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Dynamics of clinical manifestations of gonarthritis in overweight hypertensive women under the influence of complex therapy

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The aim of the work was to study the dynamics of clinical manifestations of gonarthritis in women with hypertension and overweight under the influence of complex therapy.

Materials and methods. A two-stage study was conducted on the effectiveness of Rosuvastatin and Arginine in the complex therapy for patients with gonarthritis in combination with hypertension and excess body weight. At the first stage, on the basis of the inpatient Rheumatology Department, 198 women hospitalized in the period 2018–2020 were prospectively examined after receiving their informed consent. The follow-up study of the second stage (2019–2021) was carried out at the outpatient department. At the follow-up stage, 134 women were examined. Depending on the accompanying pathology, the patients were divided into three groups.

Results. The use of the proposed treatment option in the complex treatment for selected contingent of patients contributed to a significant reduction in the proportion of patients with movement restriction in Group 2 and Group 3 by 62.21 % and 52.12 %, pain during active movements by 24.89 % and 52.12 % and swelling of the joints by 13.8% and 12.65 %, respectively; a decrease in IL-6 levels in Group 2 and Group 3 by 3.64 and 1.36 times, CRP by 1.97 and 1.12 times, and an increase in IL-10 by 3.57 and 1.62 times, respectively; improvements in WOMAC scores in all studied groups with a significant increase in Group 2 and Group 3.

Conclusions. The combination of Rosuvastatin 20 mg per day for the 3-month course and Arginine 100 ml intravenously No. 10 with subsequent oral administration of 5 ml 4 times daily for 1 month has been found to increase the effectiveness of treatment for patients with gonarthritis combined with hypertension and overweight, reduce the intensity and duration of joint pain syndrome and significantly improve the functional capacity of joints.

Ключові слова: гонартрит, гіпертонічна хвороба, надлишкова маса тіла, ревматологія, комплексна терапія.

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Динаміка клінічних проявів гонартриту в жінок із гіпертонічною хворобою та надлишковою масою тіла під впливом комплексної терапії

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Мета роботи – вивчити особливості динаміки клінічних проявів гонартриту в жінок з артеріальною гіпертензією та надлишковою масою тіла під впливом комплексної терапії.

Матеріали та методи. Здійснили двоетапне дослідження ефективності застосування розувастатину та аргініну в рамках комплексної терапії хворих на гонартрит у поєднанні з артеріальною гіпертензією та надлишковою масою тіла. На першому етапі на базі стаціонара ревматологічного відділення (за умови наявності попередньо підписаної інформованої згоди) проспективно обстежили 198 жінок, які перебували на стаціонарному лікуванні в період 2018–2020 рр. Катамнестичне обстеження другого етапу (2019–2021 рр.) здійснили в поліклінічному відділенні. На цьому етапі обстежили 134 жінки. Залежно від супутньої патології пацієнток поділили на три групи.

Результати. Застосування запропонованого варіанта лікування в рамках комплексної терапії обраного контингенту хворих сприяло достовірному зменшенню частки випадків з обмеженням рухів у Г2 і Г3 (на 62,21 % та 52,12 % відповідно), вираженим больовим синдромом під час активних рухів (на 24,89 % та 52,12 % відповідно), припухлостями суглобів (на 13,8 % та 12,65 % відповідно); зниженню вмісту IL-6 у крові пацієнтів Г2 та Г3 (у 3,64 та 1,36 раза), С-реактивного білка (у 1,97 та 1,12 раза), збільшенню IL-10 (у 3,57 та 1,62 раза відповідно); покращенню показників WOMAC у всіх групах дослідження; достовірне підвищення зафіксували в пацієнток Г2 і Г3.

Висновки. Застосування комбінації розувастатину 20 мг на добу курсом 3 місяці та аргініну 100 мл внутрішньовенно № 10 із переходом на пероральне приймання по 5 мл чотири рази на добу протягом одного місяця підвищує ефективність лікування жінок, хворих на гонартрит у поєднанні з гіпертонічною хворобою та надлишковою масою тіла, зменшує інтенсивність і тривалість суглобового больового синдрому та значно покращує функціональну здатність суглобів.

