ISSN 2409-9988

Inter Collegas

Experientia docet

2016

N2(3)

INTER COLLEGAS

2016

Vol. 3 No.2

OFFICIAL JOURNAL OF
KHARKIV NATIONAL MEDICAL UNIVERSITY
ISSN 2409-9988

Recommended for publishing
by Scientific Council of Kharkiv National Medical University

16-June- 2016

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

Periodicity:
4 times a year

INTER COLLEGAS, VOL. 3, No. 2 (2016)
ISSN 2409-9988

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Novikov D.O.

HISTORICAL MODELS AND LEGAL REGULATION OF HEALTH CARE PRACTICE IN KIEVAN RUS

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Abstract: The article examines historical models and specific of legal regulation of labor in health care field in Kievan Rus. The author identifies three historical models of medicine in Kievan Rus: pagan, secular and monastery. It is noted that norms of Rus Justice and Izbornik of Svyatoslav fall into the legal regulation of labour in secular medicine; Church Charter of Prince Volodymyr the Great – the legal regulation of labour in monastic medicine; ethical norms of customary law – the legal regulation of labour in pagan medicine.

KeyWords: Kievan Rus, pagan medicine, monastery medicine, secular medicine, legal regulation, customary law

INTRODUCTION

Legal regulation of health care practice in Ukraine has its own genesis. The development of health care and various health care constituents stems from the time of national statehood formation among the Eastern Slavic tribes in the ninth century. First physicians in Kievan Rus distributed medical knowledge and skills, formed the foundations of deontological rules of conduct and professional duties which made government take on the obligation to provide health care services to the population. A historic research on basic strategic characteristics of legal state impact on health care practice considering the reforms being launched in the field of the present health care system is therefore regarded as a priority.

Conflict of interests

There is no conflict of interests.

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2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of the study was to investigate the historical models and legal regulation of health care practice in Kievan Rus.

3 RESULTS AND DISCUSSION

According to the literature on the history of medicine, the assessment of national health care service formation should be made on the basis of the following scientific hypotheses: 1) humanity has always been affected by diseases, requiring treatment; 2) the territory of present Ukraine has been inhabited since ancient times and was the cradle of Indo-European civilization, and therefore was the source of their medical and pharmaceutical knowledge; 3) there are no grounds to believe that the people who inhabited the territory of modern Ukraine, lived in isolation and evolved separately from the development of world civilization and medicine in particular [1, p. 436].

Ukrainian health care history originates from the formation of a written language on the national territory, i.e. Kievan Rus, from the moment those who took care of the patients' health, namely various healers, shamans,

magicians, quacks who cured not only the body but also (or primarily) the soul, fending off "evil spirits", taking off "magic spell" etc., started to prepare medicinal agents [2, p. 11]. Various cults and beliefs developed much later than the primitive medicine, thus the annalistic references concerning the magicians, diviners, healers, sorcerers provide evidence supporting the existence of health care services long before the development of the written language [3, p. 19]. Thus, these services are of the same age as a primitive man [4, p. 9].

Consequently, medical service in Kievan Rus was mediated by the natural process of labour division, necessitating elaboration of a population-wide health care system.

Historical literature draws generalizing conclusion on the existence of three types of Kievan Rus health care: 1) ancient or pagan; 2) monastery; 3) city secular health care [5].

Ancient health care in Kievan Rus was based on traditional pagan medicine, which empirically accepted rational therapies. Pagan medicine preserved many traces of those times. Pagan medicine is characterized by many common archaic methods and approaches acquired over the period of centuries of experience imparting knowledge by oral communication from generation to generation. Pagan medicine is the experience rich in the number of rational means received over the ages. In pagan medicine, as in the domestic daily life in general, nothing was used or brought into service without a cause [6, p. 254].

In early period of Kievan Rus pagan medicine "experts" had some knowledge and skills to manage patients with infections, described and tried to identify and treat lupus, itching, inflammation of the thoracic membrane and joints, bronchial and cardiac asthma, jaundice, typhus, plague, anthrax, epilepsy, nerve paralysis, etc. with the traditional methods. This treatment was provided by magicians, cutters, wizards and quacks [7, p. 301]. In various areas of Kievan Rus most popular pagan doctors were quacks, prymivnyks, bayilnyks. A quack treated with potions, prymivnyk with the power of words, when a quack was powerless to help. Quacks were multiskilled, i.e. they provided treatment of all diseases; however there were those who specialized in the treatment of certain diseases. Rational and irrational aspects were combined not only in pagan practice, but also in traditional therapies, views on diseases and their causes.

With the spread of Christianity, the church and state engaged in the attempts to eradicate quackery and sorcery. In particular, the Prince Volodymyr Church Charter "On ecclesiastical courts" (995) [9], zeleynytstvo, a type of quackery, was referred to as a crime against faith. Quacks and sorcerers were identified as servants of the devil. Nevertheless, in terms of traditional therapies the attitude was ambiguous; they had their supporters and defenders even among the contemporary elite, including Prince Gleb who supported sorcerers [8, p. 18].

Paragraph 38 of the Prince Yaroslav Church Charter "On ecclesiastical courts" mentions the following: "If the wife is a sorcerer, enchantress or quack the husband has to execute her" [10, p. 39]. This norm provides two points: first, the additional confirmation of the government's direction towards eradication of pagan medicine; second, the evidence supporting the fact that female physicians were also engaged in providing treatment. It should be noted that women were granted the official right to work in the field of medicine only in the middle of the nineteenth century [11, p. 13]. Besides these norms of criminal law, no legal document of Kievan Rus mentions provisions for folk medicine practice. Such activities were obviously regulated by moral and ethical norms of customary law.

Fig. 1. Pagan medicine.
F. Zhuravlyov. "Quack" (1870)

Alternatively, the practice of monastic and secular physicians required legal regulation.

A monastic hospital became a new form of medical care and an important step in the development of medical knowledge [12, p. 201]. Having acquired a certain level the monastic medicine necessitated regulation. It was performed by the Prince Volodymyr the Great Church Charter which included norms on hospitals and physicians [13, p. 145]. According to the Church Charter, hospitals were referred to as church institutions, and most of the lichets were considered to be churchmen who obeyed the bishop [14, p. 43]. The definition lichets originated as a specification of a particular activity of quackery with transition from pagan medicine under the patronage of monastic medicine and narrowing of specialization of using therapeutic methods and tools, adapting them to the new philosophy of life [15, p. 32]. Thus, first legal reference of lichets was emphasized by the Church Charter.

One of the greatest orthodox literature landmarks "Kievan Cave Patericon" includes basic information on monks-doctors and organization of their work. A chapter of this landmark The life of Theodosius Pechersky mentions a special place given to hospitals, which were separated by a fence from other buildings. Pimen's life story, who lived in a separate monastic cell, proves that monasteries had special hospital beds [5, p. 69]. Kievan Cave Patericon also lists the monks-doctors' duties. Monks-doctors looked after patients and performed menial jobs, having good bedside manner and not caring for personal enrichment [16, p. 23].

The author of Kievan Cave Patericon proclaims modesty to be the best quality of the doctor. All doctors of Kievan Cave monastery were accessible, vanity was unknown to them. Doctors had to be free of any opinion aimed at enrichment owing to their practice (famous monk-doctor Agapit ordered to give all the money to the poor and churches and refused to take fees) [17, p. 58]. Thus, Christian humility, renunciation of worldly fame and wealth was emphasized among the high moral qualities of monks-doctors.

Thus, Kievan Cave Patericon developed the concept of treatment as a spiritual ministry. The ability to treat people was interpreted as a gift of God, which opens to righteous by their spiritual exploit. Accordingly, the treatment was perceived primarily as an integral part of the service of the God. Gratuity and inability to pay for treatment is regarded in relation to the treatment as the gift of God. Monk-doctor Agapit said: "...I do not take money for healing because healing power is not mine, but Christ's" [15, p. 33]. So monks-doctors performed medical care free of charge.

Fig.2. Monastic medicine.
Monastic bed. Miniature from manuscript "Life of Antoniy Siyskiy" (1648).

Apart from monks-doctors health care in medieval Kievan Rus was provided by numerous secular, professional lichets who studied the basics of their profession through apprenticeship, often in families of hereditary healers. They mainly specialized in general practice, e.g. kamchuzhni (treatment of body pains, currently referred to as rheumatism), ochni (treatment of eye diseases), chepuchynni (treatment of syphilis), those who treated "bedevilment" (ancestors of modern neuropsychiatrists) and others [18]. For instance, these "doctors" were mentioned in the annals of seventeenth century "Posthumous miracles of St. Nicholas the Wonderworker".

Some of these lichets were permanent residents of cities, including the princely court lichets, and rambling lichets, as indeed in other countries of medieval Europe [19, p. 41].

Izbornik of Svyatoslav (1076) named the first professional duties of secular lichets. It indicated that lichets should be able to provide surgical care (be able to cut the skin, amputate limbs, causticize wounds, treat suppuration [20, p. 15].

Unlike monks, who did not leave their monastery, secular lichets treated the patients in their homes and unlike monks treated on a fee for service basis. Izbornik of Svyatoslav (1076) notes the following about the fees for secular lichets: "If lichets is needed, he should be brought to the sick and be given payment for treatment".

Rus Justice greatly contributed to the regulation of ancient treatment and social relations in the field of medical practice, despite the relatively small number of articles relating to the regulation of medicine. First of all, it is necessary to note the fact of referencing lichets engaged in treatment. Secondly, the norms of Rus Justice contain the provision about charged nature of health care in secular medicine [21, p. 7]. Paragraph XIII of Rus Justice named About sword notes the following: "If the person was wounded with a sword but did not die, one hryvna should be paid for wound care". From this text it is clear that "wound care" was administered by a professional who received a certain payment, probably not less than one hryvna.

Thus, the relationship of health care services provided by secular doctors had civil law nature and differed from the monastic medicine which was considered to be the monks' commitment. In this context it should be noted that at this stage in Kievan Rus the ecclesiastic law was the main source of legal regulation of labour in health care.

Fig.3. Secular medicine.
In lichets' residence. Manuscript. XIV century.

Regarding the right to provide health care services in Kievan Rus we must note that the norms of the Church Charter, Rus Justice and Izbornik of Svyatoslav and Kievan Cave Patericon do not contain special requirements for medical practice. Social and professional status of doctors in Kievan Rus entirely depended on the will of the rulers and their opinion on health care activities, which continuously underwent changes [16, p. 24].

4 CONCLUSIONS

Social and legal status of health care professionals in Kievan Rus underwent separation within the processes of labour division and manifestation of particular importance of public health in the life and development of the society. As for the types of Kievan Rus medicine (pagan, monastery and secular) it should be noted that norms of Rus Justice and Izbornik of Svyatoslav deal with legal regulation of secular medicine; the Prince Volodymyr the Great Church Charter provides legal regulation of monastic medicine and ethical norms of customary law cover legal regulation of pagan medicine. It is worth emphasizing that fundamental characteristics of legal regulation of health care services in Kievan Rus may be used in the context of the current health care reform for the formation of its basic principles and specific areas of implementation.

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Received: 01-May. – 2016
Accepted: 29-May. - 2016

INTER COLLEGAS, VOL. 3, No. 2 (2016)
ISSN 2409-9988

PHARMACOLOGY

Smirnov A.S.

THE IMPACT OF EPICHLOROHYDRIN, ECHINACEA PURPUREA EXTRACT AND THIOTRIAZOLINE ON THE PYLORIC GLANDS OF THE STOMACH IN RATS

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Abstract: The study involving white male rats was performed to assess the pattern of epichlorohydrin action on the pyloric gland of the stomach and evaluate the possibility of Echinacea purpurea extract and thiotriazoline administration for the correction of changes developing in the pyloric glands. Prolonged epichlorohydrin inhalation was shown to trigger a decrease in the length of the pyloric glands in rats. A decrease in the length of glands occurred within thirty days after discontinuation of inhalation. Echinacea purpurea extract and thiotriazoline administration in rats not exposed to epichlorohydrin was accompanied by an increase in the length of the pyloric glands, which persisted after discontinuation of administration of each agent. Echinacea purpurea extract and thiotriazoline administration secondary to epichlorohydrin inhalation reduced the degree and duration of the effect of a decrease in the length of the pyloric glands caused by epichlorohydrin. Thiotriazoline was shown to have a more significant corrective action.

KeyWords: stomach, pyloric glands, epichlorohydrin, Echinacea purpurea extract, thiotriazoline

INTRODUCTION

The state of the gastric mucosa depends on various environmental factors such as temperature, hypoxia, vibration, electromagnetic radiation and some other [2, 4, 6, 10]. A significant amount of various substances which are man-made pollutants enters the human body. As a result of exposure the changes occur in the stomach, triggering the development of diseases [1, 9]. Epichlorohydrin is one of such substances. The products manufactured on the basis of epichlorohydrin include paints, varnishes, adhesives, synthetic fibers, ion exchange resins, epoxy resins, rubbers. Due to its volatility epichlorohydrin is capable of polluting the air and entering the body, producing a negative impact on human health [3, 7, 8]. Epichlorohydrin is known to be able to influence the state of the gastric mucosa [5]. However, the features of action of epichlorohydrin on the pyloric glands are not investigated. Contemporary scientific literature offers no data on the possibility of using antioxidants and adaptogens to correct changes occurring in the pyloric glands.

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2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of the study was to study characteristics of epichlorohydrin action on the pyloric gland of the stomach, to evaluate the possibility of using Echinacea purpurea extract and Thiotriazoline to correct the changes in pyloric glands.

