динамика в состоянии пациентки: уменьшилась кратность и объем мочеиспусканий, в течение ночи частота мочеиспускания снизилась до 1-2 раз.

При выписке проведено повторное исследование анализа мочи по Зимницкому. Общий диурез составил 1980 мл, дневной диурез – 810 мл, ночной – 1170, колебания удельного веса мочи находились в диапазоне от 1006 до 1014. Следовательно, проведенное лечение было эффективным, купирована полиурия, улучшилась концентрационная способность почек.

Пациентка была выписана с рекомендациями продолжить начатое лечение в амбулаторных условиях. Учитывая высокую вероятность ремиссии послеоперационного ЦНД у данной пациентки, которая обычно приходится на 3-6 месяцы после операции, рекомендуется контроль водного баланса и электролитных показателей крови (натрий,калий, глюкоза).

Заключение: таким образом, в данном клиническом случае четко прослеживается причинная связь предшествующего нейрохирургического вмешательства в гипоталамо–гипофизарной области по поводу пролактинсекретирующей макроаденомы гипофиза и развившихся сразу после операции проявлений несахарного диабета (сухость во рту, полиурия), и эффективностью назначенной терапии синтетическим аналогом вазопрессина. Совокупность указанных фактов в сочетании с данными лабораторно-инструментальных исследований подтверждают центральный генез развития несахарного диабета.

Можно полагать, что анализ данного клинического случая улучшит осведомленность врачей о данной патологии и позволит своевременно распознавать и начинать лечение ЦНД.

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FEATURES OF THE COURSE AND TREATMENT OF KNEE OSTEOARTHROSIS IN PATIENTS WITH LOW BONE MINERAL DENSITY

Abstract. Osteoarthritis and osteoporosis are one of the most common diseases among the elderly, which significantly impair the quality of life and even reduce its duration in patients. The study of the relationship between osteoporosis and rheumatic diseases is of considerable interest not only among rheumatologists but also specialists from other branches of medicine. In the article the features of the course and clinical manifestations of osteoarthrosis (OA) of the knee joints, as well as the effect of anti-inflammatory drugs on its course in patients with reduced bone mineral density. According to current guidelines for the treatment of osteoarthritis, symptomatic slow-acting anti-inflammatory drugs (SYSADOA) are used. Due to the influence of osteoporosis on OA, namely, the more severe course, more pronounced X-ray changes, increased CRP is an important consideration to date of the features of the flow of OA with reduced bone mineral density.

Key words: osteoarthritis, osteoporosis, mineral density of bone tissue, anti-inflammatory effect, diacerein.

The relevance of the topic:

Today, a considerable amount of attention is paid to the treatment of diseases of the musculoskeletal system associated with lesions of the skeletal system, such as osteoarthritis and osteoporosis, which by their prevalence compete with cardiovascular diseases and

often lead to incapacity and disability. Osteoarthritis and osteoporosis are one of the most common diseases among elderly patients, they significantly worsen the quality of life and even reduce the lifespan of patients. [7] The study of the relationship between osteoporosis and rheumatic diseases is of considerable interest not only among rheumatologists but also specialists from other branches of medicine. [8]

Osteoarthritis (OA) is the most common form of arthritis and the main cause of disability. [1] The most common localization of OA is the knee joint, 24% of the total population. [2] In Ukraine in recent years, the prevalence of osteoarthritis has remained high.

The prevalence of OA is 2200.6 per 100 thousand. The population varies in different regions from 13.6 percent to 41.7 percent and increases significantly as the population ages, and the incidence is 497.1 cases per year. [6]

There has been a discussion about the relationship in the development of these diseases for many years. There are different points of view. One of them suggests that in old and elderly age osteoporosis can trigger the pathogenetic chain of osteoarthritis, and an alternative view is based on the fact that osteoarthritis and osteoporosis are independent nosological forms that are independent of each other. [5]

Recent studies have shown that there are common and dependent interaction mechanisms between the bone and cartilage tissues [3]. Osteoblasts and chondrocytes have a common embryological origin with mesenchymal tissue.

