis.

Main laboratory criteria of congenital leukemia are myeloid line (promyelocytes, myelocytes), anemia, thrombocytopenia or thrombocytosis, increased ESR.

Bone marrow aspiration and biopsy with the detection of blast cells in myelogram (more than 25%) are known to be the diagnostic gold standard.

Megakaryocytic leukemia is characterized by the following:

- Hyperthrombocytosis in blood, varying from 700×109/L to 1000×109/L and higher (sometimes up to 2000-4000×109/L)
- Abnormal forms of platelets in peripheral blood
- Occasional slight polycythemia, leukocytosis with a shift of leukocyte formula to the left
- Histological specimens are suggestive of bone marrow hyperplasia of megakaryocytic lineage (more than 5-7 megakaryocytes in the field of view)
- In the majority of cases the spleen is not or slightly enlarged and is palpable at the costal margin. The tendency to thrombosis is triggered by hyperthrombocytosis.
- Bleeding results from impaired platelet aggregation, disseminated intravascular coagulation.

By hematological signs congenital leukemia is similar to chronic myeloid leukemia, which allowed several authors [17] to suggest that congenital leukemia is a chronic myeloid leukemia, but with a rapidly progressive course.

However, the majority of experts regard congenital leukemia as acute myeloid leukemia.

When considering the development of thrombocythemia, some authors [18] suggest the following mechanism: in megakaryocytic leukemia myelopoiesis of all lineages is clonal. The descendants of the mutated cell have an ability to proliferate uncontrollably, retaining the ability to differentiate into mature forms, which can explain the histologic similarity of acute myeloid and chronic megakaryocyte leukemia.

CONCLUSIONS

1. Congenital leukemia is a rare abnormality that is not yet well understood.
2. Groups of patients requiring further follow-up with a heamatologist with oncohemological approach include patients with sepsis, pneumonia, congenital syphilis, congenital hepatitis, hepatolienal syndrome of unknown origin and other, which implies that the non-responsive diseases require early intervention.
3. Patients with sepsis due to polyorganic clinical manifestations present the greatest challenge when providing diagnosis of congenital leukemia.
4. In case of doubt, urgent bone marrow examination is mandatory.

CONFLICT OF INTERESTS

There is no conflict of interests.

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PEDIATRICS

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RISK FACTORS OF CARDIOVASCULAR DISORDERS IN NEWBORNS FROM MULTIPLE DICHORIAL BI-AMNIOTIC TWIN PREGNANCIES

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Abstract: The research deals with the study of characteristics of obstetrical, intrapartum and early neonatal periods. Dichorial biamniotic twin pregnancy was the inclusion criterion. One of the risk factors was threatened abortion and/or premature labor. Anemia of pregnancy, acute respiratory viral infections and urogenital infections had no statistically significant differences among the groups of observation. Every third woman 29% with multiple dichorial biamniotic twin pregnancy was found to have a trend towards an increase in incidence of polyhydramnios, and every third woman 30.4% with singleton pregnancy and IUGR had oligohydramnios.

KeyWords: aorta, IUGR, multiple pregnancy

INTRODUCTION

According to leading scientists, clinicians and health care authorities, diagnosis of hemodynamic disorders in "mother-placenta-fetus" system and prognosis of placental dysfunction in multiple pregnancy is one of the current challenges in obstetrics, perinatology and neonatology, which should be dealt with to reduce perinatal morbidity and mortality [1-5].

Dopplerometric examination of fetal aorta is performed in the thoracic section between the aortic arch and the diaphragm, i.e. before the branching point of arterial trunks of the abdominal cavity. The aorta is visualized in the longitudinal scan as an echo-free area limited by pulsating echo-free margins [6]. Nowadays the mechanisms of blood flow redistribution during distress are explained in terms of adrenoreception physiology. Cerebral vessels are mainly represented by ß-receptors, as compared to other organs, which means that cerebral blood flow remains intact in distress. Redistribution of blood to the brain secondary to distress results from an increase in the density of ß-adrenoreceptors of the cerebral vessels.

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Normal indices of blood flow in cerebral vessels and non-physiologic ones in the aorta or umbilical artery may indicate a delayed diagnosis of fetal abnormality with decompensation of cerebral circulation [6, 7].

As it has already been established, blood in the umbilical artery, aorta and cerebral arteries flows from the heart to the periphery during the whole cardiac cycle [7].

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of the study was to study risk factors of cardiovascular disorders in newborns from multiple biamniotic pregnancies.

2.2 Subjects & Methods

The study involved 37 newborns from multiple dichorial biamniotic twin pregnancies without intrauterine growth retardation (Group 1); 25 newborns from multiple dichorial biamniotic twin pregnancies with intrauterine growth retardation (Group 2); 27 infants from singleton pregnancies without IUGR (Group 3 – control group); 23 infants from singleton pregnancies with IUGR (Group 4 – the group of comparison). The research implied determination of characteristics of obstetrical, intrapartum and early neonatal periods.

Dichorial biamniotic twin pregnancy was the inclusion criterion. Median (Me), quartile values (Uq; Lq) and Mann-Whitney (MW) criteria were used to compare the indices with non-Gaussian distribution. Statistically significant difference was considered at $p < 0.05$.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

Women with multiple pregnancy were significantly more likely to require implementation of reproductive technologies ($p < 0.05$) and their infants required observation in the maternity hospital for a more prolonged period ($p < 0.05$).

It stands to mention that newborns from singleton pregnancies with IUGR (Group 4) required significantly more prolonged observation in the maternity hospital compared with newborns from multiple pregnancies and the control group ($p < 0.05$). None of the children from any group under investigation died in the early neonatal period. The results of the study of obstetrical medical history of the mothers involved in the investigation are given in Table 1. Multiple pregnancy statistically significant in frequency ranked second when compared to singleton pregnancy with IUGR (Group 3), ($p > 0.05$). Threatened abortions and/or premature labor occurred significantly more often in mothers with singleton pregnancy and IUGR of the fetus (73.9%) compared to women in the control group (40.7%), ($p < 0.05$). Women with multiple pregnancies were found to have an increased incidence of threatened abortions and/or premature labor (up to 65% with no statistical difference when compared to other groups of observation). Perinatal loss, such as spontaneous abortions, death of children from previous pregnancies and stillbirths occurred with equal frequency in the groups of observation. Anemia of pregnancy, acute respiratory viral infections and urogenital infections did not have any statistically significant differences among the groups of observation.