2.2 Subjects

The trial involved albino outbred sexually mature adult male rats. The rats were divided into six experimental groups with thirty rats in each group. Group I rats constituted the control group. Group II rats were administered epichlorohydrin in a dose of 10 MPC (10 mg/kg) by inhalation for two months, five days a week for five hours a day. Group III rats were given Echinacea purpurea extract in a dose of 200 mg per kg of the body weight through a gastric tube for two months, five days per week. Group IV rats were administered thiotriazoline in a dose of 117.4 mg per kg of the body weight as an injection of 2.5% solution

intraperitoneally for two months, five days a week. Group V rats were exposed to epichlorohydrin and Echinacea purpurea extract, and Group VI rats were exposed to epichlorohydrin and thiotriazoline according to the above described procedure.

2.3 Methods

After two-month administration of epichlorohydrin, Echinacea purpurea extract and thiotriazoline, under chloroform anesthesia, six rats from each experimental group were taken out of the experiment on the first, seventh, fifteenth, thirtieth and sixtieth day. The stomach was fixed in 10% solution of neutral formalin. Histological processing was performed according to the standard method by dehydration in ethanol solution followed by alcohol extraction with xylene. The specimens were set in paraffin. In order to study the gastric wall, its cross sections obtained on sliding microtome were stained with hematoxylin and eosin by Van Gieson method. Microscopy was carried out by a laboratory Micros microscope MC 100 series (Austria). The height of the pyloric gastric glands of rats was determined using Microvisible software. Excel program was used for the statistical analysis of the results. Significance of differences was assessed by Mann-Whitney U test. The differences were considered significant at $p<0.05$.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The length of the pyloric glands of the stomach in rats after inhalation of epichlorohydrin decreased compared to the same indicator in intact rats of the control group on the first day by 32.6% ($p<0.01$), 31.6% ($p<0.01$) on the seventh day, 26.1% ($p<0.01$) on the fifteenth day of, and by 10.5% ($p<0.01$) on the thirtieth day. Temporar dynamics of changes was found in the length of the pyloric glands in rats of the experimental group undergoing epichlorohydrin administration. It was manifested by a gradual increase in this indicator by 49.2% ($p<.01$) from the first day to the sixtieth day of the study (Table 1).

On the first and on the seventh day after the cessation of Echinacea purpurea extract administration the length of the pyloric glands of the stomach in rats was greater than the length in intact rats of the control group by 13.4% ($p<0.01$) and 15.0% ($p<0.01$), respectively. The comparison of this indicator value in rats treated with Echinacea purpurea extract in different periods of observation revealed a decrease in the length of the pyloric glands by 10.9% ($p<0.05$) in the period from the first to the sixtieth day (Table 1).

The length of the pyloric glands of the stomach in rats after thiotriazoline administration in comparison with the length of the pyloric glands in intact rats of the control group was more on the seventh day by 4.9% ($p<0.05$), by 11.9% ($p<0.01$) on the fifteenth day, by 5.6% ($p<0.05$) on the thirtieth day, by 5.0% ($p<0.05$) on the sixtieth day. The length of pyloric glands in rats treated with thiotriazoline was increasing in the period from the seventh to the fifteenth day by 9.9% ($p<0.01$), but the differences in this indicator in the period from the first to the sixtieth day were not statistically significant ($p>0.05$) (Table 1).

Table 1.

The length of the pyloric glands of the stomach in rats (M±MSD, μm)

Day of observation	No of rats per group	Gp1	Gp2	Gp3	Gp4	Gp5	Gp6
1	n = 6	231.57 ±13.50	156.18 ±12.04 *	262.64 ±10.67 *	241.89 ±10.65	204.54 ±8.77* #	217.79 ±10.23 #
7	n = 6	226.82 ±10.70	155.21 ±10.17 *	260.92 ±14.38 *	237.93 ±11.13 *	210.27 ±18.81 *#	208.21 ±9.78* #
15	n = 6	233.33 ±12.37	172.33 ±9.11*	243.01 ±12.68	261.16 ±13.17 *x	219.26 ±13.75 #	237.71 ±10.82 #
30	n = 6	237.64 ±6.93x	212.59 ±12.74 *	243.87 ±8.03	250.98 ±8.82*	247.67 ±8.35* #x	240.48 ±8.98#
60	n = 6	233.35 ±11.63	233.06 ±10.44 x	233.89 ±10.42 x	244.91 ±11.74 *	234.62 ±11.55 x	237.80 ±9.85x

Notes:
* - $p<0.05$ as compared to the indices in rats of the control group;
# - $p<0.05$ as compared to the indices in rats undergoing epichlorohydrin inhalation;
x - $p<0.05$ as compared to the indices in rats of the same experimental group at different periods of observation.

The length of the pyloric glands of the stomach in rats following epichlorohydrin inhalation and Echinacea purpurea extract administration was reduced on the first day by 11.7% ($p<0.01$), by 7.3% ($p<0.05$) on the seventh day, but increased on the thirtieth day by 4.2% ($p<0.05$) in relation to the length of the pyloric glands in intact rats of the control group.

In comparison with the length of the pyloric glands in rats undergoing epichlorohydrin inhalation, the length of pyloric glands in rats treated with epichlorohydrin and Echinacea purpurea extract was increased on the first, seventh, fifteenth, and thirtieth day by 31.0% ($p<0.01$), 35.3% ($p<0.01$), 27.2% ($p<0.01$), and by 16.5% ($p<0.01$), respectively. Following the cessation of epichlorohydrin inhalation and Echinacea purpurea extract administration, the experimental group was found to have changes in the length of the pyloric glands. In the period from the first day to the thirtieth day this indicator value increased by 21.1% ($p<0.01$), whereas in the period from the thirtieth day to the sixtieth day it decreased by 5.3% ($p<0.05$) (Table 1).

The length of pyloric glands in rats after discontinuation of inhaled epichlorohydrin and thiotriazoline administration compared with length of pyloric glands in intact rats of the control group was lower on the seventh day by 8.2% ($p<0.05$). In conditions created after the action of epichlorohydrin and thiotriazoline this indicator was higher than in rats undergoing epichlorohydrin inhalation, by 39.4% ($p<0.01$) on the first day, by 34.1% ($p<0.01$) on the seventh day, by 37.0% ($p<0.01$) on the fifteenth day, and by 13.1% ($p<0.01$) on the thirtieth day. In the period from the first day to the sixtieth day of the study the length of the pyloric glands in the experimental group of rats treated with epichlorohydrin and thiotriazoline increased by 9.2% ($p<0.05$).

Scientific data obtained in the study is consistent with the results of earlier trials [5] and give a possibility to demonstrate that epichlorohydrin causes the development of changes in the gastric mucosa.

4 CONCLUSIONS

1. Long-term inhalation of epichlorohydrin triggers a reduction in the length of the pyloric gastric glands in rats. Reduction in the length of glands occurs within thirty days after discontinuation of inhalation.

2. Echinacea purpurea extract administration in rats not exposed to epichlorohydrin was accompanied by an increase in the length of the pyloric glands which persisted for seven days after discontinuation of extract administration.

3. Thiotriazoline causes an increase in the length of the pyloric glands in rats not exposed to epichlorohydrin which was observed from the seventh to the sixtieth day after the agent administration.

4. Echinacea purpurea extract and thiotriazoline administration secondary to epichlorohydrin inhalation reduces the degree and duration of the effect of reduction in the length of the pyloric glands caused by epich-?orohydrin. Thiotriazoline was found to have a more significant corrective action.

Prospects for further research. Continued studies of patterns in epichlorohydrin action on the gastric mucosa and its structural components can provide additional scientific information on the mechanisms of changes facilitating the elaboration of experimental basis for the informed choice of the ways to develop effective methods for the correction of changes triggered by the exposure to epichlorohydrin and other xenobiotics.

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Received: 13-May. – 2016
Accepted: 20-May. - 2016

INTER COLLEGAS, VOL. 3, No. 2 (2016)
ISSN 2409-9988

NEUROLOGY

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THE PECULIARITIES OF LIPID METABOLISM AND ENDOTHELIAL DYSFUNCTION IN YOUNG PATIENTS WITH SPONDYLOGENIC VERTEBROBASILAR INSUFFICIENCY

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Abstract: To determine consistent patterns of changes of lipid metabolism and condition of an endothelium in patients of young age with the spondylogenic vertebrobasilar insufficiency we examined 98 patients (women - 56, men - 42) with manifestations of SVBI on the background of neurovascular and radicular syndromes of osteochondrosis of cervical vertebral column. Patients, age 18 to 40 years (middle age of 28.5±3.8 years) were included in this study. All study subjects underwent functional X-ray examination, cervical spine MRI and duplex scanning of neck vessels for verification diagnosis. The dynamics of blood flow indices in suboccipital (VA3) segments of vertebral and basilar arteries (BA) by dopplerography were calculated. The received data of correlation analysis confirmed the assumption of interrelation between lipid metabolism and state of an endothelium in patients with SVBI, having revealed positive correlation between the TCh level and endothelin-1 level ($r = + 0.58$; $p \leq 0.05$), with the same index in control group ($r = + 0.28$; $p \leq 0.05$). The negative correlation dependence between S-NO and LDL ($r = - 0.1$, $p \leq 0.05$) in patient's group was detected, in control group – ($r = - 0.02$, $p \leq 0.05$). Revealed in the examined patients reliable ($p \leq 0.05$) positive correlation between the LDL level and TCh ($r = +0.89$) against positive correlation between the HDL level and TCh ($r = +0.52$) shows the sanogenetical activation of reserves in the young contingent patients and strengthening of development of an anti-atherogenous reserve. The received correlation showed that lipid metabolism plays a significant role in the promotion of endothelium dysfunction.

KeyWords: lipid metabolism, endothelial dysfunction, spondylogenic vertebra-basilar insufficiency

INTRODUCTION

Vertebrobasilar insufficiency (VBI) is a broad classification describing the condition characterized by an insufficient supply of blood via the vertebral and/or basilar arteries to the brain [14].

Blood is delivered to the brain via the carotid and vertebral arteries. The vertebral arteries are located at the back of the neck and merge at the base of the brain to form the basilar artery. The vertebral and basilar arteries supply blood to several structures in the brain including the occipital cortex, the brainstem consisting of the midbrain, pons and medulla, the cerebellum and the thalamus. As a result of decreased blood flow, the symptoms vary and are often broadly referred to as VBI or vertebral basilar ischemia.

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The symptoms can include vertigo (dizziness), visual disturbances (blurring, graying, double vision), drop attack (sudden falls), numbness or tingling and slurred or lost speech. Since the portions of the brain most typically impacted are responsible for movement and balance, symptoms of VBI can often result in falls [7]. More significantly, patients with VBI are at increased risk for transient ischemic attack (TIA) and stroke. Treatable VBI may be underdiagnosed in comparison to carotid disease. Patients with vertebrobasilar ischemia do represent a significant cohort of patients. Twenty-five percent of all transient ischemic attacks and ischemic strokes involve areas of the brain supplied by the vertebrobasilar circulation. For patients who experience vertebrobasilar transient ischemic attacks, disease identified in the vertebral arteries portends a 30-35% risk for stroke over a 5-year period. Medical refractory disease of the vertebrobasilar system carries a 5-11% risk of stroke or death at 1 year. Consequently, mortality associated with a posterior circulation stroke is high,

ranging from 20-30% and this disease entity should not be ignored [5,7].

Transient ischemic symptoms referable to the posterior vascular systems are quite variable, which is consonant with the many functional systems packed into the relatively small structure of the brain stem and posterior portions of the hemispheres. These symptoms may be precipitated by rotation and hyperextension of the cervical spine which may result in temporary occlusion of the vertebral artery followed by relative ischemia at the base of the brain. This syndrome commonly presents with a combination of cerebrovascular arteriosclerosis and cervical spondylosis as fundamental clinicopathological components. [1,7]. In young patients (under 45 years) spondylogenic mechanism of VBI is more apparent, therefore the so called spondylogenic vertebrobasilar insufficiency (SVBI) is of exceptional interest.

Biochemical changes developing in patients are essential for understanding and early diagnosing of vertebrobasilar ischemia.

Interactions between blood lipid metabolism and the state of endothelium are of considerable scientific and practical interest. That is because development of endothelial dysfunction (DE) plays an essential role in vascular disorders progression.

When functioning, the endothelium involves production of biologically active agents ensuring maintenance of the vessels tone and anatomic structure, facilitating the processes of blood clot formation, regulating local inflammation [6,19]. DE can result in angiospasm, thrombi formation and adhesion of leukocytes to the endothelium. Ischemia and tissue hypoxia, hypertension, hyperglycemia, endogenous and exogenous intoxications, action of cytokines, lipid metabolism disorder, other local and general influences which strengthen death of endotheliocytes promote endothelium dysfunction and cause their defective regeneration [3,15,18].

At the same time, lipid metabolism disorders play one of the leading roles in the development of vascular complications in patients with SVBI [5,7,8,10,12,14,20]. Increased level of low density lipoproteins promotes formation of the final products of proteins oxidation and atherogenous modification of LDL also possessing cytotoxicity towards endothelial cells. Besides, hypercholesterolemia depresses formation of nitrogen oxide (NO), main vasodilatator [3,4,11,16]. The oxidized LDL promotes formation of adhesion molecules, increases smooth muscles proliferation and causes thromboses. Additionally, oxidized LDL stimulates synthesis of vasoconstrictors (endothelin-1, prostacyclin 12) and suppresses the activity of vasodilatators (serotonin, bradykinin) [1]. All the above mentioned factors contribute to endothelium dysfunction and subsequent brain blood dyscirculation [2,13].

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of the study was to determine consistent patterns of changes in lipid metabolism and endothelium condition in young patients with SVBI.

2.2 Subjects

The study involved examination of 98 young patients, of them 56 women and 42 men, with signs of SVBI secondary to neurovascular and radicular syndromes of cervical osteochondrosis of the vertebral column. The study comprised patients aged 18 to 40 (middle age of 28.5±3.8 years).

