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ESSENTIAL ELEMENTS ROLE IN PATHOGENESIS OF OCCUPATIONAL CHRONIC LUMBOSACRAL RADICULOPATHY IN COAL MINERS

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Ключові слова: *хронічна попереково-крижова радикулопатія, остеопенія, кістково-м'язова система та сполучна тканина, есенційні елементи*
Ключевые слова: *хроническая пояснично-крестцовая радикулопатия, остеопения, костно-мышечная система и соединительная ткань, профессиональная патология, эссенциальные элементы*

Abstract. Essential elements role in pathogenesis of occupational chronic lumbosacral radiculopathy in coal miners. Basanets A.V., Andrusyshyna I.N., Lashko O.N. *The problem of diagnosis in the early and preclinical stages of diseases is of importance for the prevention of occupational diseases and their complications, because this is the key to the timely initiation of treatment, the implementation of preventive measures. Chronic lumbosacral*

radiculopathy (CLSR) or low back pain (LBP) is one of the most common diseases in the structure of occupational pathology in Ukraine, which usually develops in those of working professions associated with physical activity, forced work posture, effect of high levels of general vibration, etc. The highest levels of occupational morbidity are recorded in the coal industry, which accounts for about 80% of occupational pathology in Ukraine. Above 1600 cases of CLRS are diagnosed annually in the country. A risk factor for the development of the CLSR is osteopenia, which arises due to the impairment of quantitative and qualitative characteristics of bone tissue and is characterized by a decrease in its strength, an impairment of microarchitecture with a further increase in risk of fractures. One of the modern methods of assessing condition of bone tissue is determination of the content of macro- and microelements (MaE and ME) in the biological environments of patients. Ca, Al, Mg, B, P are the most important in the formation and development of bone and connective tissue. To date, studies of bone tissue status in patients with CLSR of professional etiology have not been conducted (small in numbers). Goal – to determine the role of essential elements Ca, Al, Mg, B, P in serum and urine in the formation of occupational CLSR in miners. The research was conducted in 20 miners with CLRS (slaughterer, mining worker of a clearing face (MWCF), drifter) of coal mining industry of Donbass and Lviv-Volyn basins. The results were analyzed in two groups: I group consisted of patients with work experience of 10-15 years (n=10), II group with work experience of 16-32 years (n=10). The control group included 22 patients without pathology of the musculoskeletal system and connective tissue. The inductively coupled plasma atomic emission spectroscopy method (ICPAE) was used to determine the MaE and ME concentrations. The study revealed that the average serum aluminum (Al) concentration in miners with occupational CLSR (115.07 μmol/l) exceeded control group level (3.3 μmol/l) by almost 30 times (p<0.05). Serum boron (B) concentration in both age groups (25.90 μMol/l and 19.43 μMol/l, respectively) were lower than in the control (62.90 μMol/l), (p<0.05). The average serum calcium (Ca) concentration in patients with occupational CLSR (2.82 mMol/l) was 1.3 times higher than the same indicator in the control group (2.16 mMol/l), with a significant difference between the two age groups (p<0.05). It was revealed that the average level of phosphorus (P) in the urine of patients with occupational CLSR (19.0 mMol/l) significantly exceeded its content in patients of control group (11.96 mMol/l) (p<0.05). The concentration of Al in the urine of patients with CLSR in both age groups (1.26 μMol/l and 1.334 μMol/l, respectively) was higher that in control (0.85 μMol/l), (p<0.05). Reduction of Ca and Mg levels in the serum of miners in increasing work experience in harmful working conditions, exceeding average concentration of aluminum in patients' blood compared to the normative value and indicators of the control group patients was established.