Table 1.

Characteristics of obstetrical medical history of the mothers involved in the investigation

Indices		Observation group		
		Group 1, n=31	Group 2, n=27	Group 3 n=23
		abs. ($p\%\pm s_{p\%}$)	abs. ($p\%\pm s_{p\%}$)	abs. ($p\%\pm s_{p\%}$)
Consecutive number of pregnancy	1-st	8 (25.8±7.8)	10 (37.0±9.2)	8 (34.7±9.9)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
	2-nd	14 (45.1±8.9)	10 (37.0±9.2)	4 (17.3±7.8)
		$p_{1-3} = 0.0352$		
	3-rd	4 (12.9±6.0)	3 (11,1±6,0)	0 (0±2.3)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
	> 3-rd	5 (16.1±6.6)	4 (14.8±6.8)	4 (17.3±7.8)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
Obstetrical pathology	Placentation abnormality	4 (12.9±6.0)	3 (11.7±6.0)	4 (17.3±7.8)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
	Threatened miscarriage and/or premature labor	20 (64.5±8.5)	11 (40.7±9.4)	17 (73.9±9.1)
		$p_{2-3} = 0.028$, $p_{1-2} > 0.05$, $p_{1-3} > 0.05$		
	Preeclampsia	4 (12.9±6.0)	0 (0±3.7)	3 13.0±7.0)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
Children mortality in previous pregnancies and stillbirth	Spontaneous abortion	6 (19.3±8.9)	6 (22.2±7.9)	2 (8.6 ± 5.8)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
	Anemia of pregnancy	11 (35.4 ± 8.5)	8 (29.6 ± 8.7)	9 (39.1 ± 10.1)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
	Urogenital infection of the mother	6 (19.3±7.0)	5 (18.5±7.4)	2 (8.6±5.8)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
	Acute respiratory diseases during pregnancy	8 (45.1±8.9)	7 (25.9±8.4)	7 (25.9±8.4)
		$p_{1-2} > 0.05$, $p_{1-3} > 0.05$, $p_{2-3} > 0.05$		
	Gestational pyelonephritis	2 (6.4±4.3)	2 (7.4±5.0)	6 (26.0±9.1)
		p1-2> 0.05, p1-3> 0.05, p2-3> 0.05		
Abnormalities of fetal membranes and amniotic fluid	Hydramnion	9 (29.0±8.1)	0 (0±2.7)	3 (13.0±7.0)
		$p_{1-2} = 0.0053$, $p_{2-3} > 0.05$, $p_{1-3} > 0.05$		
	Oligohydramnios	6 (19.3±7.0)	0 (0±2.7)	7 (30.4±9.5)
		$p_{1-2} = 0.0305$, $p_{2-3} = 0.0045$, $p_{1-3} > 0.05$		

Every third woman (29%) with multiple dichorial biamniotic twin pregnancy was shown to have an increase

in incidence of polyhydramnios compared to controls (p <0.05) and every third women (30.4%) with singleton pregnancy and IUGR was found to have oligohydramnios (p < 0.05).

4 CONCLUSIONS

1. One of the factors is that threatened abortions and/or premature labor occurred significantly more frequently in mothers with singleton pregnancy and IUGR of the fetus, 73.9% compared to 40.7%, (p <0.05) of the control group. Women with multiple pregnancies were shown to have a trend towards an increase in the frequency of threatened abortions and/or premature labor up to 65% without statistical differences with other groups of observation.

2. Anemia of pregnancy, acute respiratory viral infections and urogenital infections had no statistically significant differences among groups of observation.

3. Every third woman 29% with multiple dichorial biamniotic twin pregnancy was found to have an increased incidence of polyhydramnios compared to the control (p<0.05) and every third woman 30.4% with singleton pregnancy and IUGR had oligohydramnios (p <0.05) .

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PEDIATRICS

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COMPARATIVE ANALYSIS OF THE ROLE OF DOMESTIC ALLERGENS IN ATOPIC RHINITIS IN CHILDREN

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Abstract: The study implied examination of 304 children aged 4 - 18 years, the patients with allergic rhinitis during the period of stable remission by the method of prick-test. The incidence of allergic rhinitis was found to be progressively increasing with age. Allergic rhinitis in children is predominantly caused by Dermatofagoides farina mites, resulting in allergic reactions in most patients, especially in adolescence.

KeyWords: allergic rhinitis, children, domestic allergens.

INTRODUCTION

One of the leading causes of allergic rhinitis (AR) in children is sensitizing to different domestic allergens [1-6]. The majority of authors [6-8] note that allergenic aggressiveness of the house dust depends primarily on the number and kinds of mites inhabiting it, which belong, generally, to Dermatophagoides genus of Pyroglyphidae family, among them Allergenum e pulvere domesticum e Dermatophagoides pteronyssinus, Allergenum e pulvere domesticum e Dermatophagoides farinae, Allergenum e pulvere domesticum ex Acarus siro. Besides, domestic allergens include Allergenum e pulvere bibliothecae, Allergenum e pluma pulvini, and Allergenum e Daphnia magna.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The study design involved a comparative assessment of domestic aeroallergens in etiologic spectrum of allergic rhinitis in children according to the age and sex by prick-test in the period of stable remission of the disease.

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2.2 Subjects & Methods

The objective of the study implied a comparative assessment of domestic aeroallergens in etiology of allergic rhinitis in children. The study implicated examination of 304 children aged from 4 to 18 with atopic rhinitis. The research was carried out in the Regional children's allergy center based in Kharkov Regional Children's Clinical Hospital No.1.

Skin testing with allergens is a comprehensible and informative method of allergy testing. The tests were performed to confirm the role of allergens in the disease development, which was suggested by hypersensitivity history. This highly sensitive method determines specific sensitization by injecting percutaneous allergen and evaluation of the extent and nature of edema or inflammatory reaction. Testing can be carried out using scratch test, injection test, prick test and the intradermal test techniques. We performed allergy prick test to discover first-type reactions.

Indications for skin testing with allergens included past history, clinical and laboratory findings.