2.3 Methods

All the patients underwent ultrasonic dopplerography and transcranial dopplerography of cerebral vessels with functional loading tests (head rotations) to assess spondylogenic influence on vertebral arteries. The study implied evaluation of blood flow dynamics indices in suboccipital (VA3) segments of vertebral and basilar arteries (BA) on head rotation. Velocity was estimated initially in the patients' prone position with the head's neutral position, then on the maximum rightwards rotation, and after that on maximum leftwards rotation. Reactivity ratio on head rotation (RR, %) was calculated by the following formula:

$RR = (Vr / Vn - 1)*100$

Vr – Velocity in VA (BA) in the prone position

Vn - Velocity in VA (BA) in the head's neutral position

Duplex color-coded ultrasonography was used for the exclusion of atherosclerotic changes in the arteries. All study subjects underwent functional X-ray examination of the cervical vertebral column with bending and extension, cervical spine MRI, ultrasonography of the neck and head vessels with functional probes of rotation of the head, and duplex scanning of the neck vessels using the device Echo-cardiograf-320 (Moscow, Russia). Parameters of serum lipid metabolism were determined by spectrophotometry. The levels of total cholesterol (TCh), triglycerides (Tg) and high density lipoproteins (HDL), very low density lipoproteins (VLDL) and low density lipoproteins (LDL) indices were estimated by Friedewald's method (Friedewald, 1972) recalculation. The study also involved calculation of atherogenic coefficient (CoA). Endothelin-1 concentration in blood serum was evaluated by immunoenzyme assay. The control group consisted of 30 gender- and age-matched healthy subjects. The obtained values were analyzed by the Student t-test. The difference was considered statistically significant at P≤ 0.05 [9].

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

Doppler research showed reduction of blood velocity by 32.9% in posterior cerebral artery (PCA), by 23.1% in vertebral artery (VA) and by 23.4% in basilar artery (BA) as compared to corresponding indices in the control group. It also determined signs of vascular tone increase in the vertebobasilar system according to the level of index pulsatility (PL) and resistance index (RL) [17] (table 1).

The change in linear velocity according to the degree of head rotation was significantly higher in patients with VBI. The group was found to have variations in the number of Vr changing cases by 30 % and more (P < 0.05).

Significant differences were detected during functional loading tests (head rotations) by defined reactivity ratio on rotational probe (RR). The study showed that the RR for BA in patients with SVBN was higher when compared to the control (31.0±12.2 % vs. 6.5±2.5 %) (p≤0.05),

Table 1

Hemodynamic indices of blood supply in intra- and extracranial vessels (M±m)

Vessel	Linear velocity of blood flow (sm/s)		PL, conv.units		RL, conv.units	
	SVBI	Control	SVBI	Control	SVBI	Control
ICA right	58.1± 1.95*	53.2± 6.4	1.06± 0.02*	0.85± 0.21	0.58± 0.02*	0.55± 0.16
ICA left	51.1± 1.96*	51.9± 5.9	0.95± 0.06*	0.83± 0.19	0.55± 0.06*	0.53± 0.15
MCA right	53.5± 5.7*	62.4± 11.3	0.86± 0.10*	0.56± 0.14	0.52± 0.15*	0.50± 0.10
MCA left	57.2± 6.2*	65.2± 10.7	0.82± 0.13*	0.57± 0.14	0.50± 0.13*	0.51± 0.09
ACA right	43.1± 2.3*	46.2± 6.8	0.82± 0.11*	0.85± 0.16	0.48± 0.11*	0.50± 0.19
ACA left	41.8± 2.19*	44.5± 7.1	0.83± 0.12*	0.83± 0.14	0.51± 0.09*	0.49± 0.12
PCA right	30.1± 1.8*	34.2± 6.9	0.89± 0.13*	0.86± 0.17	0.55± 0.06*	0.54± 0.17
PCA left	31.6± 1.67*	37.1± 5.3	0.87± 0.12*	0.85± 0.18	0.56± 0.04*	0.53± 0.15
VA right	28.9± 1.98*	37.6± 7.8	2.39± 0.15*	0.78± 0.11	0.94± 0.08*	0.52± 0.08
VA left	29.3± 2.1*	38.1± 8.7	1.01± 0.07*	0.74± 0.10	0.59± 0.02*	0.52± 0.07
BA	35.2± 2.52*	46.0± 5.6	0.82± 0.06*	0.54± 0.19	0.51± 0.02*	0.56± 0.09

Notes: * - The difference was more significant (p≤0.05) when compared between the study and control groups

the same direction was detected while analyzing RR for VA (23.4±8.2 % vs. 5.1±2.2 %) (p≤0.05). Hemodynamic changes detected in the study confirmed spondylogenic influence on patients under investigation. The analysis of lipid metabolism indices in patients with SVBN revealed the disorder of transport system of lipids in all the values (Table 2).

Table 2

Lipid metabolism indices in patients with spondylogenic vertebrobasilar insufficiency and healthy donors (M ± m)

INDICATOR	Study group (n=98)	Controls (n=30)
TCh (μmol/l)	5.68±0.94*	3.51±0.08
Tg (μmol/l)	0.94±0.3	0.78±0.06
VLDL (μmol/l)	0.42±0.14	0.26±1.04
LDL (μmol/l)	3.7±0.77*	2.02±0.07
HDL (μmol/l)	1.53±0.25*	1.14±0.03
CoA	2.76±0.59	2.14±0.09

Notes: * - The difference was more significant (p≤0.05) when com-

pared between the study and control groups

It was confirmed by a significant increase in TCh levels in the study group (5.68±0.94 μmol/l vs. 3.51±0.08 μmol/l). The Tg level was slightly increased as compared to the control (0.94±0.3 μmol/l vs. 0.78±0.06 μmol/l). The VLDL level was also increased in patients of the study group as compared to the control group indices (3.7±0.77 μmol/l vs. 2.02±0.07 μmol/l).

The assessment of anti-atherogenous reserve in patients under investigation showed a compensatory increase in the body defenses in terms of HDL level (1.53±0.25 μmol/l vs 1.14±0.03) ($p \leq 0.05$). Thus, a 1.3-fold increase in CoA reflected the balance of atherogenous and anti-atherogenous fractions retention in blood as evidenced by the overstrain of the body defenses, an increase in atherogenous potential of blood and, therefore, an increased risk of atherosclerosis development in the examined patients.

Moreover, the study determined an increase in the concentration of endothelin-1 as a marker of serum endothelium functional state in the study group (2.84±0.09 fentamol/ml vs. 1.25±0.08 fentamol/ml) ($p \leq 0.05$) and a decrease in S-NO level (0.18±0.07 μmol/l vs. 0.45±0.02 μmol/l). These changes confirmed vasoconstriction shift in endothelial vasoregulation.

Correlation analysis confirmed an interrelation between lipid metabolism and endothelium state in patients with SVBI, having revealed a positive correlation between TCh level and endothelin-1 ($r = + 0.58$; $p \leq 0.05$), with the same index in the control group ($r = + 0.28$; $p \leq 0.05$). The study group was found to have a negative correlation dependence between S-NO and LDL ($r = - 0.1$, $p \leq 0.05$), with ($r = - 0.02$, $p \leq 0.05$) in the control group. A significant ($p \leq 0.05$) positive correlation between LDL level and TCh ($r = +0.89$) revealed in the examined patients against a positive correlation between the HDL level and TCh ($r = +0.52$) showed a sanogenetical activation of reserves in young patients and an intensification of the anti-atherogenous reserve.

4 CONCLUSIONS

1. Development of SVBI is accompanied by lipid metabolism changes characterized by multidirectional shifts of TCh, LDL and HDL levels, confirmed by an increase in plasma indices of lipid system towards atherogenesis.

2. Endothelial dysfunction in these patients is characterized by an increased endothelin-1 concentration, being a factor of vasoconstriction opposite to a reduction of an active metabolite of nitrogen oxide – S-NO, possessing vasodilatation properties.

3. The received correlation showed that lipid metabolism plays a significant role in the promotion of endothelium dysfunction.

ACKNOWLEDGEMENTS:

We thank all volunteers who participated in this study. The wholehearted support of clinicians, nurses and lab personnel who contributed their effort made this study possible. Our gratitude is expressed to many experts in neurology field who kindly shared with us their opinions and critiques prior to and after this study was completed.

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Received: 18-May. – 2016
Accepted: 29-May. - 2016

INTER COLLEGAS, VOL. 3, No. 2 (2016)
ISSN 2409-9988

PEDIATRICS

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FAMILIAL HYPERCHOLESTEROLAEMIA IN PEDIATRIC PRACTICE: CURRENT GUIDELINES & CLINICAL CASE

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Abstract: High risk for the population health due to hypercholesterolemia demands routine screening for the children from hyperlipidaemic parents and/or with acute cardiovascular events in family history. The article provides current European Atherosclerosis Society guidelines concerning diagnosis and management of patients with familial hypercholesterolaemia. A case of familial hypercholesterolaemia in a five-year-old girl is presented. Phenotypic presentation together with lipids and genetic analysis are common for the problem diagnosed.

KeyWords: children, familial hypercholesterolaemia, cardiovascular risk

INTRODUCTION

Coronary heart disease (CHD) is one of the leading causes of premature death of adults [1]. Despite the extremely rare clinical presentation of CHD in children and adolescents, Framingham Heart Study shows that high relative risk at a young age will likely be transformed into high absolute risk later in life [2].

In 2006, as soon as risk factors and risk behaviors that accelerate the development of atherosclerosis began in childhood, the Director of the National Heart, Lung, and Blood Institute (NHLBI), Dr. Elizabeth Nabel, appointed an Expert Panel to develop cardiovascular (CV) health guidelines for pediatric care providers. The final report of Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents was published in 2012 [3]. High population coronary risk is also linked to the fact of underdiagnosis and undertreatment of familial hypercholesterolaemia [4].

Familial hypercholesterolaemia (FH) was recognized as a common genetic cause of CHD. FH in vast majority of cases is an autosomal dominant disorder.

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FH is most often caused by mutations in the LDLR gene, resulting in absent or dysfunctional receptors on the surface of hepatocytes, identifying the liver as the principal site of LDL catabolism. More than 1700 mutations in the LDLR gene on chromosome 19 have been identified, of which 79% are probably expressed as a hyper-?holesterolaemic phenotype [5]. Defects in the genes encoding apolipoprotein B (APOB) and proprotein convertase subtilisin/kexin type 9 (PCSK9) account for 5% and 0,1% of FH cases, respectively. The LDL receptor adaptor protein (LDLRAP1) gene is a very rare recessive form of FH [6].

However, 5–30% of cases of phenotypic FH may arise from mutations in unidentified genes, or have a polygenic cause [7]. All of the monogenic defects result in reduced efficiency of LDL uptake and clearance in hepatocytes and increased circulating total cholesterol and LDL-C concentration. Many individuals considered homozygous have two different genetic defects related to LDLR (i.e. compound HeFH), with mutations in APOB or PCSK9 genes, as well as an LDLR mutation [8].Both homozygous and heterozygous FH result in markedly reduced hepatic capacity to clear atherogenic cholesterol-rich low density lipoproteins (LDLs) from the circulation, with consequent accumulation of LDL cholesterol (LDL-C)

[9]. Circulating LDL penetrate and then accumulate in the artery wall, become oxidatively modified, and subsequently initiate an inflammatory response, which results in vascular injury and formation of atherosclerotic plaque [10]. Additional alterations in the lipoprotein profile in FH may involve elevated levels of lipoprotein(a) [Lp(a)] and triglyceride-rich lipoprotein remnants, together with low levels of dysfunctional high-density lipoproteins (HDLs), which collectively may contribute to accelerated atherosclerosis and CHD [11].

The calculation of risks during elaborating Risk Scores shows that every 0.25 mmol/L (10 mg/dL) increment in non-HDL-C is associated with an increase in atherosclerotic burden equivalent to 1 year of aging [12].

At the same time just children with FH display a variety of changes reflecting both the lipid and the inflammatory arm of atherosclerosis, as well as early atherosclerotic development [13].

Familial hypercholesterolaemia is diagnosed either on phenotypic criteria, involving an elevated LDL-C level plus a family history of elevated LDL-C, premature CHD, and/or genetic diagnosis, or with genetic testing. As soon as the clinical presentation in childhood is rare, the systematic screening strategies are recommended [14].

Diagnosis of familial hypercholesterolaemia in children and adolescents [15]

- Family history of premature CHD + high LDL-C levels are the two key selective screening criteria
- Cholesterol testing should be used to make a phenotypic diagnosis.
- An LDL-C level ≥ 5 mmol/L (190 mg/dL) on two successive occasions after 3 months diet indicates a high probability of FH.
- A family history of premature CHD in close relative(s) and/or baseline high cholesterol in one parent, together with an LDL-C ≥ 4 mmol/L (160 mg/dL) indicates a high probability of FH. If the parent has a genetic diagnosis, an LDL-C ≥3.5 mmol/L (130 mg/dL) suggests FH in the child.
- Secondary causes of hypercholesterolaemia should be ruled out.
- DNA testing establishes the diagnosis. If a pathogenic LDLR mutation is identified in a first-degree relative, children may also be genetically tested.
- If a parent died from CHD, a child even with moderate hypercholesterolaemia should be tested genetically for FH and inherited elevation in Lp (a).

Clinical management of FH in children and adolescents (by European Atherosclerosis Society Consensus Panel [15])

- Early identification of children with FH ensures that adherence with lifestyle intervention is already established before puberty.
- Children with HeFH should be treated with a fat-modified, heart-healthy diet at diagnosis, and begin statins at age 8–10 years.
- In HeFH, pharmacologic treatment should start at diagnosis: statins are the cornerstone of FH management; in the case of homozygous FH combination with ezetimibe must be started at diagnosis and , if available, lipoprotein apheresis should be started as soon as technically possible.
- Early initiation of lifestyle is essential for ensuring long-term adherence.
- Children diagnosed with FH should have lipoprotein(a) [Lp(a)] measured for risk stratification.
- Boys and girls should start treatment at similar ages.
- For children aged 8–10 years, the Panel recommends that LDL-C is ideally reduced by 50% from pre-

treatment levels.