Реферат. Роль эссенциальних элементов в патогенезе развития хронической пояснично-крестцовой радикулопатии профессионального генеза у шахтеров. Басанець А.В., Андрусишина И.Н., Лашко О.Н. *Проблема диагностики на ранних и доклинических стадиях занимает особое место в вопросе профилактики профессиональных заболеваний и их осложнений, ведь это является залогом своевременно начатого лечения, применения профилактических мероприятий. Хроническая пояснично-крестцовая радикулопатия (ХПКР) является одним из наиболее распространенных заболеваний в структуре профессиональной патологии в Украине, диагностируется обычно у работающих профессий, и связана с выполнением тяжелой физической работы, пребыванием в вынужденной рабочей позе, действием высоких уровней общей вибрации, неблагоприятного микроклимата и тому подобное. Самые высокие уровни профессиональной заболеваемости регистрируются в угольной промышленности, которая формирует около 85% профессиональной патологии в Украине. Ежегодно в стране диагностируется около 1600 случаев профессиональной ХПКР. Кроме опасных факторов производства, которые являются этиологическими факторами развития ХПКР, фактором риска развития заболевания является остеопения, которая возникает вследствие нарушения количественной и качественной характеристик костной ткани и характеризуется снижением ее прочности, нарушением микроархитектоники с последующим увеличением риска возникновения переломов. Одним из современных методов оценки состояния костной ткани является определение содержания макро- и микроэлементов (МаЭ и МЭ) в биологических средах пациентов. Ca, Al, Mg, B, P имеют наиболее значимый вес в формировании и развитии костной и соединительной ткани. До этого времени исследования состояния костной ткани у больных ХПКР профессиональной этиологии не проводились (малочисленные). Цель – определить роль эссенциальных элементов Ca, Al, Mg, B, P в сыворотке крови и мочи в формировании хронической ХПКР профессиональной этиологии шахтеров. Исследования проведены в группе 20 шахтеров основных профессий (забойщик, горный рабочий очистного забоя (ГРОЗ), проходчик) угледобывающей промышленности Донбасса и Львовско-Волынского бассейнов, страдающих ХПКР. Анализ результатов проводился в двух стажевых группах: I группу составили пациенты со стажем работы от 10 до 15 лет (n=10), II – от 16 до 32 лет (n=10). В контрольную группу вошли 22 пациента без патологии костно-мышечной системы и соединительной ткани. Для определения концентрации МаЭ и МЭ использовался метод атомно-эмиссионной спектроскопии с индуктивно связанной плазмой (АЭС-ИСП). Концентрация бора в сыворотке крови в обоих стажевых группах (25,90 мкмоль/л и 19,43 мкмоль/л соответственно) была ниже по сравнению с показателем контрольной (62,90 мкмоль/л), (p<0,05). Установлено превышение концентрации алюминия в моче больных ХПКР в обеих стажевых группах (1,26 мкмоль/л и 1,334 мкмоль/л соответственно) по сравнению с контрольной (0,85 мкмоль/л), (p<0,05). Показатель средней концентрации кальция в сыворотке крови у больных ХПКР профессиональной этиологии (2,82 ммоль/л) в 1,3 раза превышал аналогичный показатель в контрольной*

группе (2,16 ммоль/л), при этом установлена достоверная разница между показателями обоих стажевых групп (p<0,05). В исследовании установлено, что средняя концентрация алюминия в сыворотке крови шахтеров, больных ХПКР (115,07 мкмоль/л), превышала показатель в контрольной группе (3,3 мкмоль/л) почти в 30 раз (p<0,05). Установлено, что средний уровень фосфора в моче больных ХПКР (19,0 ммоль/л) достоверно превышал его содержание у пациентов контрольной группы (11,96 ммоль/л) (p<0,05). Выявлено снижение концентрации бора в крови шахтеров с хронической радикулопатией профессиональной патологии по сравнению с контрольной группой. Установлено снижение уровня Ca и Mg в сыворотке крови шахтеров при увеличении стажа работы во вредных условиях труда, превышение средней концентрации алюминия в крови пациентов в сравнении с нормативным значением и показателями контрольной группы.

In the structure of occupational morbidity in Ukraine pathology of the connective tissue and musculoskeletal system ranks second and makes up more than 20%, reaching 1568 cases each year. Chronic lumbosacral radiculopathy occupies a prominent place among this group of diseases, the risk factors for which are: rough labor, forced or fixed working posture, forced bendings, unfavorable microclimate, general vibration [4]. Disorders of the quantitative and qualitative characteristics of bone tissue are one of the causes for the development of this pathology. Osteoporosis is one of the most important biological risk factors for the development of chronic radiculopathy, and the condition of bone tissue depends on many factors, an important place among which is the quantitative composition of a number of MaE and ME [5, 7]. To date, a significant number of these elements are known to affect both bone and muscle tissue. Vitamin D and essential elements Ca, P, Al B, Mg, which are part of the enzymatic systems, play the greatest role in the formation of bone and connective tissue [9].