The connection of microtraumas of the subchondral bone with cartilage damage has been established. As a result of mechanical compression of osteoblasts of the subchondral bone, the production of interleukin-6 (IL) increases and the level of osteoprotegerin decreases (osteoprotegerin, OPG). A decrease in the osteoprotegerin (OPG) / ligand ratio of the nuclear activator receptor kappa B receptor activator (RANKL) causes damage to both bone and cartilage. It has been established that a decrease in the OPG / RANKL ratio significantly accelerates the progression of OA. [4]

In Ukraine, signs of systemic osteoporosis and clinical and radiological symptoms of gonarthrosis are found in 14.3% of women in the age group of 40-44 years, and at the age of 65-69 years, the combination of these diseases occurs in 83.2% of women.[9]

Due to the effect of osteoporosis on the course of OA, namely, a more severe course, more pronounced X-ray changes, increased CRP, it is important today to study the features of OA with a reduced BMD.

According to current guidelines for the treatment of osteoarthritis, symptomatic slow-acting anti-inflammatory drugs (SYSADOA) are used. Among them, the most common are chondroitin sulfate, glucosamine sulfate, diacerein, unsaponified soybean and avocado compounds and ginger root extract and others.

Objective: To investigate the features of the course, clinical manifestations and the effect of anti-inflammatory drugs on the course of OA of the knee joints in cases of reduced bone mineral density.

Materials and research methods:

The study was conducted on a basis of the therapeutic department №1 of the Kiev City Clinical Hospital №7. The study included 100 patients (60 women and 40 men) aged 34 to 80 years. OA patients were divided into 3 groups depending on the index of bone mineral density (BMD). First group included patients with OA and normal BMD, second group included patients with osteopenia, third group – with osteoporosis. General characteristics of examined patients are presented in table.1.

Table 1

CHARACTERISTICS OF EXAMINED PATIENTS

Indicator	Group
Number of patients of them: men women	100 40 60
Middle age, years	57,00 (IQR 51,00-68,00)
Average body mass index, kg/m²	30,00 (IQR 25,50-35,50)
Patients with: Normal weight Excessive weight Obesity 1 Obesity 2 Obesity 3	 20 30 24 18 8
Number of patients who had a stage for Kellgren-Lawrence: I II III	 9 73 18
Number of patients who had: Normal BMD Osteopenia Osteoporosis	 32 38 30

Criteria for inclusion of the examined:

1. The diagnosis of osteoarthritis of the knee to the criteria of EULAR.

2. Men and women are aged 30-80 years.

3. Before beginning of the study, patients suffered from pain for at least 15 to 30 days, and general symptoms of the disease were observed for at least six months.

4. Patient consent to participate in the study.

Exclusion criteria for subjects:

1. Refusal to participate in the study

2. The presence of malignant neoplasms.

4. Untimely laboratory and instrumental methods of research.

Research methods:

1. General clinical: a collection of complaints and anamnesis, objective examination, assessment of arthrological status of patients, questionnaires (filling in cases of adapted questionnaires from WOMAC, Leken, VAS).

2. Laboratory: cholesterol, blood glucose, bilirubin, ALT, AST, creatinine, uric acid in the blood, CRP, IL-1, IGF-1, NO.

3. Instrumental (X-ray examination of the knee joints, ultrasound densitometry)

4. Methods of biomedical statistics.

Results and discussion:

Table 2

DEPENDENCE OF X-RAY STAGE OF OA ON THE REDUCTION OF BMD

Indicator	Group 1 normal BMD (n=32)	Group 2 osteopenia (n=38)	Group 3 osteoporosis (n=30)
Number of patients who had a stage for Kellgren – Lawrence: I II III	6 24 2	3 29 6	0 20 10

As can be seen from the data in table 2, more pronounced radiological changes are observed in cases of osteopenia and osteoporosis. Such data indicates a more severe course of OA in cases of reduced BMD.