- For children aged ≥10 years, especially if there are additional cardiovascular risk factors, including elevated Lp (a), the target LDL-C should be 3.5 mmol/L (130 mg/dL).
- The benefits of LDL-C reduction should be balanced against the long-term risk of treatment side effects.
- Adherence should be checked if HeFH children fail to achieve LDL-C targets with combination lipid-lowering treatment. If patients are non-adherent, consider referral to a dedicated, multidisciplinary clinic.
- Children with HeFH should be referred to and cared for at a specialised centre.

As soon as early diagnosis of FH and treatment this category of children is under the priority from the point of potential ongoing early atherosclerosis in young adults, we providing case history of the pediatric patient with FH.

CASE STUDY

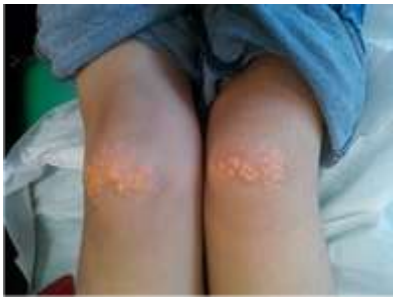
Presentation & medical history:

Otherwise healthy 5 y.o. middle-east origin girl attended the clinic for the assessment due to hyperlipidemia in the siblings. The only complaint is the presence of skin problems on both of her elbows and both knees.

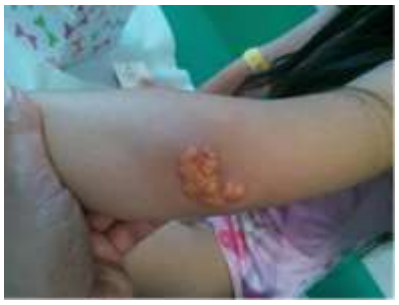
Her parents are known to be affected by hyperlipidaemia a swell as 4 of their 5 children. Her elder brother (21 y.o) suffers from severe hyperlipidemia and had the same skin problems in childhood and has been taking antihyperlipidemic medication together with lipid apheresis for years.

Physical examination:

- Height – 101 cm, weight – 18,75 kg, BMI = 18,67 kg/m2 (body composition – asthenic, adipose tissue distribution – normal)
- HENT – normal;
- Eyes – circumferential extent of arcus in the peripheral cornea is detected (arcus corneae)
- Lungs – normal
- Cardiovascular system – normal
- Abdomen – normal
- Musculoskeletal system – normal
- CNS - normal
- Lymph nodes – normal
- Skin – regular color, no problems with nails and hair. On the extension surface of both elbows and knees the multiple yellowish papulae were found. No underlying lesions. No pain or itching. Typical presentation of Xanthomas (fig.1).



(a)



(b)

Figure 1. Xanthomas on the skin of knees (a) and elbows (b) in a 5 y.o. girl

Laboratory data are pesented in Table 1.

Table 1.

Laboratory data of patient with FH

Parameter	*UNIT*	*RESULT*
CALCIUM total	MMOL/L	2,5
PHOSPHORUS INORGANIC	MMOL/L	1.67
SODIUM	MMOL/L	138
POTASSIUM	MMOL/L	4,95
CHLORIDE	MMOL/L	102
CHOLESTEROL TOTAL	MG/DL	> 650
TG	MG/DL	206
HDL-Cholesterol	MG/DL	22
LDL-Cholesterol	MG/DL	very high (out of measure)
ALAT	U/L	22
ASAT	U/L	29
GGT	U/L	<10
ALKALINE PHOSPHATASE	U/L	143
CHOLINESTERASE	kU/L	7.0
LIPASE	U/L	69
ALPHA-AMYLASE	U/L	79
BILIRUBIN, TOTAL	MG/DL	0.98
PROTEIN, TOTAL SERUM	G/L	71
ALBUMIN	G/L	44
GLUCOSE	MG/DL	97
CREATININE ENZ, SER	MMOL/L	0.45
Apolopoprotein A1	MG/DL	61
Apolopoprotein B	MG/DL	> 400

- Cardiac ultrasound: normal
- Duplexsonography of carotid vessels: A.carotis communis intima-media thickness (IMT) dextra = 0,38; sinistra = 0,32 mm – normal. A. carotis interna, A. carotis externa, A. vertebralis – normal structure and speed of blood flow

Genetics:

LDLR: E12: c.1729T>C, p. Trp577Arg (FH Marburg) homozygous

Clinical diagnosis: Homozygous familial hypercholesterolemia (LDLR - mutation)

Genetics of family members:

- Mother, Father, 1 brother, 1 sister - LDLR: E12: c.1729T>C, p. Trp577Arg heterozygous
- 1 brother - LDLR: E12: c.1729T>C, p. Trp577Arg homozygous (the similar course of disease, takes statins + lomitapide together with lipid apheresis)
- 1 brother – no mutations detected

Final diagnosis: E78.0 – Familial hypercholesterolemia (Pure hypercholesterolemia)

Diet: heart-healthy, fat-modified - 30% of calories from total fat, 7% of calories from saturated fat, and 200 mg of cholesterol/day

Medication: Patient takes treatment by simvastatin (current dosage 30 mg) in combination with ezetimibe 10 mg. Because the therapy does not completely improve the lipid profile in the patient, the procedure of lipoprotein apheresis should be started as soon as technically possible.

4 CONCLUSIONS

The discussed above clinical case demonstrates strong necessity of examination of the children from families with dyslipidaemia. Presentation seen is the common one for the patients with familial hypercholestherolemia as well as the form of genetic mutation.

High risk for the population health due to hypercholesterolemia demands routine screening for the children from hyperlipidaemic parents and/or with acute cardiovascular events in family history.

CONFLICT OF INTERESTS

There is no conflict of interests.

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Received: 01-Apr. – 2016
Accepted: 20-May. - 2016

PEDIATRICS

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THE FEATURES OF NUTRITIONAL STATUS IN CHILDREN WITH BRONCHOPULMONARY DYSPLASIA

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Abstract: The features of nutritional status of children with bronchopulmonary dysplasia were analyzed based on the analysis of anthropometric data and laboratory findings. The children with bronchopulmonary dysplasia were shown to have significantly lower physical development indices than healthy ones. Dependence between blood serum hypoproteinemia and pathological changes in the coprogram of children with bronchopulmonary dysplasia was revealed, which should be taken into account during clinical management of this group of children.

KeyWords: bronchopulmonary dysplasia, nutritional status, physical development, children.

INTRODUCTION

The Concept of the State Program «Healthy Child for 2008-2017» notes that the health of children is a priority for the Ukrainian state policy and modern society [1]. However, despite the rapid introduction of new technologies in neonatology, neonatal mortality rates in Ukraine have not diminished [2, 3]. An increase in the proportion of preterm birth is observed in many countries secondary to demographic crisis and deterioration of reproductive and somatic health [4]. This in turn emphasizes the need for a thorough research from the perspective of evidence-based medicine and implementation of the results in health care establishments providing medical care for children from the group of high risk of death or forming a stable combined organic pathology of various organs and systems [4, 5]. Therefore, reducing infant mortality is one of the most important tasks for Ukrainian pediatrics [6]. Of the causes of death of children under 1 year of age, 70% depend on maternal health and access to and quality of health care for women during pregnancy, childbirth and children in the neonatal period [7].

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Main problems occurring in children in the neonatal period include hypoxia, respiratory disorders, hypothermia, intraventricular hemorrhage, sepsis, intrauterine infections and others. These conditions result in overstrain of immature non-specific adaptive mechanisms, which was described in 1936 by Hans Selie [3]. Despite the increase in the absolute number of children surviving in intensive care units for newborns over the recent decades, nearly 50% of preterm infants are at risk of chronic disease and disability [8].

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of the study was to study characteristics of epichlorohydrin action on the pyloric gland of the stomach, to evaluate the possibility of using Echinacea purpurea extract and Thiotriazoline to correct the changes in pyloric glands.

2.2 Subjects

The study involved 83 children aged from 1 month to 3 years with bronchopulmonary dysplasia. BPD diagnosis was made according to the International Classification of Diseases, 10th revision. Informed consent was signed by the parents prior to the study.

2.3 Methods

Evaluation of physical development was carried out using centile graphs [20]. The comparison group included 20 age-matched children who were born prematurely, but later did not have clinical and radiological signs of BPD and any chronic disease.

Statistical analysis was performed using statistical package «EXCELL FOR WINDOWS» and «STATISTICA 7.0. FOR WINDOWS» [21]. Depending on the chosen statistical model both parametric and non-parametric methods were used to test the hypotheses of the work. For samples of distribution that did not comply with Gaussian law, median (Me) and interquartile scope (Lq - lower quartile; Uq - upper quartile) were determined. To compare dispersions, Fisher's criterion (F) was used, comparing sample particles, the method of angular transformation with F-test assessment was used. To determine the association between quality characteristics, Pearson x2 test (Fisher's exact test in the case of 2x2 tables) was used. The results were considered statistically significant at $p < 0.05$.

Conflict of interests
There is no conflict of interests.

3 RESULTS AND DISCUSSION

Age- and sex-dependent distribution of the examined children is presented in Table 1.

Table 1.
Age- and sex-dependent distribution of the examined children

Indicator	Distribution feature	Children with BPD (n=83)		Controls (n=20)	
		N	%	N	
Gender	Males	50	60.2	12	60.0
	Females	33	39.8	8	40.0
Age	1 mo – 11mo 29 d	60	72.3	14	70.0
	1 mo – 11mo 29 d	15	18.1	4	20.0
	2 yr – 2 yr 11 mo 29 d	8	9.6	2	10.0

Among the examined children of the main group boys prevailed in the number (60.2±5.4% and 39.8±5.4%, respectively; F = 7.01, p<0.01). Group age-dependent patterns in children with BPD agreed with the relevant general trends among the investigated children, namely boys prevailed among the children both of the first year of life (K = 1.72) and aged 2 - 3 years (K = 1.66). This predominance of boys in the group of investigated children corresponds to the literature, according to which bronchopulmonary dysplasia is more common in boys and can be considered one of the unmodified risk factors of bronchopulmonary dysplasia [10, 22].

The study of the age ratio in the investigated groups shows that bronchopulmonary dysplasia was most likely under 1 year of life (72.3±4.9%; F = 35.43, p <0.001). Reduction of the relative number of patients with the age is due to the fact that the clinical manifestations of the disease regress during the growth of the child [10, 22].

Indicators of physical development of children with bronchopulmonary dysplasia are important in assessment of both the severity and prognosis of the disease. The analysis of anthropometric indices revealed that 89.2±3.4% of children with BPD had disharmonious physical development (F = 134.8; p<0.001). Of them, 60.2±5.4% of children (overwhelming majority, F=20.7; p<0.001) had disharmonious physical development due to low or very low body weight; in 3.6 ± 2.1% due to great body length. The physical development of the controls was regarded as harmonic mean in the majority of children (90.0 ± 6.8%). and only in two children as disharmonious due to low body weight (Table 2).

In our opinion, delayed weight gain or growth in children with bronchopulmonary dysplasia may result from low basic growth potential in the neonatal period, which is caused by energy deficiency against a background of mechanical ventilation, higher expenditure for minute pulmonary ventilation, higher metabolism level, prolonged chronic respiratory failure, which is supported by many authors [9, 18, 23-25].

The changes in the physical development of children with BPD do not contradict the known literature data on

slow weight gain, requiring increased caloric intake (140-150 kcal/kg) with sufficient protein content (3.0-3.5 g/kg) [10, 11, 12].

Table 2.

Physical development of children from the both groups

Assessment of physical development	Children with BPD (n=83)		Controls (n=20)		Difference
	N	p %±sp%	N	p %±sp%	
Harmonic	9	10.8±3.4	18	90.0±6.8	F=53.9; p<0.001
Disharmonious:	74	89.2±3.4	2	10.0±6.9	F=53.9; p<0.001
- below average in weight and height	21	25.3±4.8	0	0	F=17.9; p<0.001
- low in weight	50	60.2±5.4	2	10.0±6.9	F=20.7; p<0.001
- tall	3	3.6±2.1	0	0	F=2.35; p>0.05

Objective examination of the digestive system demonstrated in the vast majority of children with BPD (97.6±1.6%; F=263.3, p<0.001) hepatomegaly and in 9 (10.8±3.4%) children splenomegaly. These changes can be related to compensation reaction of the organism to chronic inflammation of the respiratory system. Fifteen (18.1±4.2%) children had predisposition to constipation, most probably of central origin.

Diagnostic measures in children with BPD revealed certain changes in the laboratory findings. The changes in coprogram were detected in the majority of children, i.e. 71 (85.5 ± 3.9%; F = 103.5, p <0.001), of them 45.8% demonstrated undigested or digested fiber, 22.9 % steatorrhea, 21.7% amylorrhea, 9.6% creatorrhea. These changes may be associated with decreased enzyme-secreting function of the gastrointestinal tract in children born prematurely indicating a lack of absorption function of the gastrointestinal mucosa, which adversely affects a child's development.

According to the literature [26, 27], the patients with bronchopulmonary pathology demonstrate activation of lipid peroxidation processes, which leads to increased levels of cholesterol, ß-lipoprotein and is accompanied by decrease in antioxidant activity. In our study 11 (13.3 ± 3.7%) children had marked increase in ß-lipoprotein (62.0 (59.0; 68.0) c. u.), 2 (2.4±1. 6%) children increased cholesterol level (7.6 (7.5; 7.7) mmol/l). Fifteen (18.1±4.2%) children had reduction in ß-lipoprotein level (28.0 (23.0. 29.0) c.u.) and 14 (16.9±4.1 %) patients increased cholesterol level (2.545 (2.4; 2.7) mmol/l). The increase in alkaline phosphatase (8400.0 (7600.0. 11000.0) nmol/s*l) was noted in 15 (18.1±4.2%) children. Increased transaminases level was observed in 8 (9.6±3.2%) children, alanine aminotrasferase (0.810 (0.69; 1.04) mmol/l·h) and aspartate aminotransferase (0.910 (0.560; 1.25) mmol/l·h) being equally increased. These children were conducted investigation for markers of hepatitis B, C, namely HBsAg. HBcAg. HCV. All results were negative, which allowed to exclude the presence of viral hepatitis. In our opinion, these changes in transferase activity can be explained by the reaction of the liver to chronic inflammation of the bronchopulmonary system.