Standard serial allergens containing 10,000 PNU in 1 ml made of pollen, house dust, wool, food etc. were used for skin testing (producer LRS Immunolog, 21036, Vinnica, P.O.B. 4283, Zbyzhka street, 5). Skin testing technique is based on the allergen interaction with Langerhans cells

and macrophages. Such interaction, in case of sensitization, results in a release of allergic mediators and the development of local allergic reaction. Technique of the skin test with allergens

Prick testing has no age restrictions. Allergens, test control fluid (negative control) and 0.01% histamine solution (positive control) are applied aseptically. Skin tests are performed on the inner surface of the forearm at the distance 30 ± 10 mm from one another.

One drop (0.10 ml) of a standard water-salt allergen extract for diagnosis, the control test fluid and 0.01 % histamine solution was applied on the skin disinfected with 70˚ ethanol using a sterile plastic dropper. We pricked the skin through a drop of allergen fluid and 0.01% histamine solution against the stopper of the lancet.

The skin test results were assessed in 15 to 20 minutes (immediate reaction). The reaction was evaluated according to the pattern demonstrated in Table 1.

Table 1.

Skin test assessment pattern

Allergic reaction types	Prick testing	
	Papule size, mm	Conventional signs
Negative	0	-
Slightly positive	1-2	+
Positive	3-5	++
Strong positive	8-12	+++
Hyperergic	13 and more	++++

Skin reaction to histamine should be positive, in case of negative reaction allergen test should not be performed. Skin reaction to test control fluid should be negative, in case of positive reaction the allergen tests should be ignored [8]. Test results were analyzed by the extent of skin reaction to the specific allergen to determine the most probable allergens in case of the development or exacerbation of atopic dermatitis in children. The range of allergic reactions from (++) to (+ + + +) was considered causally significant in the etiologic spectrum of the disease.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The study implied a comparative assessment of indoor aeroallergens in etiologic spectrum of allergic rhinitis in children according to the age and sex by prick-test in the period of stable remission of the disease. We examined 304 children aged from 4 to 18 with atopic rhinitis. Table 2 demonstrates sex- and age-dependent distribution of the children. According to sex and age, the distribution is as follows

Table 2.

Distribution of patients according to sex and age

Parameter	Age (years)					
	4-8		9-12		13-18	
	M	F	M	F	M	F
	n=48		n=42		n=204	
abs.	n=30	n=18	n=20	n=42	n=82	n=112
p% ±sp%	9.9 ±1.7	5.9 ±1.3	6.6 ±1.4	13.8 ±1.99	27.0 ±2.5	36.8 ±2.7
P	P >0.05		P >0.05		P >0.05	
p% ±sp%	15.8±2.1		13.8±1.9		67.1±2.7	
p	P (4-8)/(9-12) >0.05; P (4-8)/(13-18) <0.05; P(9-12)/(13-18) >0.05					

Notes: M – males; F – females

According to the findings presented in Table 2, the number of children suffering from AR, is increasing progressively with age, especially in puberty; these results are statistically significant (P<0.05).

Table 3 shows that the allergens prevailing in the etiological range to allergic rhinitis to house dust include Dermatophagoides farina (Allergenum e pulvere domesticum e Dermatophagoides farina).

Table 4 demonstrates the prevalence of hyperergic reactions to domestic allergens in girls with AR, aged 4-8 years.

Table 5 shows the prevalence of hyperergic reactions to domestic allergens in girls with AR, aged 9-12 years.

Table 4

Allergic reaction to domestic allergens in children with AR,

aged 4 to 8 years

Sex	**Boys (n=111)**				**Girls (n=139)**			
Allergy grade	1+	2+	3+	4+	1+	2+	3+	4+
Allergens	($p\%\pm s_{p\%}$)				($p\%\pm s_{p\%}$)			
A.D. pteronissimus	6.7±4.5	16.7±6.8	3.3±3.3	0	11.1±7.4	5.6±5.6	16.7±8.7	5.6±5.6
A.D. farina	20.0±7.3	20.0±7.3	0	20.0±7.3	61.1±11.5	11.1±7.4	50.0±11.8	0
A.P. bibliothecae	10.0±5.4	16.7±6.8	0	0	11.1±7.4	5.6±5.6	16.7±8.8	5.6±5.6
A.D. Acarus siro	3.3±3.3	13.3±6.1	6.7±4.6	0	5.6±5.6	11.1±7.4	22.2±9.7	0
A.P. pulvini	3.3±3.3	13.3±6.1	3.3±3.3	0	11.1±7.4	5.6±5.6	16.7±8.8	0
A. Daphnia magna	3.3±3.3	16.7±6.8	3.3±3.3	0	5.6±5.6	11.1±7.4	22.2±9.7	0

Table 5

Allergic reaction to domestic allergens in children with AR,

aged 9 to 12 years

Sex	**Boys (n=49)**				**Girls (n=41)**			
Allergy grade	1+	2+	3+	4+	1+	2+	3+	4+
Allergens	($p\%\pm s_{p\%}$)				($p\%\pm s_{p\%}$)			
A.D. pteronissimus	10.0±6.7	10.0±6.7	0	0	9.5±4.5	2.4±2.4	11.9±4.9	4.8±3.2
A.D. farina	65.0±10.6	55.0±11.1	5.0±4.8	20.0±8.9	26.2±6.7	33.3±7.2	14.3±5.4	9.5±4.5
A.P. bibliothecae	15.0±7.9	0	5.0±4.8	0	7.1±3.9	9.5±4.5	9.5±4.5	2.4±2.4
A.D. Acarus siro	10.0±6.7	10.0±6.7	5.0±4.8	0	11.9±4.9	4.8±3.2	9.5±4.5	2.4±2.4
A.P. pulvini	5.0±4.8	5.0±4.8	0	0	7.1±3.9	11.9±4.9	7.1±3.9	2.4±2.4
A. Daphnia magna	5.0±4.8	15.0±7.9	0	0	4.8±3.3	9.5±4.5	9.5±4.5	2.4±2.4