Table 3

DYNAMICS OF VAS AND LEKEN INDICATORS DEPENDING ON THE BMD

Indicator	Group 1 normal BMD (n=32)		Group 2 osteopenia (n=38)		Group 3 osteoporosis (n=30)	
	Me	IQR	Me	IQR	Me	IQR
VAS to rest, mm (0-100)	14,50	4,25-20,25	26,00*	21,50-31,00	40,00**	31,75-47,25
VAS while walking, mm (0-100)	51,00	34,75-61,00	59,00*	52,50-65,00	79,00**	68,25-87,25
Leken Index, points (0-25)	6,00	5,00-12,00	9,00*	8,00-12,50	13,50**	11,00-15,00

* The reliability of the differences $p < 0,05$
** The reliability of the differences $p < 0,05$ in comparison with the 2nd group

Analyzing the intensity of pain according to the VAS scale, a statistically significant difference was established between the three groups of patients. The most pronounced pain intensity was observed in cases of osteoporosis and osteopenia compared with normal BMD (Tabl. 3). So, patients with normal BMD had VAS indices at rest 14.50 (IQR 4.25-20.25), VAS when walking 51.00 (IQR 3.75-61.00), in cases of osteopenia, VAS at rest was 26 00 (IQR 21.50-31.00), VAS while walking - 59.00 (IQR 52.50-65.00), respectively, and in cases of osteoporosis - 40.00 (IQR 31.75-47.25) and 79.00 (IQR 68.25-87.25), respectively.

With the help of Leken algo-functional index severity of gonarthrosis was estimated. It turned out that indicators of the Leken index among three groups statistically differed significantly. Patients with normal BMD showed better performance (6.0 (IQR 5.00–12.00)) than patients with osteopenia (9.00 (IQR 8.00–12.50)), and patients with osteoporosis (13.50 (IQR 11.00-15.00) - worse than patients with osteopenia (Tabl. 3). This indicates a more severe course of gonarthrosis in cases of reduced BMD.

Table 4

DYNAMICS OF WOMAC INDICATORS DEPENDING ON THE BMD

Indicator	Group 1 normal BMD (n=32)		Group 2 osteopenia (n=38)		Group 3 osteoporosis (n=30)	
	Me	IQR	Me	IQR	Me	IQR
WOMAC (pain), mm (0-500)	219,50	183,00-254,50	304,00*	232,00-381,50	390,00**	282,50-469,75
WOMAC (stiffness), mm (0-200)	68,50	33,25-98,50	74,00*	49,00-107,00	129,00**	83,25-151,25
WOMAC (functional activity), mm (0-1700)	467,50	324,50-714,25	674,00*	428,00-830,50	1052,50**	734,00-1278,00
Total index WOMAC, mm (0-2400)	781,50	569,25-1080,75	1044,00*	825,00-1277,5	1503,00**	1170,50-1876,25

* The reliability of the differences p <0,05

** The reliability of the differences p <0,05 in comparison with the 2nd group

When assessing the WOMAC index, a statistically significant difference in the indices among patients with normal and low BMD was also detected, as can be seen from the table. 4. Yes, the pain was intense in cases of reduced BMD, especially in cases of osteoporosis. Stiffness was also most pronounced in cases of osteoporosis and somewhat less of osteopenia. Functional activity was less pronounced among the 1st group, more in the 2nd group and the largest in the 3rd group of the examined.

Table 5

IMMUNOLOGICAL INDICATORS DEPENDING ON THE REDUCTION OF BMD

Indicator	1 group normal BMD (n=32)		2 group osteopenia (n=38)		3 group osteoporosis (n=30)	
	Me	IQR	Me	IQR	Me	IQR
IL-1,pg/ml	18,00	11,00-37,50	27,00*	3,00-40,50	31,73*	19,75-54,17
NO, mkmol/l	2,80	1,70-6,00	3,80	2,00-6,70	5,80**	2,85-8,36
IGF-1,ng/ml	589,00	502,00-600,00	524,00*	363,50-585,00	519,00*	449,00-600,00
CRP, mg/l	4,00	4,00-6,00	6,00*	6,00-8,00	17,00*	6,00-23,25
ESR, mm/hr	13,00	8,25-17,00	14,00	10,00-18,00	20,50*	15,00-24,25
Uric acid, umol/l	317,17	254,75-343,75	321,3	267,5-364,00	403,77*	324,50-499,00

* The reliability of the differences p <0,05

** The reliability of the differences p <0,05 in comparison with the 2nd group

When analyzing the indicators of the inflammatory process between patients with normal and lowered BMD, a statistically significant difference between these indicators were found. As can be seen from the table. 5, the most pronounced inflammatory process was observed in cases of osteoporosis, as evidenced by higher levels of ESR, CRP, IL-1, NO, and reduced levels of IGF-1. The inflammatory process was less pronounced in cases of osteopenia compared with patients with normal BMD. Higher uric acid levels were also observed in cases of osteoporosis.