An important role belongs to Ca, which is one of the most common elements in the human body. Optimal levels of Ca^{2+} and HPO_4^{-2} (based on phosphorus ions) in the serum contribute to normal bone mineralization, however, these ions are associated with active metabolites of vitamin D, which are 25-hydroxycholecalciferol and 1,25-dihydroxychoxylecalciferol. In osteoblasts 1,25 $(OH)_2D$ induces the expression of the transmembrane ligand of receptor activator of the nuclear factor kB (receptor activator of nuclear factor-kBligand – RANKL), which in turn affects the maturation of osteoclasts that are directly involved in resorption of phosphorus and calcium from bone tissue, and thus maintain normal levels of these elements in the serum. Calcium is known to actively affect bone metabolism, which provides impulses for neuromuscular transmission, causes a positive inotropic effect, activates and controls neurotransmitters and hormones.

Element B plays an important role in bone metabolism, which regulates the metabolism of parathyroid hormone, affects the metabolism of vitamin D, essential elements P, Ca, Mg and in interaction with these substances prevents the development of osteoporosis, which is one of the biological risk factors of developing chronic lumbosacral radiculopathy [1, 6].

Thus, Al participates in the maturation of chondrocytes and osteocytes, affects the regeneration of connective, bone and epithelial tissues, improves the formation of phosphate and protein ligands, has the ability to affect the function of the parathyroid and thyroid glands and its excess, according to research, inhibits assimilation of phosphorus, magnesium, calcium by replacing of enzyme E activator, which is a cellular regulator of metabolism of these elements with the cations Al^{3+}

That is why the study of the content of these MaE and ME in the biological environments of patients with chronic lumbosacral radiculitis, caused by the action of physical factors in the process of work is considered appropriate.

MATERIALS AND METHODS OF RESEARCH

In the clinic of occupational diseases of State Institute "Kundiev Institute of Occupational Health of the NAMS of Ukraine" 20 miners of coal mines of Ukraine with a diagnosis of chronic lumbosacral radiculopathy were examined. The average age of patients was 48.25 years, the average work experience in underground working conditions was 17.45 years. The control group consisted of 22 patients without pathology of connective tissue or musculoskeletal system.

Determination of Al, Ca, Mg, P, B levels in the serum and urine of patients was performed in the laboratory of analytical chemistry and monitoring of toxic substances of the SI "Kundiev Institute of Occupational Health of the NAMS of Ukraine". Patients' serum and urine were collected according to the sampling protocol [8, 10]. By the method of atomic emission spectroscopy with inductively coupled plasma (AES-ICP) the content of essential elements (Ca, Mg, B, Al, P) was determined in the samples using the device "Ortima 2100 DV" of Perkin-Elmer (USA). To determine the elemental composition of blood serum, 0.5 ml of centrifuged plasma was taken, then 4.5 ml of 10% solution of HNO_3 (Merck) was added and centrifuged for about 20 minutes at 5000 rpm The supernatant was put

into a flask and was brought to a volume of 10ml. To determine the concentration of elements in 5 ml of urine, 5 ml of 4% HNO_3 solution (Merck) was added [3]. Processing was performed by the method of parametric statistics using standard programs "Microsoft Office Excel" and the program "Statistica" (licensed statistical program) [2].

RESULTS AND DISCUSSION

The study found an excess of the average concentration of Al in the serum of miners with CLSR (115.07 μMol/l) compared with the control group (3.3 μMol/l) by 34 times, and in the group of miners with work experience from 10 to 15 years, the concentration was 6 times higher (20.01 μMol/l), while in the group with work experience from 16 to 32 years – by 36 times (118.98 μMol/l) compared with the control group ($p<0.05$) (Table 1). This may be due to the fact that the miners under study were exposed to many hazards in the production environment (apart from work loading in the performance of their professional duties), among which a special place is occupied by exposure to waste dust, which contains a significant list of chemicals.

Table 1

Concentration of MaE and ME in serum of miners with CLSR of occupational genesis (mg/l, μMol/l, mMol/l), M±m, median

Essential element	Concentration of elements in patients under study				
	control group, n=22	Concentration of elements in groups of patients by work experience			p
		total, n=20 (2)	work experience 10-15 years, n=10 (3)	work experience 16-32 years, n=10 (4)	
Al (mg/l)	0.10±0.03	0.62±0.05	0.34±0.065	1.31±0.56	$p_{1-4}<0.05$
μMol/l	3.3	115.07	20.01	118.98	
Median	0.09	3.11	0.54	3.21	
B (mg/l)	0.070±0.02	0.17±0.05	0.17±0.044	0.15±0.04	$p_{1-3}<0.05$
μMol/l	62.90	25.90	25.91	19.43	$p_{1-4}<0.05$
Median	0.68	0.27	0.28	0.21	
Ca (mg/l)	86.44±5.54	93.44±12.68	109.87±9.82	79.17±6.33	$p_{1-3}<0.05$
mMol/l	2.16	2.82	3.20	1.98	$p_{3-4}<0.05$
Median	86.44	113.13	128.4	79.25	
Mg(mg/l)	17.43±1.40	18.86±2.32	21.30±1.92	16.86±0.86	$p_{1-3}<0.05$
mMol/l	0.72	0.97	0.82	0.65	$p_{3-4}<0.05$
Median	17.40	23.57	19.90	15.79	
P(mg/l)	98.5±2.20	76.91±5.74	109.85±57.13	43.45±2.63	$p_{1-3}<0.05$
mMol/l	3.20	1.66	11.83 366.41	1.43	$p_{1-4}<0.05$
Median	99.30	51.37		44.43	