Changes in proteinogram were noticed in 37 (44.6±5.4%) children with bronchopulmonary dysplasia. Of them hypoproteinemia was observed in 28.9±5.0% of children, dysproteinemia in 22.9±4.6% of patients. These changes in children with BPD can be interpreted as the body's response to inflammation or nutritional disorders due to failure in intake of main ingredients or disorders in absorption and digestion functions of the gastrointestinal mucosa.

To clarify these issues tetrachoric indicator was used to analyze the relationship between qualitative criteria: presence or absence of hypoproteinemia and pathological changes in coprogram (amylorrhea, steatorrhea, creatorrhea) in children with BPD (Table 3). The above calculations led to the conclusion that the level of protein in the serum of children with BPD depends on the digestive function of the gastrointestinal tract (x2 =4.08; p=0.043), disorders of which may be inherent to preterm infants due to immaturity of enzyme systems the gastrointestinal tract

[18, 24, 25]. These factors are not directly associated with the disease, but can significantly enhance severity of its course and sequellae. All this leads to functional load to all organs and systems.

Table 3.

Characteristics of association between hypoproteinemia and abnormal coprogram changes in children with BPD

Feature	Children with BPD (n=49)		χ^2	p
	Group 1 n=6 abs.	Group 2 n=43 abs.		
Reduced protein level	1	26	4.08	0. 043
Blood protein level within the norm	5	17		

Note. x2 - Pearson criterion to evaluate statistical significance of Pearson coefficient of association; p - level of statistical significance.

If adverse internal or external factors are present, this may result in repeated episodes of the disease exacerbation and development of complications. These findings should be considered when conducting examination, treatment and rehabilitation of this group of patients.

4 CONCLUSIONS

1. The vast majority of children with bronchopulmonary dysplasia (F=20.7; p<0.001) were characterized by disharmonious physical development due to low or very low body weight, which requires increased calorie intake with sufficient protein content.

2. Blood serum protein level of children with bronchopulmonary dysplasia depends on the digestive function of the gastrointestinal tract, the disorders of which are inherent in preterm infants due to immaturity of the enzyme system of the gastrointestinal tract.

3. Solution of a multifactorial problem of improving the quality of life of children with bronchopulmonary dysplasia is promising, which is possible only if a comprehensive rehabilitation program including organization of early detection and correction of various disorders in postnatal adaptation of preterm infants is created.

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Received: 21-Apr. – 2016
Accepted: 23-May. - 2016

INTER COLLEGAS, VOL. 3, No. 2 (2016)
ISSN 2409-9988

PEDIATRICS

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THE ROLE OF MONOCYTE CHEMOATTRACTANT PROTEIN 1 IN IMMUNE RESPONSE FORMATION IN CHILDREN WITH HEMORRHAGIC VASCULITIS

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Abstract: The goal of the investigation is to define the role of monocyte chemoattractant protein 1 in immune response formation in children with hemorrhagic vasculitis. The study included 60 patients with hemorrhagic vasculitis at the age of 1 to 18 years. To achieve the target goal of the investigation we analyzed MCP-1 concentration in blood serum and studied cellular and humoral component of immune system and phagocytosis. Increased levels of MCP-1 and cellular component of immune system indices levels show that this chemoattractive agent takes part in T-lymphocyte and natural killer cells involvement into inflammation lesion. Present inverse correlation relationships of MCP-1 levels and phagocytic activity may indicate compensation abilities decrease whereas in the presence of humoral component of immune system underactivity the synthesis of MPC-1 increases for the purpose of macrophages involvement into inflammation lesion and depletion process compensation. Resulting data indicate direct involvement of MPC-1 into hemorrhagic vasculitis immunopathogenesis as immunodefence activation marker or as a possible trigger of pathologic process activation.

KeyWords: children, hemorrhagic vasculitis, monocyte chemoattractant protein 1, immunity.

INTRODUCTION

Hemorrhagic vasculitis is a part of widespread vasculitis and represents generalizable immune complex microthrombovasculitis [1, 2, and 3]. In spite of the spectrum of known in modern times etiologic factors the diagnostics of hemorrhagic vasculitis occurs to be inadequately timed and identification of provoking factor succeeds not in all cases. Since pathogenesis of hemorrhagic vasculitis is not completely known active involvement of immune system into pathologic process occurs. Currently most of investigators conceive that in the presence of vasculitis several immune and perhaps non-immune pathogenic mechanisms simultaneously play role in the development of vascular damage [4].

Over the past decade, studies showed that one of the principal molecular markers of vasculature endothelium damage was the monocyte chemoattractant protein 1 (MCP-1) [5].

MCP-1 is produced by several cells including monocytes, T-lymphocytes, fibroblasts, vessel endotheliocytes, epithelial and smooth muscle cells of bronchi [6]. MCP-1 is effective chemoattractant for monocytes, activated CD4 and CD8 T-lymphocytes binding with them through CCR2 receptor. As a result of binding, cells draw toward focus of inflammation. Besides MCP-1 can induce integrin expression required for chemotaxis [7, 8]. MCP-1 is not only chemoattractant that provides migration and extravasation of mononuclear cells into inflammation focus but also is a mediator of inflammation at the same time activating resident cells. Consequently, involvement of above-mentioned pathological mechanisms in hemorrhagic vasculitis pathogenesis appears to be possible taking into account immune complex nature of disease that belongs to systemic diseases and develops pathologic process in endothelium.

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2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

To define the role of monocyte chemoattractant protein 1 in immune response formation in children with hemorrhagic vasculitis.

2.2 Subjects

Study included 77 children of 1 to 18 years old. 60 patients with hemorrhagic vasculitis (25 girls and 35 boys) who received medical treatment at Communal Health Protection Institution "Kharkiv Municipal Children's Hospital No.16". Control group included 17 apparently healthy children of similar sex and age. Diagnosis of disease was verified and determined with the help of commonly accepted clinical laboratory and instrumental findings according to protocol of Ministry of Health Care of Ukraine No. 676 of 12.10.2006 "Clinical protocol of delivery of healthcare to patients with Henoch-Schonlein syndrome (hemorrhagic vasculitis, Henoch-Schonlein purpura) (HSP)".

2.3 Methods

The activity rate of pathologic process and severity of disease course were measured according to such parameters as clinical evidence and laboratory method data of investigation i.e. leukocyte level in peripheral blood, ESR, indicators of acute phase of inflammation (seromucoids, glycoproteins), and gamma-globulins.

To achieve the target goal of the investigation we analyzed MCP-1 concentration in blood serum with the help of immunoenzymatic set for quantitative test of human MCP-1 Bender MedSystems GmbH (Austria) and studied cellular and humoral component of immune system and phagocytosis. Identification of T- and B-lymphocytes subpopulations (CD3, CD4, CD8, CD16, CD22) in absolute and relative value using the method of their identification with the help of diagnostic agent "НВЛ Гранум" (Ukraine), blood serum Ig A, Ig M and Ig G levels using method of G.Mancini (1965) with the help of Federal State Unitary Enterprise SPA "Microgen" (The Ministry of Healthcare of The Russian Federation, Russia), circulating immune complex (CIC) using method of V. Haskova et al. in modification of Yu.A.Grynevich and A.N.Alfyorov (1978), phagocytosis indices (phagocytizing neutrophils, phagocytic number and neutrophil index activity) according to ability of polymorphonucleocytes and monocytes of peripheral blood to bind on their surface, absorb and digest microbial testing culture, NST-test according to Stuart (1975) in modification of B.S. Nagoev (1983). We calculated mean cytochemical coefficient of myeloperoxidase content in neutrophils according to the Graham-Knoll's method and mean cytochemical coefficient of lysosomal cationic protein content according to M.G. Shubich method (D.V.Belokrynytskiy, 1987). Using statistical programs „EXCELL FOR WINDOWS" and „STATISTICA 7.0. FOR WINDOWS" received data underwent statistical processing. For samples other than Gaussian sample we calculated median (Me) and interquartile range (Lq – low quartile; Uq – up quartile). By comparison of values that involved comparison of more than 2 points, we used H criterion of Kruskal-Wallis dispersion analysis (KW). Level of significance was identified taking into account Bonferonni adjustment. To analyze statistical significance of differences between two independent groups we used nonparametric U-test of Mann-Whitney (MW). Analysis of indices range connection was performed according to Spearman rank correlation method (r). Results had statistical significance when $p < 0.05$.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

Classification of children by sex in total number of patients did not show statistical significant difference: 35 boys (58.3%), 25 girls (41.7%). Analysis of age peculiarities of children from main group showed that 29 children (48.3±6.42%) got into the group of 1-6 year old patients, 23 children (38.3±6.2%) got into the group of preschool age and only 8 patients (13.3±4.3%) got into the group of puberty. Now, therefore, 86.6±4.3% (p=0.003) of children suffer from hemorrhagic vasculitis at the age under 12 that indicates significant "youthification" of this pathology.

Study showed that 30 (50±6.4%) patients from main group had allergic disposition of the body, that is 11 (18.3±4.9%) children had gastrointestinal allergy, 5 (8.3±3.5%) children had medicamentous allergy, and 14 (23.3±5.4%) children had combined allergy.

Frequent acute respiratory diseases (4 and more times a year) occurred in 44 (73.3±5.7%) children, chronic center of nasal infection occurred in 27 (45±6.4%) children, frequent inflammatory airway disease occurred in 6 (10±3.8%) patients and persistent herpetic infection occurred in 8 (13.3±4.3%) children.

While investigating nasal structure of examined children we found that dermic form of the disease occurred in 8 (13.3±4.3%) patients, dermic-articular form of the disease occurred in 24 (40±10%) patients, 19 (31.6±6%) patients had combined form of hemorrhagic vasculitis and 9 (15±4.6%) children had combined form of the disease with renal syndrome. 40 (66.6±6.2%) children were registered with acute course of the disease, 3 (5±2.8%) children had chronic course of the disease and 17 (28.3±5.8%) had recidivating course of hemorrhagic vasculitis. Taking into account severity of the course and activity rate of pathologic process all children were divided into following groups: 1st group included patients with mild disease or I degree of activity (n=19), 2nd group included children with moderate course of the disease or II degree of hemorrhagic vasculitis activity (n=22) and 3rd group included children with severe course of disease or III degree of activity (n=19). T-lymphocytes content in blood in children with I degree of pathologic process activity significantly did not differ from values in control group. Children with II degree of activity were registered with increase of total count of absolute and relative T-lymphocytes number (2.50 (2.20; 3.20) *109/L, 73 (68; 80) %) versus values in control group. In addition, we detected increase of correlation index of T-helpers and T-suppressors at the cost of increase of the former and decrease of the latter ones versus values in control group. The level of natural killer cells was twice higher than data levels in control group.

In children with III degree of hemorrhagic vasculitis activity, we detected similar changes of T-cellular component but more expressive. CD8 function decrease provides prevalence of stimulating effect of T-helpers as well as B-lymphocytes that produce antibodies (Table 1).

Table 1.

Values of the cellular component of immune system according to degree of hemorrhagic vasculitis activity in children in acute episode of disease (Me (Lq; Uq)).

Value	Degree of activity			Control group (n=17)
	I (n=19)	II (n=22)	III (n=19)	
CD_3 (T total), $*10^9$/L	1.60 (1.56;1.68)	2.50 (2.20; 3.20)*	5.70 (4.00; 6.90)*	1.60 (1.40; 1.80)
%	67 (65; 68)	73 (68; 80)	79 (76; 80)*	69 (65; 72)
CD_4 (T helper), $*10^9$/L	0.90 (0.90; 1.00)	1.75 (1.50; 2.00)*	3.90 (3.20; 4.50)*	0.90 (0.80; 1.00)
%	36 (34; 40)	37 (36; 39)	53 (51; 60)*	37 (35; 40)
CD_8 (T count), $*10^9$/L	0.75 (0.65; 0.75)	0.75 (0.70; 0.80)	1.70 (1.00; 2.00)*	0.74 (0.70; 0.80)
%	32 (30; 34)	26 (22; 30)	27 (24; 30)	30 (27; 32)
CD_4/ CD_8	1.28 (1.20; 1.53)	2.31 (1.50; 2.85)*	2.38 (1.85; 2.73)*	1.17 (1.12; 1.25)
CD_{16} (NK), $*10^9$/L	0.34 (0.30; 0.35)	0.60 (0.50; 0.90)*	1.80 (0.90; 2.00)*	0.30 (0.20; 0.30)
%	12 (11; 12)	18 (15; 19)*	23 (18; 25)*	12 (10; 14)

Note.*-p<0.01- probable difference with values in children from control group.

Represented data are confirmed by analysis of cellular effectors levels of humoral component of immune system

(CD22) which indicates their increase and direct dependence on severity of hemorrhagic vasculitis course (Table 2). Statistical processing of received data indicates significant difference of circulating immune complex levels in children with minimal to maximal degree of hemorrhagic vasculitis activity (67 (59; 74) c.u., 81 (76; 86) c.u., 136 (100; 162) c.u., respectively).

Table 2.

Values of the humoral component of immune system according to degree of hemorrhagic vasculitis activity in children in acute episode of disease (Me (Lq; Uq)).