Table 6

Allergic reaction to domestic allergens in children with AR,

aged 13 to 18 year

Sex	**Boys (n=82)**				**Girls (n=112)**			
Allergy grade	1+	2+	3+	4+	1+	2+	3+	4+
Allergens	($p\%\pm s_{p\%}$)				($p\%\pm s_{p\%}$)			
A.D. pteronissimus	20.7±4.4	6.1±2.6	3.7±2.1	1.2±1.2	6.3±2.3	15.2±3.4	6.3±2.3	1.8±1.3
A.D. farina	28.0±4.9	37.8±5.3	3.7±2.1	14.6±3.8	17.9±3.6	24.1±4.0	4.5±1.9	3.6±1.7
A.P. bibliothecae	17.1±4.1	11.0±3.4	2.4±1.6	1.2±1.2	8.9±2.6	12.5±3.1	7.1±2.4	8.9±2.6
A.D. Acarus siro	17.1±4.2	9.8±3.2	3.7±2.1	1.2±1.2	7.1±2.4	12.5±3.1	5.4±2.1	4.5±1.9
A.P. pulvini	22.0±4.5	6.1±2.6	1.2±1.2	1.2±1.2	6.3±2.3	16.1±3.4	3.6±1.7	3.6±1.7
A. Daphnia magna	12.2±3.6	7.3±2.8	7.3±2.8	4.9±2.3	7.1±2.4	9.8±2.8	8.0±2.5	5.4±2.1

As shown in the Tables, the number of children with allergic rhinitis is progressively increasing with age.

The findings of the study suggest that domestic allergens play an important role in the etiological spectrum of AR in children. Dermatophagoides farina which causes hyperergic skin reactions in children of all age groups, especially at puberty should be considered causally significant in the development of atopic rhinitis among the domestic triggers.

Assessment of the test results with the other household allergens showed the prevalence in the group of girls at puberty, aged 9-12. However, the significance of other household allergens in AR exacerbation in children aged 4-8 and boys aged 9-12 should be considered questionable.

However, there was an increased sensitivity to Daphnia magna allergens in children at preschool and early school age, especially boys aged 4-8, suggesting the cause and significance of AR at this age. Daphnia allergens are not causally significant in children at elder age (Tables 3 to 6).

4 CONCLUSIONS

1. The study showed that the causally significant allergens from house dust morbidize atopic rhinitis in children of certain age and sex.

2. The number of children with allergic rhinitis is progressively increasing with age, especially at puberty.

3. Positive reactions to Dermatophagoides farina prevail in children with allergic rhinitis.

4. These findings give a possibility to elaborate specific immunotherapy.

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PEDIATRICS

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TWO-DIMENSIONAL ECHOCARDIOGRAPHIC CHARCTERISTICS IN PREADOLESCENT ATHLETES

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Abstract: Data of echocardiographic characteristics of 59 children 10-11 years old, involved in football is presented in article. Depending on the duration of sports activities the children were divided into 3 groups: group 1 - children who play football up to 3 years (24 children), Group 2 - children who play football from 3 to 5 years (23 children), Group 3 - training duration over 5 years (12 children). It was found that the linear size of the heart was not significantly different in the groups studied, which may indicate that myocardial remodeling as cardiac adaptation to sporting loads takes more time. It was revealed that more trained children (group 3) have significantly higher left ventricular ejection fraction compared with group 1 (p = 0.05) and Group 2 (p = 0.0051).

KeyWords: athletes, children, echocardiography

INTRODUCTION

Among professional athletes the risk of sudden death is more than 2 times higher at 1.6 per 100 000 compared with 0.75 per 100 000 in the general population [1]. In the structure of the sudden death of athletes more than 50% of cases are caused by cardiovascular diseases [2]. However, in sportsmen with high achievements economic motivation may affect the decision to continue sports career, despite the presence of established and perceived by the athletes with health problems.

Whether the hypertrophy found in the hearts of athletes is physiologic or a risk factor for the progression of pathologic hypertrophy remains controversial. The diastolic and systolic functions of athletes with left ventricular (LV) hypertrophy are usually normal when measured by conventional methods [3].

However, echocardiographic findings in young athletes remain unremarkable and provoke discussion on its inclusion in screening program [4].

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2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of study was to evaluate echocardiographic parameters in pre-adolescent athletes depending on the duration of training process.

2.2 Subjects & Methods

The study involved examination of 43 boys aged 10-11 from different football teams. Weekly duration of training was 6-8 hours. Depending on the duration of football playing, children were divided into three groups:

The first group: children who play football up to 3 years, n = 24;

The second group: children who play football 3-5 years, n = 23;

The third group: children who have been playing football for more than 5 years, n = 12.

Based on the values obtained during two-dimensional echocardiography end-diastolic (EDV) and end-systolic (ESV) left ventricular volume (ml), stroke volume (SV), ejection fraction (EF), myocardial mass and left ventricular myocardial mass index were determined by formulas according to Recommendations for Quantification Methods During the Performance of Pediatric Echocardiogram [5].

Checking for Gaussian division was performed with Shapiro-Wilk or x2 Pearson criteria, which proved the use of

nonparametric methods (non-parametric U-Mann-Whitney criterion (the MW), Wilcoxon (T), Fisher criterion (F)). The difference in the results was considered statistically significant at p <0.05. During the multiple comparison ANOVA and Kraskal-Wallis tests were used, and the difference was assessed with Bonferroni correction (at p ^ = p / k, where k - the number of paired comparisons) as follows: p '= p / m -1, where m - number of groups in the experiment. Statistical analysis was performed using the statistical software "Microsoft Excel 2010", "StatSoft 7.0. for Windows".

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

Mean training experience of boys from the first group was 2.07 ± 0.7 years, second group 4.34 ± 0.5 years and third group 5.75 ± 0.3 years. Comparison of linear echocardiographic measurements was performed. The results of measurement statistical analysis are presented in Table 1.

Table 1.