According to the results of the study, the average content of Ca in the serum of patients with CLSR (2.82 mMol/l) was 1.3 times higher compared to the control group (2.16 mMol/l) ($p<0.05$) and in the group of miners with work experience from 10 to 15 years, the concentration of Ca (3.20 μMol/l) was 1.6 times higher than in the group with a longer work experience (1.98 mMol/l) ($p<0.05$). A decrease in Ca concentration with increasing underground work experience may explain the increased risk of fractures of the tubular bones, vertebral bodies due to reduced quality bone structure, and, as a result, the development of chronic diseases of the connective tissue and musculoskeletal system.

The average concentration of element B in the blood of patients with chronic lumbosacral radiculopathy (25.90 μMol/l) was determined to be 2.5 times lower compared to the control group (62.90 μMol/l). It should be noted that this indicator was the lowest in the group of subjects with the work experience from 16 to 32 years (19.43 μMol/l) and this difference between the indicators of both groups compared with the control was characterized by a high degree of significance ($p<0.05$) (Table 1). These data explain the increased risk of osteopenia or osteoporosis in miners with chronic lumbosacral radiculopathy, with decrease in the concentration of B in the body, as this chemical element has a

regulatory effect on the functioning of sex hormones and parathyroid hormone, which affect the quality bone structure.

The average level of Mg (0.97 mMol/l) in the serum of patients with occupational CLSR exceeded the same indicator in the control group (0.72 mMol/l) by 1.34 times. The level of Mg in the group of patients with work experience in underground working conditions from 16 to 32 years (0.65 mMol/l) was lower than the same indicator of the control group and the indicator in the group with work experience from 10 to 15 years (0.82 mMol/l) and the difference between the indicator in the first group and the indicator of the control and second groups was significant ($p<0.05$). Decreased levels of Mg in the blood of patients can lead to its insufficiency and imbalance in the system Mg^{2+} - Ca^{2+}, resulting in dysfunction of the musculoskeletal system, the pathology of which is a risk factor for CLSR, especially in workers with work experience for more than 15 years in hazardous conditions.

As a result of the study, it was found that the average concentration of P in the serum of patients with occupational CLSR (1.66 mMol/l) was 1.5 times lower than this figure in the control group (3.20 mMol/l). In the group with shorter work experience the concentration of P (11.83 mMol/l) was 3.6 times higher and in the group with longer work experience (1.43 mMol/l) was by 50% lower compared to the concentration in the control group (3.20 mMol/l). In addition, a significant difference was found between the indicators of the control and both groups under study ($p<0.05$) (Table 1).

For the correct interpretation of the level of MaE and ME in the body of patients with chronic lumbosacral radiculopathy, the level of these elements in the urine of miners was determined. Analyzing the obtained data, it was found that the average concentration of Al in the experimental group (1.26 μMol/l) was exceeded by 46% compared to the control group (0.85 μMol/l) ($p<0.05$). It was also determined that the level of Al was higher in both groups compared to the control by 51% (1.334 μMol/l – in group I and 1.14 μMol/l – in group II), therewith difference between the indicators in the control and both groups under study was significant ($p<0.05$) (Table 2).

Table 2

Concentration of MaE and ME in the serum of miners with CLSR of occupational genesis (mg/l, μMol/l, mMol/l), M±m, median