Value	Degree of activity			Control group (n=17)
	I (n=19)	II (n=22)	III (n=19)	
CD_{22}(B-lymph) $*10^9$/L	0.60 (0.50; 0.65)*	1.21 (1.10; 1.32)*	1.90 (1.60; 2.40)*	0.50 (0.40; 0.60)
%	18 (17; 20)	26 (22; 29)*	35 (27; 37)*	17 (13;19)
Ig A, g/L	2.29 (2.12; 2.43)*	3.25 (2.90; 3.50)*	2.70 (2.20; 3.30)*	1.22 (0.90; 1.62)
Ig M, g/L	1.70 (1.10; 2.00)*	2.15 (2.00; 2.60)*	1.55 (1.26; 2.40)*	0.98 (0.82; 1.11)
Ig G, g/L	10.70 (9.98; 12.30)	14.35 (13.00; 15.70)*	9.98 (8.00; 12.70)	9.95 (8.16; 11.24)
CIC, c.u.	67 (59;74)*	81 (76; 86)*	136 (100;162)*	29 (25; 34)

Note.*-p<0.01- probable difference with values in children from control group.

While analyzing Ig A levels in blood serum in acute episode of hemorrhagic vasculitis we detected statistically significant differences with values in control group. The most expressive differences were detected in children with II degree of activity (3.25 (2.90; 3.50) g/L). Concerning Ig A levels in blood serum, significant increase was registered in children with moderate course of hemorrhagic vasculitis (14.35 (13.00; 15.70) g/L). Ig M level in blood serum was significantly increased in acute episode of the disease in children of all degrees of activity.

Patients with minimal degree of activity in acute episode of the disease appeared to have significant increase of values of phagocytizing neutrophils and phagocytic number (88 (85; 94) %, 6.0 (4.3; 6.5), respectively).

In children with II and III degree of hemorrhagic vasculitis activity we registered systemic decrease of these values which may indicate low reserve of compensative capacity of phagocytosis in patients of given groups and their exhaustion associated with their involvement into elimination of inflammation products and circulating immune complex from the body. In all patients with different degrees of activity of the disease, we registered significant increase of NST-test values versus values in control group. The highest points were registered in children with II degree of activity (35 (30; 38), %).

Activity of leukocytes myeloperoxidase according to mean cytochemical coefficient data in acute episode was decreased in patients of all groups versus values of control group particularly in children with II degree of hemorrhagic vasculitis activity (2.00 (1.88; 2.50), mean cytochemical coefficient). Lysosomal cationic protein values in children with I and II degrees of activity did not statistically differ from values of control group, significant increase of them was registered in children with III degree of activity (1.24 (1.12; 1.26), mean cytochemical coefficient) (table 3).

Table 3

Values of phagocytosis according to degree of hemorrhagic vasculitis activity in children in acute episode of disease (Me (Lq; Uq)).

Value	Degree of activity			Control group (n=17)
	I (n=19)	II (n=22)	III (n=19)	
Phagocytizing neutrophils, %	88 (85; 94)*	67 (64; 77)*	50 (47; 55)*	82 (78; 86)
Phagocytic number	6.0 (4.3; 6.5)*	3.2 (3.1; 5.0)	2.4 (2.2; 3.1)*	4.2 (3.8; 4.8)
Neutrophil activity index	0.98 (0.90; 1.00)*	1.10 (0.90; 1.30)	0.92 (0.78; 0.92)*	1.09 (1.00; 1.15)
Myeloperoxidase, mean cytochemical coefficient	2.30 (2.25; 2.45)*	2.25 (2.25; 2.34)*	2.00 (1.88; 2.50)*	2.56 (2.55; 2.57)

Lysosomal cationic protein, mean cytochemical coefficient	1.26 (1.20; 1.30)	1.27 (1.22; 1.35)	1.24 (1.12; 1.26)*	1.23 (1.22; 1.24)
NST-test, %	26 (24; 30)*	35 (30; 38)*	18 (14; 20)*	9 (7;12)

Note.*-p<0.01- probable difference with values in children from control group.

Analysis of MCP-1 values according to pathologic process activity in children who suffer from hemorrhagic vasculitis indicates a significant increase of its values particularly the dependence of MCP-1 levels in blood serum on degree of hemorrhagic vasculitis activity should be noted. The remarkable thing is that criterion of Kruskal-Wallis of MCP-1 levels among represented groups equals to 70.53 where p=0.0000, that indicates occurrence of differences in represented groups. Data obtained by pairwise comparison indicate a significant difference in children with different degrees of hemorrhagic vasculitis activity versus values of control group as well as among each other (table 4).

Table 4

Values of MCP-1 in blood serum in children according to degree of hemorrhagic vasculitis activity in acute episode of the disease

Value	Statistical value	Degree of activity			Control group (n=17)
		I (n=19)	II (n=22)	III (n=19)	
MCP-1, pg/ml	Me	870.4	1280.6	2350.6	370.6
	Lq	786.5	1127.4	2050.2	350.3
	Uq	955.3*	1430.2*	2780.6*	400.0
KW H=70.53, p=0.0000, p_{I-II}=0.0000**, p_{I-III}=0.0000**, p_{II-III}=0.0000**, p_{c-I}=0.0000*, p_{c-II}=0.0000*, p_{c-III}=0.0000*					

Notes:* - p<0.01- probable difference with values in children from control group; ** - statistical significance level according to Bonferonni adjustment versus values of different groups – p<0.01; I, II, III – degree of hemorrhagic vasculitis activity.

It is important to note that in children with I degree of activity a significant correlation relationship was not found. In children with II degree of hemorrhagic vasculitis activity, direct significant coefficients of correlation of MCP-1 levels in blood serum and absolute and relative CD4 levels, by CD4/CD8 ratio (rxy = +0.87, rxy = +0.72, rxy = +0.84 respectively, n=22), and inverse correlation relationship of MCP-1 levels and absolute and relative CD8 levels (rxy = -0.65, rxy = -0.91, respectively, n=22) indicate MCP-1 involvement into activation of T-cellular component of immune system. Present positive correlation relationship of MCP-1 levels and CD16 levels indicates significant role of this chemoattractive agent in Th1 way formation of immune response in patients with hemorrhagic vasculitis. Irreversible correlation relationship of MCP-1 levels and absolute and relative CD22 amount likely indicates expression of MCP-1 by B-lymphocytes (rxy = +0.50, rxy = +0.50, respectively, n=22). Analyzing correlation relationship of MCP-1 and phagocytosis values we noted inverse correlation coefficients of phagocytizing neutrophil levels, phagocytic number and MCP-1 levels in blood serum (rxy = -0.51, rxy = -0.53, respectively, n=22). In addition, we registered direct correlation relationship of Ig A, Ig M, Ig G levels and MCP-1 levels (rxy = +0.45, rxy = +0.48, rxy = +0.45 respectively, n=22).

In the process of correlation analysis of immunological indicators and indicators of MCP-1 in blood serum in children with III degree of hemorrhagic vasculitis we received similar data. Direct coefficients of correlation registered between absolute, relative amount of CD4, absolute, relative amount of CD16, absolute, relative amount of CD22, Ig A, Ig M and MCP-1 (rxy = +0.71, rxy = +0.74, rxy = +0.80, rxy = +0.64, rxy = +0.76, rxy = +0.50, rxy = +0.72, rxy = +0.55 respectively, n=19). Inverse correlation relationship was registered between absolute, relative amount of CD8, phagocytic neutrophils, phagocytic number and MCP-1(rxy = -0.68, rxy= -0.72, rxy = -0.83, rxy = -0.54 respectively, n=19).

4 CONCLUSIONS

MCP-1 in the presence of hemorrhagic vasculitis serves as chemoattractant not only for monocytes and for basophils but also involves T-lymphocytes and natural killers into focus of inflammation. Present inverse correlation relationship of MCP-1 levels and phagocytic

activity may indicate compensative capacity decrease of phagocytosis that in the presence of active inflammation reaction focused on elimination of inflammation product and circulating immune complex. Whereas in the presence of insufficient activity of phagocytic component of immune system a MCP-1 synthesis increases for the purpose to involve macrophages into focus of inflammation and compensate exhaustion process. Thus, MCP-1 high levels and present correlation relationship with immune response indicators can be from one side as a marker of activation of immunodefences and from another side as a possible trigger of pathologic process activation. Received data indicate direct involvement of MCP-1 into hemorrhagic vasculitis immunopathogenesis.

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Received: 17-May. – 2016
Accepted: 29-May. - 2016

PEDIATRICS

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THE ROLE OF VASCULAR INTERCELLULAR ADHESION MOLECULE-1 (SVCAM-1) IN INFLAMMATION DEVELOPMENT ACCOMPANYING BRONCHIAL ASTHMA IN CHILDREN

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Abstract: The goal of the investigation is to evaluate the role of sVCAM-1 in inflammation development in children suffering from bronchial asthma at the period of exacerbations and remission. The study included 91 patients with persistent bronchial asthma at the age of 6 to 17 years. The serum levels of sVCAM-1 was determined with enzyme-linked immunosorbent assay. Intima media complex thickness of common carotid artery was detected applying to the method of Pignolli P. (1986). Clinical investigations of blood were performed according to common methods. Statistic analysis was performed using Statistics packages such as "EXCELL FOR WINDOWS" and "STATISTICA 7.0. FOR WINDOWS". The study of sVCAM-1 level in blood serum of children suffering from BA showed its significant increase in mentioned patients both at the exacerbation and remission periods, and it depends on disease severity; its decrease was reported at remission period. sVCAM-1 was found to directly participate in inflammatory cells adhesion processes (neutrophils, eosinophils, and monocytes) on vascular endothelium with their further migration not only at the period of BA exacerbation but also at remission period. It leads to development of local inflammation and thickening of vascular wall. The present correlations with external respiration function suggest direct participation of sVCAM-1 in development of endothelial dysfunction and severity of BA manifestation.

KeyWords: bronchial asthma, children, inflammation.

INTRODUCTION

Bronchial asthma (BA) is considered to be the most widespread chronic condition among children, and remains a global problem of health protection [4, 9]. Inflammation specific for this pathologic process can be caused by different factors including allergens, viruses, physical activity, etc., and results from changes in immune system including cellular, humoral mechanisms, and resembles a complex process which results in immune balance disorder [1,2]. BA pathogenesis is influenced by IgE-mediated allergic reactions which also result from changes in immunoregulation system [5]. At the time of inflammatory reaction development endothelium, thrombocytes, leukocytes, coagulation plasma system, and complement system always interact [3, 7,10].

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Vascular remodeling molecular mechanisms of which are complex and underinvestigated plays a significant role in pathogenesis of chronic process in respiratory tract [4, 8]. Endothelium plays many important functions including barrier and transport ones, synthesis of proteins and vasoactive substances, takes part in angiogenesis, blood coagulation processes, regulates vascular tone and immunoinflammatory reactions [11, 14]. Moreover, endothelial cells express a significant number of biologically active substances (anti-inflammatory cytokines, chemokines and enzymes, anticoagulants, vasoconstrictors and vasodilators, and also adhesion molecules) which directly take part in inflammatory process, and not only initiate but also support it [12, 13, 14]. Inflammation leads to activation of endothelial cells which are participants and regulators of inflammatory process expressing intercellular adhesion molecules [12]. Hereafter it causes the increase of vascular penetration [12, 13].

It appears that the perspectives of further scien-

tific search for investigation of BA development mechanisms, formation and progressing can include extended detection of vascular and endothelial factors in genesis of chronic inflammatory process of bronchopulmonary system [3].

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

To evaluate the role of sVCAM-1 in inflammation development in children suffering from bronchial asthma at the period of exacerbations and remission.

2.2 Subjects

`We examined 91 children suffering from persistent BA (50 boys and 41 girls) at the age of 6-17 years at the periods of exacerbations and remission of the disease. The examination was performed at Pulmonology Department of Communal Health Institution "Kharkiv Municipal Children's Clinical Hospital #16". The diagnosis was made taking into account the demands stated in corresponding protocol with BA (order #868 Ministry of Healthcare of Ukraine d.d. 08.10.2013). The research also included examination of 15 apparently healthy children who belonged to control group.

Depending on disease severity children were divided into 3 groups: 1st group – children with light persistent disease course (40); 2nd group – children with moderately severe BA (34); 3rd group – with severely persistent BA (17)

2.3 Methods

The level of sVCAM-1 was detected in blood serum with the help of BenderMedsystems kit (Austria) for sVCAM-1 identification. Clinical investigations of blood were performed according to common methods (В.Е. Предтеченський, 1960), levels of glycoproteins and seromucoids based on unified method (В.В.Меньшиков, 1987). Intima media complex thickness of common carotid artery (IMC CCA) was detected applying duplex sonography in the distal third of the common carotid artery according to the method of Pignolli P. (1986). The function of external respiration was assessed according to the method of computed pneumotachography using "Custo-Vit" apparatus (Germany).

Statistic analysis was performed using Statistics packages such as "EXCELL FOR WINDOWS" and "STATISTICA 7.0. FOR WINDOWS". For sampling methods with allocation different from the normal one median (Me) and interquartile range were defined (Lq – lower quartile; Uq – upper quartile).

While comparing values which were characterized by comparison of more than 2 points Kruskal-Wallis H-test dispersion analysis was applied. Significance point was defined using Bonferonni adjustment. To compare two independent samples non-parametric Mann-Whitney U-test was applied. To compare two dependent samples non-parametric Wilcoxon test was used. The relation between values was assessed by the method of Spearman rank correlation. Significance point was detected taking into account $p<0.05$.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

sVCAM-1 in blood serum depending on disease course severity was assessed (Table 1). It was significantly increased comparing with values of control group children.
After analysis of statistical characteristics of multiple comparison of sVCAM-1 value in blood serum of children suffering from BA it was reported that Kruskal-Wallis H-test was highly significant. It allows confirming that statistical characteristics of different groups significantly differ from one another, and its level depends on patient's belonging to this or that group (that is the disease severity). At the time of sequential comparison of the given value statistically significant increase of its level in blood serum in all people suffering from BA both in exacerbation and remission period was detected. The most expressive changes are identified in children of the 3rd group with severe stage of disease.