Results of myocardial geometry measurements

Echocardiographic parameters	Statistical values	Observed groups		
		first n=24	second n=23	third n=12
1	2	3	4	5
LV diastolic dimension, mm	Me (Lq; Uq)	41,8 (40,5; 44,3)	41,7 (39,4; 44,2)	42,5 (42,3; 44,7)
Median Test, Overall Median = 42.1000; χ^2= 4.01; df = 2, p = 0.1346; Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =2.6029, p =0.2721				
LV systolic dimension, mm	Me (Lq; Uq)	26.4 (26.4; 27.2)	25.9 (25.1; 28.2)	25.1 (24.6; 25.8)
Median Test, Overall Median = 25.9000; χ^2= 3.83; df = 2, p = 0.1472; Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =2.5494, p =0.2795				
Interventricular septum, mm	Me (Lq; Uq)	7.95 (7.65; 8.65)	7.80 (7.12; 8.30)	7.70 (7.40; 8.22)
Median Test, Overall Median = 7.90000; χ^2=0 .18; df = 2, p =0.9126; Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =1.1067, p =0.5750				
LV posterior wall, mm	Me (Lq; Uq)	8.15 (7.53; 8.78)	8.20 (6.90; 8.50)	7.90 (7.68; 8.50)
Median Test, Overall Median = 8,00000; χ^2=0,68; df = 2, p = 0,7092; Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =1,1662, p =0,5582				

Table 1 (continuation)

1	2	3	4	5
LV mass, g	Me (Lq; Uq)	106,9 (96,8; 129,4)	102,1 (88,1; 124,6)	120,8 (110,6; 129,1)
Median Test, Overall Median = 109.067; χ^2=1.03; df = 2, p = 0.5959; Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =1.9574, p =0.3758				
LV mass index, g/m^2	Me (Lq; Uq)	87,9 (76,9; 91,8)	78,6 (72,9; 90,6)	86,1 (82,9; 90,5)
Median Test, Overall Median = 82.2549; χ^2== 2.01; df = 2, p =0.3647; Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =2.0164, p =0.3649				
Relative wall thickness	Me (Lq; Uq)	0,38 (0,35; 0,43)	0,37 (0,34; 0,39)	0,36 (0,35; 0,37)
Median Test, Overall Median = 0.375296; χ^2=0.97; df = 2, p =0.6147, Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =2.0191, p =0.3644				
Left atrium, мм	Me (Lq; Uq)	30,6 (29,0; 33,3)	27,8 (25,2; 30,6)	30,4 (28,3; 30,9)
Median Test, Overall Median = 30.0000; χ^2= 4.12; df = 2, p =0.1274, Kruskal-Wallis ANOVA by Ranks;Kruskal-Wallis test: H (2, N= 41) =4.0553, p =0.1316				
Right ventricle, mm	Me (Lq; Uq)	16.7 (16.0; 18.5)	16.3 (15.7; 18.8)	17.5 (16.7; 18.4)
Median Test, Overall Median = 16.7000; χ^2= 1.13; df = 2, p = 0.5655, Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =1.2941, p =0.5236				

Based on linear measurements, there was no statistical difference in the comparison group. However, it is known that myocardial adaptation to intensive training activity includes atrial diameter enlargement and concentric remodeling [3, 6]. Received results may indicate that duration of sport involvement for 6 years is not enough for cardiac remodeling at this age group [7].

The parameters describing main left ventricle hemodynamics characteristics, such as EDV, ESV, SV and EF fraction were calculated and compared in different groups. The obtained results are presented in Table 2.

Table 2.

Results of left ventricle function assessment

Calculations	Statistical values	Observed groups		
		first n=24	second n=23	third n=12
EDV, ml	Me (Lq; Uq)	77,5 (72,0; 89,3)	77,1 (67,4; 88,5)	80,9 (79,6; 91,0)
Median Test, Overall Median = 79.2000; x^2= 3.83; df = 2, p =0.1472 Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =2.3336, p =0.3114				

Table 2 (continuation)

ESV, ml	Me (Lq; Uq)	25.5 (21.7; 28.6)	24.4 (22.8; 30.0)	22.5 (21.4; 24.2)
Median Test, Overall Median = 24.4000; x^2= 3.83; df = 2, p =0.1472, Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =2.7245, p =0.2561				
Stroke volume, ml	Me (Lq; Uq)	53.0 (44.7; 60.3)	52.0 (47.5; 60.4)	58.5 (58.0; 69.4)
Median Test, Overall Median = 53.6000; x^2= 3.84; df = 2, p =0.1460, Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =3.8558, p =0.1455				
Ejection fraction, %	Me (Lq; Uq)	68 (63; 72)	67 (63; 70)	73 (72; 75)
Median Test, Overall Median = 68.0000; x^2= 5.69; df = 2, **p = 0.0579,** Kruskal-Wallis ANOVA by Ranks; Kruskal-Wallis test: H (2, N= 43) =7.1451, **p =0.0281**				

Multiple comparison of LV ejection fraction demonstrates that it was significantly higher in the third group as compared to the first and second groups.

The Mann-Whitney test for paired group comparison demonstrated the difference in LV EF in boys of the first and third groups, and in boys of the second and third group (p I, II = 0.5257, p I, III = 0.0500, p II, III = 0.0051). We may conclude that LVEF becomes the most valuable characteristic of myocardial function in boys ages 10-11 with an increase in "experience" training over 5 years.

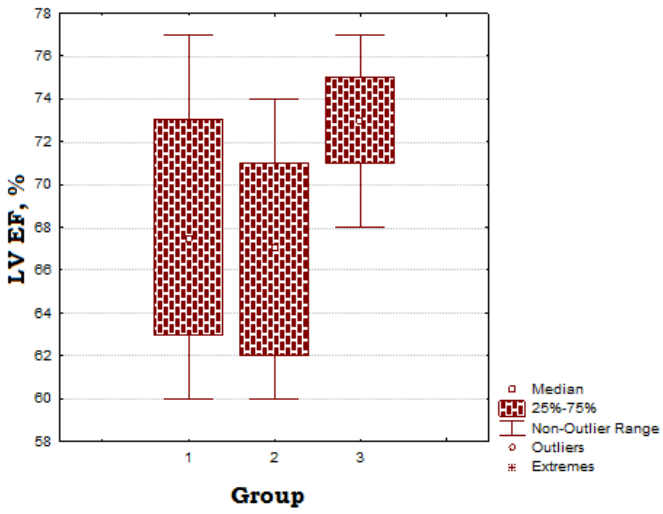

Fig 1. Left ventricle ejection fraction in boys of different training duration

4 CONCLUSIONS

1. The study did not find significant differences in morphological characteristics of the heart and great vessels with the increase of involvement in sports in the boys aged 10-11. This indicated the absence of myocardial remodeling.

2. With the increase of sports involvement over 5 years, LV EF reaches the largest value that mostly characterizes the function of left ventricular myocardium in young preadolescent athletes.

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HYGIENE

Zavgorodniy I.V., Lazarenko K.P., Chekhovskaya I.M.