Essential element	Control group, n=22 (1)	Concentration of elements in patients under study			p
		total, n=20 (2)	work experience 10-15 years, n=10 (3)	work experience 16-32 years., n=10 (4)	
Al (mg/l)	0.023±0.008	0.036±0.008	0.036±0.003	0.031±0.008	$p_{1-3}<0.05$
μMol/l	0.85	1.26	1.334	1.14	$p_{1-4}<0.05$
Median	0.023	0.034	0.036	0.031	
B (mg/l)	0.13±0.08	0.23±0.008	0.21±0.03	0.25±0.08	$P_{1-4}<0.05$
μMol/l	27.78	25.90	14.80	34.22	
Median	0.30	0.28	0.16	0.37	
Ca (mg/l)	119.07±20.19	169.07±24.19	182.55±23.76	129.52±24.19	$p_{1-3}<0.05$
μMol/l	2.944	3.195	3.252	2.671	$P_{1-4}<0.05$
Median	118.0	128.06	130.37	107.09	
Mg(mg/l)	40.97±8.36	60.97±8.36	90.03±13.79	51.95±8.36	$p_{1-3}<0.05$
mMol/l	2.036	2.406	3.287	1.886	$P_{1-4}<0.05$
Median	49.50	59.50	79.93	45.86	
P(mg/l)	370.20±48.35	552.90±99.23	533.53±56.22	511.59±99.23	$p_{1-2}<0.05$
mMol/l	11.96	19.0	18.3	19.1	$p_{1-3}<0.05$
Median	370.70	588.70	567.05	588.70	$p_{1-4}<0.05$

The average concentration of Ca in the urine of the subjects of the control group and patients with CLSR of occupational genesis was approximately the same, being 3.195 mMol/l and 2.944 mMol/l, respectively. The concentration of Ca (3.252 mMol/l) in patients with work experience from 10 to 15 years was by 10% higher than in the control group and by 18% in the group with work experience from 16 to

32 years, and the difference between the control and both groups under study was significant ($p<0.05$). This pattern indicates a decrease in the concentration of Ca in the urine of miners with CLSR with increasing work experience in hazardous conditions.

The analysis of the study results showed that the average level of B (25.90 μMol/l) in the urine of patients with CLSR was slightly lower than in the control group (27.78 μMol/). The concentration of B (34.22 μMol/l) in the second study group exceeded the similar indicator in the control group by 24% ($p<0.05$). Analyzing the results of the survey, it was found that the average level of P (19.0 mMol/l) in the urine of patients with occupational chronic radiculopathy was higher than the level in the control group (11.96 mMol/l) by 57%. Phosphorus concentrations (18.3 mMol/l and 19.0 mMol/l, respectively) in both groups under study were higher than in control group on average by 54% ($p<0.05$). An increase in the level of phosphorus in the urine of patients with occupational CLSR compared with the control group indicates its excess in the body, resulting in blocking the transition of vitamin D in its active forms and impairment of qualitative and quantitative bone structures, which are risk factors for osteoporosis.

The average level of Mg in the urine of miners with CLSR (2.406 mMol/l) exceeded this figure in the control group (2.036 mMol/l) by 20%. A significant difference was found between the indicators of Mg concentration of both study groups and the control one ($p<0.05$). It should also be noted that the concentration of Mg in the urine of miners with work experience in hazardous conditions from 10 to 15 years (3.287 mMol/l) exceeded the same indicator in the group with work experience from 16 to 32 years (1.886 mMol/l) by 70%, which indicates a decrease in the concentration of Mg in the blood of the study subjects with an increase in work in hazardous conditions.

CONCLUSIONS

1. According to the results of the study, the average concentration of Al in the blood of patients with CLSR (115.07 μMol/l) was exceeded almost by 35 times compared to the control group, which has a negative impact on the functioning of enzyme proteins by substituting of Ca^{2+} and Mg^{2+} ions in their allosteric center, and thus leading to blocking the maturation of calcium phosphate crystals and osteoid mineralization. Thus, Al can be proposed as a biomarker of disorders of quantitative and qualitative bone tissue in patients of this category.
2. Decreased levels of Ca (1.98 mMol/l) and Mg (0.65 mMol/l) in the serum of miners with occupational chronic lumbosacral radiculopathy with increasing work experience in hazardous working conditions was revealed. Such results can be used as a basis for a screening study of the level of essential elements in workers in this category with long work experience in underground conditions for timely detection of risk factors for chronic radiculopathy.
3. The study revealed a statistically significant increase in the level of P in the urine in all groups compared with the control. Increased phosphorus levels in patients with CLSR can lead to blocking the transition of vitamin D in its active forms and impairment of the quantitative and qualitative structure of bone tissue.
4. There was revealed an decrease in the concentration of B in the blood of patients with CLSR by 2.5 times (25.9 μMol/l) compared with the control group, and this may lead to a decrease in the regulatory effect of this element on the functioning of sex hormones and parathyroid hormone, which affect the qualitative structure of bone tissue.

Conflict of interest. The authors declare no conflict of interest.

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