Table 6

DYNAMICS OF BMD DEPENDING ON THE INTAKE OF INDIVIDUAL SYMPTOMATIC SLOW-ACTING ANTI-INFLAMMATORY DRUGS

Indicator	Prior treatment		After treatment	
	Me	IQR	Me	IQR
Diacerein (n=62)	-1,6	-2,7 – -0,5	-0,9*	-0,9 – 0,4
Glucosamine sulfate (n=18)	-1,7	-2,4 – 0,7	-1,6	-2,4 – 0,3
Ginger root extract (n=20)	-1,6	-2,9 – -1,1	-1,5	-2,3 – 0

* The reliability of the differences p <0.05

As can be seen from table 6, the use of symptomatic slow-acting drugs led to an increase in indicators of BMD. So a statistically significant increase in BMD was observed with patients taking diacerein. Also, the indices of BMD with patients who took ginger root extract significantly changed with positive dynamics. With patients taking glucosamine sulfate, BMD indices did not change significantly.

Table 7

DYNAMICS OF ARTICULAR INDICES IN CASES OF OA WITH DIACEREIN TREATMENT

Indicator		Normal BMD (n=26)		Osteopenia (n=21)		Osteoporosis (n=15)	
		Me	IQR	Me	IQR	Me	IQR
VAS at rest, mm (0-100)	Prior treatment	14,00	5,75-21,00	42,50	25,00-56,25	43,25	33,00-50,50
	After treatment	8,85* (-37%)	4,25-15,5	34,50* (-19%)	20,00-41,75	35,00* (-19%)	28,50-40,5
VAS while walking, mm (0-100)	Prior treatment	37,43	24,50-51,25	76,6	65,00-89,25	73,3	67,25-77,00
	After treatment	26,43* (-29%)	17,25-32,00	61,3* (-20%)	51,75-71,25	62,46* (-15%)	54,50-68,50
Leken index, score (0-25)	Prior treatment	5,00	4,25-6,00	10,00	8,00-11,50	12,69	11,00-15,25
	After treatment	3,00* (-40%)	2,75-4,25	6,9* (-31%)	8,00-11,50	10,23* (-19%)	7,75-13,25

* The reliability of the differences p <0.05

Depending on the indicator of BMD, the effectiveness of treatment of diacerein in cases of OA was evaluated. It was revealed that patients with normal BMD responded to treatment better than patients with reduced BMD, as evidenced by the data from table 7.

Table 8

DYNAMICS OF ARTICULAR INDICES IN CASES OF OA WITH DIACEREIN TREATMENT

Indicator		Normal BMD (n=26)		Osteopenia (n=21)		Osteoporosis (n=15)	
		Me	IQR	Me	IQR	Me	IQR
WOMAC (pain), mm (0-500)	Prior treatment	198,00	146,25-235,00	285,70	221,25-355,25	362,61	312,00-455,50
	After treatment	127,28* (-36%)	97,50-190,75	202,10* (-29%)	131,25-250,00	292,85* (-19%)	278,00-352,00
WOMAC (stiffness), mm (0-200)	Prior treatment	63,85	36,00-98,25	80,70	42,00-131,75	117,46	65,25-152,00
	After treatment	41,71* (-35%)	19,50-56,00	57,50* (-29%)	22,75-91,25	90,08* (-23%)	55,50-111,50
WOMAC (functional activity), mm (0-1700)	Prior treatment	377,86	218,75-482,25	562,00	404,25-800,50	933,23	732,50-128,25
	After treatment	261,43* (-31%)	160,00-368,50	459,50* (-18%)	314,75-618,25	821,46* (-12%)	641,00-994,00
Summary index WOMAC, mm (0-2400)	Prior treatment	639,71	431,25-810,76	928,40	748,50-1206,75	1431,31	1215,00-1696,00
	After treatment	430,43* (-33%)	276,00-621,75	719,10* (-23%)	521,25-889,25	1204,38* (-16%)	1006,50-1427,5

* The reliability of the differences p <0.05

As can be seen from the data in table 8, the index of BMD has a significant impact on the effectiveness of the treatment of OA. Assessing the dynamics of WOMAC indices before and after treatment, it is seen that in cases of normal BMD, pain decreased by 36%, stiffness by 35%, and functional activity improved by 31%. In cases of osteopenia, pain and stiffness decreased by 29%, and functional activity improved by 18%.