DIAGNOSIS OF SCHOOL ADAPTATION IN CHILDREN WITH SPECIAL NEEDS

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Abstract: The article deals with the problem of school adaptation of elementary school pupils studying in specialized boarding schools for children with special needs and musculoskeletal disorders. The article studies special materials and methods for diagnosis of school desadaptation. The authors presented the findings of the research identifying the peculiarities of school desadaptation diagnosis.

KeyWords: children with special needs, school adaptation, specialized boarding school, elementary school children with musculoskeletal disorders.

INTRODUCTION

School is an important stage in the life of schoolchildren, because this period is characterized by reconstructions in the consciousness of the child and his emotional sphere as well as social and psychological adaptation to school conditions.

Poor health indices in schoolchildren are an urgent problem today. Many researchers regard the steady decline in the number of practically healthy children with an increase in the number of children suffering from chronic diseases and disabled children today as a national tragedy for each country.

Preservation of the health of the growing generation, improvement of physiological systems of the growing organism in the process of training and education, working out ways and means of maintaining high working capacity of pupils are some of the major challenges for modern society.

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Humanistic paradigm of modern education and upbringing poses a problem of not only all-round development of the child, but also preserving and strengthening mental health. Recently there has been a tendency to worsening of children and teenagers' mental health. School desadaptation has been shown to have a negative influence on mental health.

Deviations in the training of schoolchildren are connected with the notion of "school desadaptation ". According to scientific definition school desadaptation is the formation of inadequate mechanisms of child's adaptation to school, manifested in the form of disorders of educational activity, behavior, as well as conflict relationships with classmates and adults, an increased level of anxiety, disorders of personal development, etc. [1].

According to studies, school desadaptation syndrome occurs in 20-30% of pupils with the tendency to further increase in their number. In the early stages of school life, desadaptation, as scientists note, is observed in 40-50% of pupils. In view of the scale and subsequent negative impacts, which are particularly manifested by resistant forms of social psychological desadaptation, behavioral disorders, reaching the level of clinical and criminal severity, the urgency of psycho-hygienic diagnostics of pupils becomes obvious for detection and prevention of school desadaptation [2, 402- 413].

Researchers often consider entering the school and the first period of adaptation to its requirements as the most

dramatic events in the life of a child. The problem of younger pupil personal development is closely related to the peculiarities of his adaptation to school.

Early school desadaptation is a negative phenomenon, which prevents a complete socialization of the child, the harmonious development of a personality, prevents further progress in training, general social and psychological adaptation. Therefore, finding ways to overcome school desadaptation is an important and urgent problem for both psychologists and doctors of clinical and hygienic specialization [3,26-30,4].

Most researchers distinguish school desadaptation as an "independent phenomenon" that occurs as a result of inappropriate socio-psychological or psycho-physiological status of the child with the requirements of a new social situation; that is, a situation of school education. Erroneous assessment of the nature and causes of the difficulties encountered at the beginning of school education, belated identification of children not ready for training activities, generates more complex problems. Problems remaining in the preschool and early school age become the basis for a variety of abnormalities in the psychosocial development of the next stages of ontogeny, gtowing especially acute in adolescence when the collective effectiveness of aid is reduced [5].

The nature of school desadaptation can be represented by a variety of factors.

1. Deficiencies in preparing a child for school, social and educational neglect.

2. Somatic weakening of a child.

3. Disorder in formation of separate mental functions and cognitive processes.

4. Movement disorders.

5. Emotional disorders.

All these factors are a direct threat, especially to the intellectual development of children. Dependence of the school success on intelligence needs no evidence [6, 7,283-292].

The assessment of adaptive capabilities of the child's body is one of the most complex and important problems of modern medicine, in particular, pediatric hygiene.

Diagnostics of first-form schoolchildren's adaptation is based on the use of different methods that can reveal the level of the child's adaptation to school and build a strategy for developing and remedial work.

First-form schoolchildren's adaptation is characterized by the following major changes:

- physiological adjustment of the child's body to new loads and new regime;

- formation of the method and receiving educational process;

- change and assessment of the child's emotional sphere.

Assessment of the level of adaptation of first-form schoolchildren to school requires identification of qualitative indices of these changes [8,9].

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The object of the study was to elaborate and implement preventive measures for prophylaxis of adaptation disorders in children with disorders of the musculoskeletal system by results of hygienic diagnostics of conditions of teaching children in a specialized boarding school taking into account current technologies.

2.2 Subjects & Methods

The study was performed as part of thesis research for the degree of Candidate of Medical Sciences on the topic: "Psycho-hygienic assessment of adaptation in children with disorders of musculoskeletal system to the conditions of education in a specialized school" and involved studies of adaptation state of primary school pupils of Community Establishment "Kharkiv sanatorium educational complex No. 13" of Kharkiv Regional Council.

To evaluate the success of adaptation of first-form schoolchildren, the study also included parents as respondents to a survey, as well as group examination of the first-form schoolchildren using specially-oriented techniques.

The study of adaptation in first-form schoolchildren implied the following methods:

- Bourdon proof-reading test for measuring the indices of switching and distribution of attention with established time of fulfilment.

- A questionnaire to assess the level of school motivation. The method of assessing the level of school motivation for primary school pupils approved by the technical council of Research Institute of Pediatric Hygiene as an innovation (N.H. Luskanova, innovation No. 138 dated 7.6.1985).

-Technique "Thermometer". The technique has been elaborated by N. Fetiskin and is intended to identify emotional states "here and now". It can be used during lessons and activities. The advantage of the method is fast fixing of conditions over time. It gives a possibility to identify the degree of anxiety in first-form children associated with educational activities in relation to the subjects.

-"Sun, cloud, rain" technique. Diagnostic "Sun, cloud, rain" technique enables to determine how the child feels in different situations. Each pupil receives a sheet of paper with the sun, cloud, rain drawn in three versions. Pupils are proposed to identify their health in the classroom, at home, with friends using weather conditions. Pupils need to answer the questions and underline the condition that suits their mood.

- A questionnaire for the parents of first-form children “Adaptation of the child to school” (Bytyanova M.R.) This questionnaire is aimed at determining the level of formation of preconditions for training and adaptation of first-form children to school.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The research identified the following characteristics:

Adaptation of a child to school. Adaptation to school was found in 41% of pupils; apparent desadaptation in 54.5% of pupils; desadaptation in 5% of pupils.