Table 1.

Statistical characteristics of sVCAM-1 level in blood serum of children suffering from BA at the period of exacerbation and remission Me (Lq; Uq

Groups of children	sVCAM-1, ng/ml	KW ANOVA by Ranks	MW U Test
Exacerbation period			
1st group (n=34)	990.27 (900.52; 1080.89)	H=67.30, p= 0.0000	p_{1-2}= 0.0000; p_{1-3}= 0.0000; p_{2-3}= 0.0000; p_{c-1}= 0.0000; p_{c-2}= 0.0000; p_{c-3}= 0.0000;
2nd group (n=31)	1280.00 (1100.27; 1380.73)		
3rd group (n=11)	1700.73 (1480.27; 1920.59)		
Control group (n=15)	730.01 (690.63; 790.19)		
Remission period			
1st group (n=40)	885.42 (800.57; 990.47)	H=76.57, p= 0.0000	p_{1-2}= 0.0000; p_{1-3}= 0.0000; p_{2-3}= 0.0000; p_{c-1}= 0.0000; p_{c-2}= 0.0000; p_{c-3}= 0.0000;
2nd group (n=34)	1150.43 (990.37;1280.77)		
3rd group (n=17)	1500.18 (1300.32; 1700.25)		
Control group (n=15)	730.01 (690.63; 790.19)		

The dependency of sVCAM-1 levels expressiveness in blood serum on disease activity is also proven by growing with severity process significant correlation factors (p<0,05) of this value and values of acute inflammation phase including levels of glycoproteins and seromucoid in blood serum: patients of the 1st group were reported to have medium strength correlation between the levels of the given values (r=+0.3492, r=+0.4487, respectively); the given correlation in children of the 2nd group equaled to r=+0,5825 and r=+0,5043, respectively; the patients of the 3rd group were reported to have strong correlation of sVCAM-1 level in blood serum with acute phase values (r=+0,8909 – glycoproteins, r=+0,9151 – seromucoid).

The analysis of sVCAM-1 level in blood serum of children suffering from BA at different disease periods demonstrated that at remission period this value remains higher than regulatory values (p<0,001), however compared with exacerbation period it is significantly reduced in patients of the 1st, 2nd, and 3rd groups (p=0.0000, T=0.00; p=0.0000, T=0.00; p=0.0033, T=0.00, respectively). It can signal about presence of pathologic process even beyond activity, and be an adverse factor in disease course.

While detecting the thickness of IMC CCA, children of the 1st, 2nd and 3rd groups were reported to have significant increase of the given value 0.9(0.8; 1.0) mm; 1.0 (0.9; 1.2) mm; 1.2(1.1; 1.3) mm, respectively, compared with values of control group – 0.6 (0.5; 0.7) mm, p<0.001).

Further statistical processing showed high direct correlation between sVCAM-1 level in blood serum and IMC CCA thickness both at exacerbation period (r=+0.8, p<0.05) and remission period (r=+0.8, p<0.05). Thus, it is possible to admit direct participation of sVCAM-1 in development of inflammatory process in vascular endothelium.

The presence of correlation between sVCAM-1 level in blood serum and IMC CCA thickness with inflammatory cells (leukocytes) in blood at exacerbation and remission periods was analyzed.

Positive correlation relationships of sVCAM-1 level of blood serum and IMC CCA thickness with leukocytes (r=+0.4, p<0.05) and neutrophils (r=+0.3, p<0.05) in children of the 1st group at exacerbation period and significant increase of bonding strength of IMC CCA thickness with neutrophils in patients of the 3rd group (r=+0.7, p<0.05) were detected.

Converse correlation of the given values with lymphocytes in children of the 1st group (r=-0.4, p<0.05) and significant increase of bonding strength of the given correlation in patients of the 3rd group (r=-0.8, p<0.05) was also identified. Analyzing inflammation from the side of tissue infiltration of leukocytes it is necessary to admit that mediators which influence endothelial cells also affect leukocytes, and vise versa. Thus, microvascular endothelial cells at inflammation site are active participants and regulators of inflammatory processes [13]. Moreover, it is necessary to note that children of the 2nd and 3rd groups have positive correlation of sVCAM-1 level of blood serum with eosinophils (r=+0.4, p<0.05 – in patients of the 2nd group and r=+0.6, p<0.05 – in patients of the 3rd group) and negative

correlation – between IMC CCA thickness and monocytes (r=-0.6, p<0.05). The identified changes can be explained by the fact that ß1-integrin which is expressed on leukocytes of some subpopulations provides selective adhesion of monocytes and eosinophils on endothelium and further sVCAM-1 causes their migration and inflammation development [71]. Thus, increased expression of sVCAM-1 by activated endothelium causes recrutization of inflammatory cells and their further transendothelial migration. It can lead to their accumulation in intima and further to thickening of vascular wall.

At remission period patients of the 1st group still have negative correlation of sVCAM-1 level of blood serum and IMC CCA thickness and lymphocytes (r=-0.5, p<0.05), children of the 2nd group have positive correlation between sVCAM-1 level of blood serum with neutrophils (r=+0.7, p<0.05), and patients of 3rd group – negative connection of the given value with monocytes (r=-0.7, p<0.05). Thus, at remission period inflammatory cellular adhesion to endothelium can continue, and it leads to its hypertrophy and further to intima thickening with formation of long-term damages of endothelium adequate functioning.

Significant dependency of external respiration function on sVCAM-1 level is proven by existing correlations (with forced vital capacity - r=-0.5; with forced expiratory volume 1- r=-0.4; with MEF25 - r=-0.5; with MEF50 - r=-0.3; p<0.05) – at the period of exacerbations; and at remission period (with forced vital capacity - r=-0.3; with forced expiratory volume 1- r=-0.5; with MEF75 - r=-0.3; p<0.05). Thus, the higher are levels of sVCAM-1 in blood serum the worse are the values of external respiration function especially those ones which are specific for BA – forced expiratory volume 1, peak expiratory flow rate that is the evidence of adhesion vascular molecule belonging to inflammatory process and external respiration dysfunction in BA.

4 CONCLUSIONS

The study of sVCAM-1 level in blood serum of children suffering from BA showed its significant increase in mentioned patients both at the exacerbation and remission periods, and it depends on disease severity; its decrease was reported at remission period. sVCAM-1 was found to directly participate in inflammatory cells adhesion processes (neutrophils, eosinophils, and monocytes) on vascular endothelium with their further migration not only at the period of BA exacerbation but also at remission period. It leads to development of local inflammation and thickening of vascular wall. The present correlations with external respiration function suggest direct participation of sVCAM-1 in development of endothelial dysfunction and severity of BA manifestation.

Thus, expression of sVCAM-1 by different cells forms pathological process which leads to stable changes in vascular endothelium and is one of the mechanisms of chronic inflammation formation.

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Received: 15-Apr. – 2016
Accepted: 23-May. - 2016

PEDIATRICS

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CEREBRAL HEMODYNAMICS IN NEWBORNS WITH SEIZURES

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Abstract: The research deals with cerebral hemodynamics in newborns with seizures. The study involved examination (including Doppler neurosonography of cerebral vessels and amplitude-integrated electroencephalography) of 56 infants undergoing neonatal intensive care. The study showed that 37.5% of neonates had convulsions (including 17.9% with atypical subclinical seizures). Disorders of cerebral hemodynamics in neonates with seizures were characterized by hyperperfusion in 52.4% and hypoperfusion in 33.3% of infants.

KeyWords: newborns, neonates, infants, seizures, convulsions, cerebral hemodynamics.

INTRODUCTION

International and domestic perinatology has made a huge step forward at the present stage of medicine development. These improvements provided possibilities to maintain pregnancy and successfully nursed newborns with low and extremely low birth weight as well as effectively treat children who had severe asphyxia at birth [1,2].

The opening of perinatal centers in Ukraine offers the opportunity to use the up-to-date equipment and render advanced neonatal monitoring and treatment technologies to provide the successful nursing of newborns at the gestational age of 22 weeks and more with a weight starting from 500 grams [1]. There has been a progress in the treatment of full-term and preterm infants with asphyxia at birth. A significant amount of these patients is admitted to the intensive care unit in a severe condition and needs a highly qualified and timely support during the early neonatal period. This group of newborns is often found to have disorders of the central nervous and cardiovascular systems. Neonatal seizures are a common manifestation of neurological dysfunction in infants [3].

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Perinatal abnormalities in a significant number of patients are triggered by a hypoxic-ischemic injury of the central nervous system caused by asphyxia [1, 3]. Disorders of cerebral hemodynamics are considered to be the leading mechanism of newborns' brain injury from the early neonatal period [4]. Seizures are a severe indicator of a grave damage to the nervous system in newborns. Contemporary studies have provided evidence that seizures can often be subclinical and cannot be detected by physical examination of newborns [5].

Disorders of cerebral blood flow are an important mechanism for the pathogenesis of perinatal injury of the central nervous system. Displacement of individual parameters of dynamic and metabolic regulation outside the physiological values promotes a disruption in the cerebral autoregulatory mechanism. It triggers cerebral hypoperfusion, vasogenic and then cytotoxic cerebral edema accompanied by an increase in intracranial pressure. As a result, these events condition the development of cerebral ischemia [4].

The amplitude-integrated electroencephalography in examination of newborns with convulsive syndrome is an important stage in the diagnosis of abnormal brain activity especially in preterm infants according to the frequency of atypical (subclinical) seizures [5,6].

The early diagnosis of cerebrovascular perinatal CNS injury is based on a comprehensive assessment of

cerebral blood flow according to Doppler neurosonography of cerebral blood vessels and edtermination of amplitude-integrated EEG patterns can improve the early diagnosis, individual therapy and may also reduce the neurological morbidity and disability in children.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

to improve diagnosis of cerebral hemodynamics disorders in neonates with seizures by means of Doppler neurosonography of cerebral blood vessels.

2.2 Subjects

The study involved the examination of 56 newborns (66.1% boys, 33.9% girls) with the assessment of obstetric records, clinical and instrumental examination (ECG, echocardiography, Doppler neurosonography of cerebral blood vessels and amplitude-integrated EEG). They were at the gestational age from 26 to 41 weeks (mean gestational age 32.1±4.8 weeks). The control group comprised 20 healthy newborns (55% boys, 45% girls) at gestational age of 39-40 weeks and within the normal fetal and early neonatal period.

2.3 Methods

All the examined newborns underwent Doppler neurosonography of cerebral blood vessels followed by the assessment of resistance index on ultrasonic unit MyLab25Gold (Italy), amplitude-integrated EEG on encephalograph “Olympic CFMTM 6000" (USA/Canada). All the infants were examined by a neurologist.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The group of examined infants included 26 (46.4%) full-term and 30 (53.6%) premature ones. Of them 25 (44.6%) children were delivered by cesarean section whereas 31 (55.4%) infants were born by vaginal delivery.

The main diagnoses of the newborns admitted to the neonatal intensive care unit of Kharkiv Regional Perinatal Center were as follows:

- birth asphyxia (R21.0 and R21.1 in ICD-10);
- respiratory distress syndrome (R22.0 in ICD-10).

Convulsive syndrome (clinical or subclinical seizures) was detected in 21 (37.5%) examined newborns. Subclinical seizures were diagnosed in 10 (17.9%) children. Subclinical seizures were identified only by the convulsive patterns on the amplitude-integrated electroencephalogram without generalized convulsions (Fig.1).

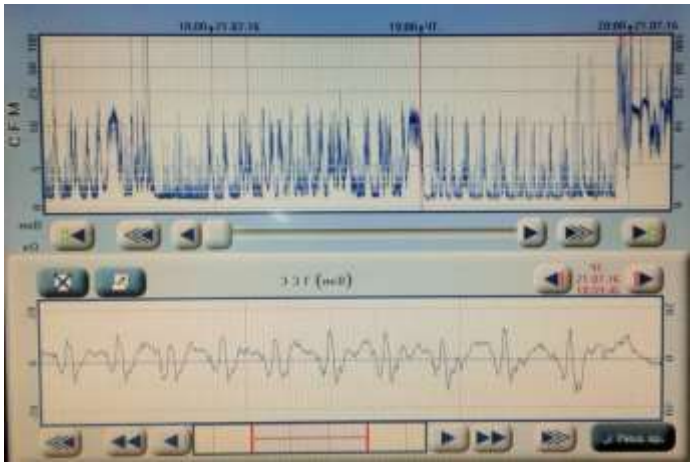

Fig.1. Subclinical seizures on the amplitude-integrated EEG

Other leading neurological syndromes diagnosed in the examined children during the neonatal period include:

- tonicity disorders syndrome – 64.3% ($p < 0.05$);
- CNS depression syndrome – 21.4% ($p < 0.05$);
- hypertension-hydrocephalic syndrome – 8.9% ($p < 0.05$);
- vegetative-visceral disorders syndrome – 8.9% ($p < 0.05$).

Echography showed the following abnormalities:

- cerebral edema in 39.3% cases,
- periventricular areas edema in 42.9% cases,
- periventricular ischemia in the late neonatal period in 64.3% of children.

Furthermore, 13 (23.2%) infants had intracranial hemorrhage including 1st degree intraventricular hemorrhage

(classification by Papile L.-A. et al, 1978) found in 8 (14.3%) children whereas 6 (75%) of them were premature newborns.