Finally, in cases of osteoporosis, pain decreased by only 19%, stiffness by 23%, and functional activity improved by 12%.

Table 9

DYNAMICS OF BMD PARAMETERS IN CASES OF OA WITH DIACEREIN TREATMENT

Indicator	Prior treatment		After treatment	
	Me	IQR	Me	IQR
Normal BMD (n=26)	0,51	-0,40 – 1,30	0,84*	0,10 –1,30
Osteopenia (n=21)	-1,60	-1,87 – -1,33	-0,95*	-1,53 – -0,4
Osteoporosis (n=15)	-3,58	-4,60 – -2,70	-3,02	-3,35 – -2,30

* The reliability of the differences p <0,05

Studying the dynamics of indicators of BMD among the three groups revealed a statistically significant increase in indicators in cases of normal BMD and osteopenia, while in cases of osteoporosis, the indicators did not significantly change (Table 9).

Table 10

DYNAMICS OF IMMUNOLOGICAL PARAMETERS IN CASES OF OA WITH DIACEREIN TREATMENT

Indicator		Normal BMD (n=26)		Osteopenia (n=21)		Osteoporosis (n=15)	
		Me	IQR	Me	IQR	Me	IQR
CRP, mg/l	Prior treatment	5,57	3,25-6,75	8,00	6,00-9,00	13,31	6,00-21,00
	After treatment	4,57* (-18%)	2,00-5,00	6,80* (-15%)	4,75-7,75	12,50 (-6%)	6,25-18,00
ESR, mm/hr	Prior treatment	8,86	6,00-12,25	15,40	10,00-21,25	19,15	14,50-24,50
	After treatment	6,42* (-28%)	6,00-8,50	12,40* (-19%)	7,50-18,50	17,30* (-10%)	12,00-22,00
IL-1,pg/ml	Prior treatment	18,43	11,25-23,00	27,10	7,50-45,75	39,77	18,98-61,50
	After treatment	12,28* (-33%)	4,75-23,00	21,30* (-21%)	6,50-35,50	34,85 (-12%)	16,50-57,50
NO, mkmol/l	Prior treatment	2,37	1,60-28,00	5,14	2,86-7,60	5,05	2,20-7,48
	After treatment	1,54* (-35%)	1,00-2,20	3,89* (-24%)	2,22-5,04	4,11 (-19%)	1,60-7,35
IGF-1, ng/ml	Prior treatment	437,29	245,00-542,00	306,90	193,25-440,50	381,14	234,75-489,00
	After treatment	574,0* (+24%)	569,25-600,00	380,9* (+19%)	227,5-534,72	437,08 (+13%)	351,75-535,00

* The reliability of the differences p <0,05

As for immunological parameters, it is also clear that a statistically significant improvement in immunological parameters was observed in cases of normal BMD and osteopenia, while in cases of osteoporosis, BMD did not significantly change (Table 10).

Findings:

1. As a result of the study, it was shown that patients with reduced BMD have a more severe course of OA.

2. It has been established that patients with reduced BMD on radiographic signs have more severe damage to knee joints according to the classification J.H. Kellgren and J.S. Lawrence.

3. It was revealed that in cases of osteopenia, pain in knee joints is more pronounced at rest and in walking compared to normal BMD, and in osteoporosis, it is much greater compared to normal BMD and osteopenia.

4. Patients with osteopenia and osteoporosis, compared with normal BMD, suffer more severe pain, stiffness, as well as reduced functional activity in knee joints.

5. It is proved that in cases of reduced bone mineral density there is a more intense inflammatory process (according to the ESR, CRP, IL-1, NO, IGF-1) than in cases of normal BMD.

6. The use of symptomatic slow-acting anti-inflammatory drugs, namely diacerein, in cases of OA led to an increase in BMD and changes towards normalization of immunological parameters and articular syndrome, more pronounced in cases of normal BMD and osteopenia while in cases of osteoporosis, immunological parameters did not change significantly.

8. So, in cases of OA with osteopenia, diacerein can be limited, and cases of osteoporosis, it is desirable to include drugs in the treatment of antiosteoporotic.

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