The level of school motivation. A high level of school motivation, educational activity was identified in 14% of pupils. These children had cognitive motivation, a desire to carry out all school requirements in high performance.

Good school motivation was found in 23% of pupils. Such level of motivation is considered an average norm.

A positive attitude to school with participation in extracurricular activities was found in 41% of pupils. Educational reasons of these children were formed to a lesser extent, and the learning process was less attractive for them.

Low school motivation was diagnosed in 18% of pupils. These children were reluctant to go to school, preferred to miss classes, experienced serious difficulties in learning activities. They were in a state of unstable adaptation to school.

A negative attitude to school was identified in 4% of pupils. Such children experienced serious learning difficulties: they could not cope with the training activities, experienced problems in communicating with classmates and mutual relations with the teacher. These pupils were often found to have neuro-psychiatric disorders.

Bourdon proofreading test showed that the rate of switching and distribution of attention was very low in 100% of children under investigation. Concentration of attention was very high in 91% of pupils, high in 9% of pupils.

Attitude to subjects.

The following subjects caused lack of interest: physical education – in 41% of pupils; English – in 32% of pupils; music - 23% of pupils, and Russian -18% of pupils.

Anxiety was caused by the following subjects: natural science and manual labor - in 14% of pupils, mathematics, music, health foundations, drawing - in 10% of pupils.

However, most pupils (73%-85.5%) considered all subjects to be interesting.

4 CONCLUSIONS

Thus, the research showed a possibility of elaboration of hygienic recommendations aimed at improving adaptation and strengthening of general and mental health of first-form pupils of specialized boarding school for children with disorders of the musculoskeletal system.

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DENTISTRY

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MORPHOFUNCTIONAL PECULIARITIES OF TISSUE OF ORAL CAVITY IN CHRONIC RECURRENT APHTHOUS STOMATITIS WITH THERAPEUTICAL CORRECTION

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Abstract: Chronic recurrent aphthous stomatitis (CRAS) belongs to the group of chronic, inflammatory, ulcerative diseases of the oral mucosa. The aim of this study was to identify the morphofunctional peculiarities in chronic recurrent aphthous stomatitis with therapeutical correction in soft tissues of the oral cavity of experimental animals in the modeling of chronic recurrent aphthous stomatitis. We performed experimental investigation for study of the morpho-functional state of tissues of the oral mucosa in CRAS and formed three groups of animals (rabbits) with different methods of treatment. Histological investigation have been performed. Conclusion of our research is that correction of tissual changes in chronic recurrent aphthous stomatitis could be obtained with application of gel with β-carotene, α-tocopherol, a mixture of vegetable oils; with ozone therapy and their combination.

KeyWords: chronic recurrent aphthous stomatitis, histology, experiment

INTRODUCTION

Chronic recurrent aphthous stomatitis (CRAS) belongs to the group of chronic, inflammatory, ulcerative diseases of the oral mucosa. Up to now, the etiopathogenesis of this condition remains unclear; it is, however, considered to be multifactorial [1, 2].

CRAS is the most common type of inflammatory efflorescence of the oral mucosa, with a prevalence of 2% to 10% in Caucasian populations. To treat them properly, physicians should know their clinical appearance and course, conditioning factors, underlying causes, and differential diagnosis [3].

The underlying etiology is not clear, though a series of factors are known to predispose to the appearance of oral aphthae, including genetic factors, food allergens, local trauma, endocrine alterations (menstrual cycle), stress and anxiety, smoking cessation, certain chemical products and microbial agents [4, 5].

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Today, many aspects of CRAS remain unexplored and there is a necessity for further experimental studies to clarify the pathogenesis of that disease and creation of primary prevention and pathogenetically based treatment of patients suffering from CRAS including their clinical manifestations in oral cavity [6, 7].

2 PURPOSES, SUBJECTS and METHODS:

2.1 Purpose

The aim of this study was to identify the morphofunctional peculiarities in chronic recurrent aphthous stomatitis with therapeutical correction in soft tissues of the oral cavity of experimental animals in the modeling of chronic recurrent aphthous stomatitis.

2.2 Subjects & Methods

We performed experimental investigation for study of the morpho-functional state of tissues of the oral mucosa in CRAS as it had been suggested in the previously proposed and widely used scheme [8]; that allows to liminate the influence of somatic pathology and social factors. Doses of used medicine were determined

according to animal body weight. Group of 8 animals with obtained mucosal changes was our comparison group. We formed three groups of animals (rabbits) after modeling CRAS also. First group was treated with application of gel with ß-carotene, α-tocopherol ("Katomas"), a mixture of vegetable oils; second group was treated by ozone therapy with the help of apparatus "Ozonimed" (exposure of 40 seconds in each ulcer at the 9th power), third group was treated was treated with application gel "Katomas" and ozone therapy as it was described for second group. The specimens of soft tissues of the oral cavity of were stained with hematoxylin and eosin (H&E) [9] after the routine proceeding. Microspecimens were performed in the Department of Pathological Anatomy of the Kharkov Medical Academy of Postgraduate Education (head of the department Irina Yakovtsova). Morphometric studies were performed. The procedure was done strictly in compliance with the Helsinki Declaration, European Convention for the protection of vertebrate animals (18.03.1986), European Economic Society Council Directive on the Protection of Vertebrate Animals (24.11.1986).

Conflict of interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

3 RESULTS AND DISCUSSION

Ulcerative defects of round or oval shape with 5 mm diameter with the imprinting surface and covered with whitish film have had been revealed on examination of the oral mucosa group of animals with modeling CRAS (fig.1).

Fig.1. Presence of aphthous defect covered whitish film on the oral mucosa of rabbit before treatment after modeling CRAS.

Performed therapeutical correction was realized in reducing or disappearance of visible ulcerative changes in all three groups of animals.

Histological investigation of obtained microspecimens shows that CRAS process is implemented by complex of pathological changes in oral mucosa. Squamous epithelium is characterized by uneven thickness with necrotic, mainly erosive injuries (Fig. 2), but ulcers have been revealed also. Intraepithelial lymphocytes, eosinophils, signs of proliferation in the basal cellular layer, moderate development of papillomatous changes have been detected in untreated animals. Inflammatory infiltration is pronounced in lamina propria of oral cavity of animals from that group.