Changes of cerebral hemodynamics in neonates with seizures were characterized by signs of hyperperfusion in 52.4%. According to neurosonography data, they had a low resistance index in the anterior cerebral artery, i.e. 0.49±0.05 ($p<0.05$) and 0.52±0.08 ($p<0.05$) standard units in the middle cerebral artery. A disruption of the cerebral blood flow autoregulation mechanism was evident due to hypotension and postnatal homeostasis changes. In 33.3% the changes of cerebral hemodynamics were characterized by signs of hypoperfusion. According to neurosonography data this group of patients had a high resistance index in the anterior cerebral artery, i.e. 0.78±0.05 ($p<0.05$) and 0.78±0.08 ($p<0.05$) standard units in the middle cerebral artery. We also examined other infants without seizures undergoing treatment in neonatal intensive care unit. Normal perfusion in the brain structures was found in 51.4% cases [7].

4 CONCLUSIONS

1. Neurological disorders in newborns were manifested mostly as tonicity disorders syndrome, convulsive syndrome and CNS depression syndrome.
2. The study showed that 37.5% of newborns had convulsions (including 17.9% of children with subclinical seizures).
3. Disorders of cerebral hemodynamics in newborns with seizures were characterized by brain hyperperfusion symptoms in 52.4% and hypoperfusion in 33.3% of patients.

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Received: 01 - May. – 2016
Accepted: 15 - May. - 2016

DENTISTRY

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MICROBIOLOGICAL EFFICACY OF PHOTO-ACTIVATED DISINFECTION AND TEMPORARY ROOT OBTURATION AS AN ADJUNCT TO THE TREATMENT OF CHRONIC APICAL PERIODONTITIS

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Abstract: Photo-activated disinfection and temporary obturation are widely used in the treatment of apical periodontitis since effective elimination of microorganisms in infected root canal systems is an important concern for endodontics. The article presents results of microbiological research in the teeth with chronic apical peridontitis before and after the treatment.

KeyWords: photo-activated disinfection, temporary obturation, calcium hydroxide, microflora, chronic apical periodontitis.

INTRODUCTION

Photodynamic therapy (PDT), also called photoradiation therapy, phototherapy, or photochemotherapy was introduced into practice in 1904 as light-induced inactivation of cells, microorganisms, or molecules. PDT involves the combination of visible light, usually through the use of a diode laser and a photosensitizer.

The photosensitizer is a compound that is capable of absorbing light of a specific wavelength and transforming it into useful energy [1, 2]. Each factor is harmless by itself, but when combined they can produce lethal cytotoxic agents that can selectively destroy cells. Thus, PDT may represent a promising alternative for reducing the bacterial load or even for eradicating certain periodontal pathogens. PDT mechanism has been described by several authors. Briefly, upon illumination, the photosensitizer is excited from the ground state to the triplet state [3, 4].

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Materials and therapeutic agents containing calcium hydroxide are extensively used in a variety of treatment modalities within endodontics and dental traumatology [7, 8]. Calcium hydroxide in endodontics and dental traumatology makes antibacterial activity, antifungal activity, effect on bacterial biofilms, the synergism between calcium hydroxide and other agents, its effects on the properties of dentine, the diffusion of hydroxyl ions

The longer lifetime of the triplet state enables the interaction of the excited photosensitizer with the surrounding molecules, and it is generally accepted that generation of cytotoxic species produced during PDT occurs while in this state. The cytotoxic product, usually O2, cannot migrate over 0.02 mm after its formation, thus making it ideal for the local application of PDT without endangering distant molecules, cells, or organs [5]. PDT is widely used in the treatment of apical periodontitis, because effective elimination of microorganisms in infected root canal systems is an important concern in endodontics. PDT has recently been used to eradicate microorganisms from root canal systems, which suggests that it might be useful as adjunctive therapy to current endodontic disinfection techniques [6].

through dentine, and its toxicity [9, 10]. Combination of PDT and root temporary obturation with calcium hydroxide in endodontic treatment is not studied enough.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

To detect the content of microflora in the infected root canals with chronic apical periodontitis before and after photo-activated disinfection and temporary obturation.

2.2 Subjects

The study was performed at KNMU Dental Centre. The main group included 18 patients with chronic apical periodontitis aged 25-40.

2.3 Methods

PDT was used in addition to the standard root canal irrigation by 3% solution of Sodium hypochlorite. Photo-activated disinfection of root canals was performed by a photosensitizer, i.e. 10% povidone-iodine solution. Laser therapeutic device "Lika-terapevt M" with a wavelength = 810 nm was used as a light source. Photosensitizer solution remained in situ for 60 seconds, following which was activated by the laser for 120 seconds. The next stage of treatment involved temporary root obturation by calcium hydroxide paste for 10 days. After this period the paste was removed by handle instruments and 17% EDTA activated by ultrasound. Then root canals were dried with paper pins, standard and constant obturation and control X-ray to detect the quality of sealing.

Sampling of root canal content was performed with sterile paper pins 15 or 20 in size, and then transferred to the transport sterile environment Ames 10 ml. The material was delivered overnight to a microbiological laboratory for a quantitative bacteriological study using anaerobic cultivation technology. Quantitative planting of the material was carried out by the secretory Gold's method (1965). Identification of the microorganisms was performed using nutrient agar intended for their cultivation. Counting was made in colony-forming units (CFU).

Detection of pure cultures was conducted according to general bacteriological rules of research. The study was conducted twice: before treatment and before permanent obturation after all scheduled medical procedures.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

Analysis of microbiological research of root canals content before treatment showed great variety of microorganisms. The study revealed thirteen type of bacteria and one type of fungus. A large number of identified microorganisms were gram-positive. According to the type of respiration there was obligate anaerobic and mixed type of respiration (facultative anaerobic and microaerophilic).

Root canals with chronic apical periodontitis were mainly found to contain Enterococcus faecalis, Staphylococcus epidermidis, Candida albicans, Pseudomonas aeruginosa and Escherichia coli. In 100% of cases the strains of Pseudomonas aeruginosa and Escherichia coli were cultured in patients undergoing repeated endodontic treatment (complications due to inadequate root canal fillings). Enterococcus faecalis, Staphylococcus epidermidis, Candida albicans, and bacteria of Streptococcus, Peptostreptococcus, Actinomyces, Lactobacillus were identified in cases of primary and secondary root canal treatment (table 1). After treatment the study identified Staphylococcus epidermidis, Streptococcus and bacteria of Pseudomonas aeruginosa in small concentrations (1.0 ± 0.01, 1.2 ± 0.02 and 1.1 ± 0.04 CFU/ ml respectively lg). Candida albicans, Enterococcus faecalis, Escherichia coli, Peptostreptococcus spp, Actinomyces spp., Lactobacillus spp. were not found in root canals. The difference between the data before and after treatment was statistically significant ($p < 0.05$).

Table 1.

Characteristics of microflora in root canals

Type of microorganism	Frequency before treatment, %	Concentration before treatment lg CFU/ml (M±m)	Frequency after PDT, %	Concentration after PDT lg CFU/ml (M±m)
Enterococcus faecalis	52.3	7.1±1.1	0	0
Staphylococcus epidermidis	43.5	5.5±0.9	25.5*	1.0±0.01*
Candida albicans	31.5	6.1±1.2	0	0
Pseudomonas aeruginosa	20.0	6.4±0.8	15.5*	1.2±0.02*
Escherichia coli	25.6	6.8±0.9	0	0
Streptococcus spp.	22.5	5.6±0.6	18.0*	1.1±0.04*
Pepto-?treptococcus spp.	6.5	5.5±0.5	0	0
Actinomyces spp.	5.0	4.4±0.8	0	0
Lactobacillus spp.	8.2	4.9 ±0.7	0	0

Note: * - statistically significant differences in the comparison of data before and after treatment, p <0.05

Comparison of microbial flora before and after treatment allowed us to develop its algorithm including temporary root obturation with calcium-hydroxide paste and photo-activated disinfection by 10% povidone-iodine, activated by 810 nm wavelength. This method of disinfection is undoubtedly advantaged by the dynamic irrigation promoting mechanical washing of microbic weight from root canals. A benefit of the photo-activated disinfection was its activity against pathogenic Enterococcus faecalis. Medicated treatment of root canals should begin with a dynamic irrigation of root chanals with sodium hypochlorite solution with the subsequent addition of photo-activated disinfection and temporary root obturation.

4 CONCLUSIONS

1. Root canals with chronic apical periodontitis were predominantly found to contain Enterococcus faecalis, Staphylococcus epidermidis, Candida albicans, Pseudomonas aeruginosa and Escherichia coli.

2. Enterococcus faecalis, bacteria of the genus Peptostreptococcus, Actinomyces and Lactobacillus were the least resistant to therapy.

3. Photo-activated disinfection of root canals with temporary root obturation is an effective method in treatment of chronic apical periodontitis, reducing the concentration of microbial cenoses to etiologically non-significant concentration.

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Received: 17-Apr. – 2016
Accepted: 14-May. - 2016

SPORT MEDICINE

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MICROBIOLOGICAL EFFICACY OF PHOTO-ACTIVATED DISINFECTION AND TEMPORARY ROOT OBTURATION AS AN ADJUNCT TO THE TREATMENT OF CHRONIC APICAL PERIODONTITIS

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Abstract: Medical career is a difficult, long and controversial process that includes a variety of content and structural components. The model consists of medical professional formation including the level of physical and mental adaptation to professional activities. Training highly qualified healthcare professionals provides the harmonious development of physical, spiritual and moral, spiritual and aesthetic qualities.

KeyWords: development, functional state, physical training, training in sports, physical activity

INTRODUCTION

A medical student is a future doctor and in this case the person is dedicated to medicine and should have a huge number of interrelated social features such as mind, emotions, willpower, skills, intuition, self-control, self-criticism, love, hate, passion, impulsiveness and more. These qualities can be both natural and generated while studying at the university. Any impact on a student is exerted through his personality, temperament, originality of character, skills, interests, inclinations, allowing to choose the most effective ways of interaction of the individual with the world. Medical career is a difficult, long and controversial process that includes a variety of content and structural components. It first of all depends on external conditions. With time the profession, the demands of the society to a certain profession and its ratio with other professions undergo changes.

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Motivational sphere of professional activity, its mentality and spiritual values may also transform.T.K. Bugayova, exploring psychological qualities in medical students, found that while studying at Medical University their professional skills undergo significant changes, largely bringing students to the identity of a real doctor, but not always the level of these qualities corresponds to the high standards of professional activity in the field of healthcare service [1].

Aggregates of qualities determining the success of training for junior and senior students differ in the ratio of cognitive abilities and communication patterns. Undergraduate students were found to develop predominantly the qualities defining the high level of cognitive abilities with a significantly less importance of organizational and volitional qualities. Cognitive abilities also remain the key ones for graduate students, but at a much lower level. Organizational skills undergo a significant improvement with the development of communicative and ethical qualities, not inherent to junior students. The aggregate of qualities professionally important to doctors, being formed in graduates, remains unchanged though undergoes further reorganization under the influence of professional activi-

ties.

According to M.M. Peysakhov the model of professional medical formation also involves the level of physical and mental adaptation to the professional activities. Abilities, developed to a high level up to the prediction and prognosis (perhaps even as a manifestation of intuition), self-regulation and decision-making (courage, creativity, timeliness, accuracy) becoming personal-professional qualities are of particular importance in the substructure of individual's professionalism. Professional adaptation (independence and autonomy, self-reliance and high resistance to stress, physical and emotional overload) plays an essential role. Thus, professional adaptation plays a significant role in the professional development of medical students. Today, professionals are concerned in the issues related to the impact of physical education and sport on personal development of healthcare professionals.

M.M. Bobyreva proposes to consider peculiarities of professional medical activities when elaborating the measures to increase the level of physical activity for students of medical specialties, such as the lack of muscular effort in relatively local movements and the growing requirements for emergent procession of the large amounts of sensory information and the need to perform fast psychomotor responses. The author states that specific working conditions in the field of healthcare require a rather high level of static endurance of muscles in the arms and torso, excellent coordination of hands and fingers in relative immobility of lower extremities [2,13] .

According to I.Y. Nikolaychuk, training of highly qualified healthcare professionals implies harmonious development of physical, spiritual, moral and aesthetic qualities. The author believes that the experts in medical field are required not only to receive professional training, but also to form spiritual and physical qualities, based on the high level of culture, humanism, good bedside manner, nice appearance, demeanor, which must match optimism self-discipline, cheerfulness, courage and confidence [3,8].

Thus, physical training is of utmost importance not only for preservation of the health of students, trained in medicine, but also for the professional development. In the study of physical capacity and health of medical students, experts emphasize that improving the health of students must first use the means of physical culture and sports, aimed at increasing the development of their motor skills. However, the health impact of employment requires a certain system of organizational measures and regular monitoring of key indices of the body to establish the physical development, functional state of the cardiovascular, respiratory and autonomic nervous systems.

Despite the fact that physical qualities are an important component of physical perfection of medical students as the ideal physical development and physical fitness, training in medical schools does not contribute to the improvement of the students' health. High level of academic load exceeding 36 - 40 hours a week, its uneven distribution during the school day and week, lack of long lunch break, disordered organization of learning activities outside classroom, all of these adversely affect functional state indices in medical students.

Analyzing physical condition in higher schools students, G.V. Korobeynikov drew a conclusion that ill health triggered a delay in physical development of medical students, causing a decrease in their physical performance [4,11].

In a research performed by O.V. Shvidky graduate medical students were shown to have signs of hypodynamia, manifested by a marked decrease in physical performance of students in the learning process. According to his estimates, the key patterns of population health include poor indices to nosologic states, low health index, a large proportion of people with health problems [5, 9].

The department of physical rehabilitation, sports medicine with a course of physical education and health created suitable conditions for individual physical training under the supervision of the teachers working at the department.

- Day physical fitness classes;
- Training at public sport clubs;
- Training in sports classes established at the course or department under the supervision of teachers-coaches or student-sportsmen;

- Training in sports classes and groups of general physical training at the place of residence (in hostels);

- Mass physical, rehabilitation and recreational activities at the weekends and holidays (competitions, tournaments, sports days, sports events, etc.).

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Received: 29-Mar. – 2016
Accepted: 12-June. - 2016