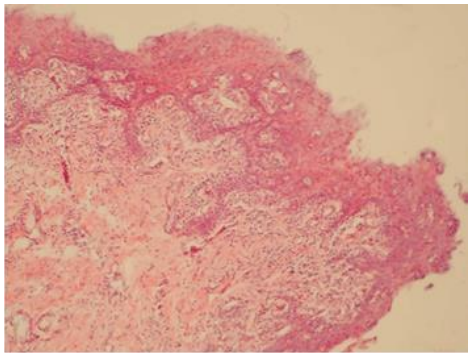

Fig.2. Pronounced focal thinning of the squamous epithelium with numeous erosion. The presence of eosinophils in inflammatory infiltrate both in the epithelium and lamina propria. Group of animals without treatment. H&E stain. Objective 10.

Examination of the oral mucosa revealed disappearance of visible pathological changes in all three investigated groups. There are no mucosal erosions, ulcers or aphthous defects in majority of experimental animals, but there are isolate no pronounced erosive changes in 2 rabbits from group which obtained treatment with gel only.

Epithelium is uniform in thickness but there are areas of no pronounced thickening (fig.3). At the same time meet its slight thickening. Superficial cells are flat, close to the spindle-shaped, the pyknosis phenomenon is not pronounced. The cytoplasm of superficial epithelial cells is represented as thin eosinophilic intensely colored rim. As approaching to basal membrane cells are increased in volume by both the nucleus and cytoplasm size. Form of cells is changed from an oval to elongate in this case with

simultaneously changing the orientation of epithelial cells and almost vertical position in the basal.

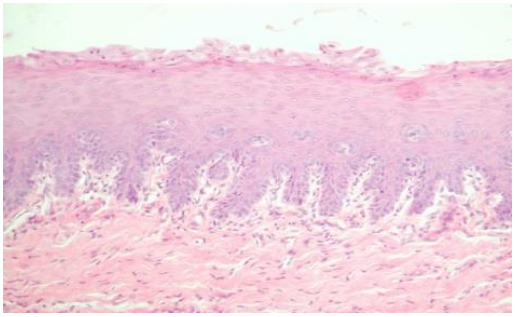

Fig.3. No pronounced necrobiotic processes in the superficial layer of the epithelium with isolate inflammatory cells. Restoration of the cellular layers of the epithelium. Moderately pronounced acanthosis. Moderately pronounced sclerosis of the papillary layer of the lamina propria. One of two rabbits with visible ulcerative changes from group which obtained treatment by gel only. H&E stain. Objective x20.

The nuclei of the basal epithelial cells well are defined, oval, uniform, hyperchromatic; cytoplasm is moderately basophilic (fig.4).

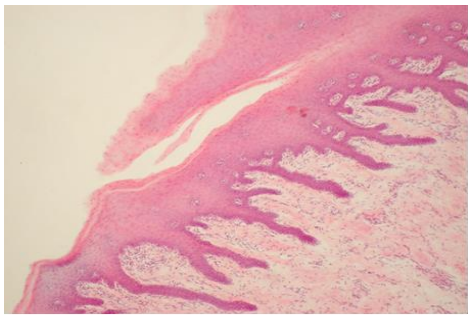

Fig.4. Well pronounced epithelialization in place of aphthous defect. Pronounced akantotic bands. Marked basophilia of basal layer. The absence of inflammatory cells in the epithelium. Group which obtained treatment by ozone therapy only. H&E stain. Objective x10.

Location of the basal cell layer is regular without "jumping" of the cells. Grouped intraepithelial lymph-leukocyte elements have been not detected. The basement membrane is uneven with non-uniform thickness. Akantotic strands of lamina propria are moderately pronounced. Superficial papillary layer of the lamina propria consists of loose connective tissue which is represented mainly elastic fibers (fig.5).

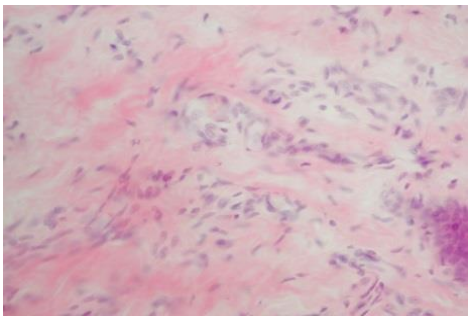

Fig.5. Superficial papillary layer of the lamina propria consists of loose connective tissue which is represented mainly elastic. Group which obtained treatment by ozone therapy only. H&E stain. Objective x40.

Reticular layer is located deeper and is represented by rough connective tissue fibers. Cellular consist of gingival mucous membrane is presented in the table 1.

Table 1.

Cellular consist (%) of gingival mucous membrane

	Comparison group (mod-eling CRAS)	Group 1* (gel)	Group 2* (ozone therapy)	Group 3* (ozone therapy and gel)
Histiocytes	4,62±0,21	31,12±3,03	32,21±2,42	39,26±2,15
Young fibroblasts	17,02±1,20	14,53±0,64	13,47±1,42	8,24±0,54
Fibrocytes	19,91±1,42	26,48±1,13	27,42±1,43	35,19±1,67
Lymphocytes	4,68±0,25	7,42±0,75	6,84±0,63	5,14±0,27
Plasma cells	4,83±0,24	6,01±0,11	4,31±0,67	3,01±0,04
Macrophages	4,72±0,38	3,68±0,42	6,02±0,42	4,17±0,33
Neutrophils	38,30±2,46	7,62±0,47	6,34±0,63	3,28±0,42
Eosinophils	5,49±0,23	2,59±0,52	3,22±0,05	1,19±0,03

*Each component of the study groups was significantly different from that in the control group ($p<0,05$ compared to the untreated animals)

Cellular elements located between connective tissue fibers (fibroblasts, histiocytes, lymphocytes, mast cells, macrophages) are isolated. Fibroblasts are presented by mature cells in papillary and reticular layers predominate. Lymphoid elements are scattered between the connective tissue fibers uniformly, without the formation of focal accumulations. Eosinophils are absent; signs of accumulation of inflammatory exudate have been not detected.

Changes which obtained as result of our treatment could be recognized as positive changes [10 ,11] with healing of injured areas.

4 CONCLUSIONS

Correction of tissual changes in chronic recurrent aphthous stomatitis could be obtained with application of gel with ß-carotene, α-tocopherol, a mixture of vegetable oils; with ozone therapy and their combination.

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