Gonarthritis (GA) is one of the diseases with the highest level of comorbidity, especially due to damage to the cardiovascular system, and a high cardiovascular risk [1]. The main target effects in the treatment of patients with GA are the reduction of pain syndrome, inflammatory process, and slowing down the degeneration of cartilage tissue. In the case of GA in combination with excess body weight (EBW) and hypertension (HTN), the main goal of treatment is to achieve a maximum reduction in the progression of degenerative processes in the joints, a decrease in body mass index (BMI) and the long-term overall risk of cardiovascular morbidity and mortality [2,3], as well as improving the quality of patients' life [4,5].

According to the Osteoarthritis Research Society International (OARSI) recommendations, the most important

in the treatment and prevention of GA progression are adequate physical exercises and joint unloading, timely termination of the inflammatory process and normalization of pro-oxidant/antioxidant balance, early prescription of disease-modifying GA drugs, appropriate use of orthopedic and surgical treatment. Basic drug therapy for GA patients should include symptom-modifying and structure-modifying drugs. Among symptom-modifying agents, preference is usually given to the use of non-steroidal anti-inflammatory drugs in combination with structure-modifying agents [6,7,8].

Aim

Considering the above, the purpose of the work was to study the dynamics of clinical manifestations of GA in women with HTN and EBW under the influence of complex therapy.

Materials and methods

The study was carried out in two stages. At the first stage, on the basis of the Rheumatology Department of "City Hospital No. 10" (Zaporizhzhia, Ukraine), 198 women hospitalized in the period 2018–2020 were prospectively examined after receiving their informed consent.

The follow-up study of the second stage (2019–2021) was carried out at the outpatient department of the "Primary Health Care Center No. 9" (Zaporizhzhia, Ukraine). At the follow-up stage, 134 women were examined.

The diagnosis of GA was made following the ICD-10 criteria, the Association of Rheumatologists of Ukraine recommendations. The diagnosis of HTN was verified by the order of the Ministry of Health of Ukraine No. 384 dated 05.24.2012. The presence of EBW was determined in accordance with the WHO recommendations (1998). BMI was calculated according to the formula: BMI = body weight (kg) / height^2 (m). If the BMI was in the range of 24.0–29.9 kg/m^2, then EBW was diagnosed, interval 30.0–34.9 kg/m^2 corresponded to class 1 obesity. Female patients with the fourth X-ray stage of GA, stage III HTN and class 2–3 obesity were not included in the study.

In order to analyze the influence of comorbid pathology on the main disease course, all the examined women were divided into three groups. The first group (G1) included 59 women with GA symptoms without accompanying pathology (36 women at the second stage of the study); the second group (G2) included 74 women with GA and HTN (53 women at the second stage); the third group (G3) included 65 women with GA, HTN and EBW (41 women at the second stage).

All the patients underwent a standard general clinical examination, including physical examination, history taking, instrumental and laboratory tests. The following questionnaires were used to assess the level of pain syndrome: the Lequesne algofunctional index and WOMAC osteoarthritis index. To evaluate the Lequesne index, questionnaires were used, based on which, the patients were interviewed, and the results were scored in points. When calculating the WOMAC functional index, the patients answered 24 questions that characterized the severity of pain (5 questions), stiffness (2 questions) and functional activity (17 questions).

The analysis of the clinical effectiveness of complex treatment was evaluated before the start of treatment, upon admission to the hospital, by determining changes in the locomotor apparatus and functional tests that characterized the degree of impaired motor activity of the joints, the intensity of the painful and inflammatory components and the expressiveness of the joint syndrome, as well as changes in BMI, dynamics of HTN indicators. Patients in G1 without concomitant pathology received standard therapy. Patients in G2, in addition to basic therapy, received Rosuvastatin 20 mg/day for 3 months and Arginine hydrochloride 4.2 % 100 ml intravenously No. 10 with subsequent oral Arginine aspartate administration (5 ml) 4 times daily for 1 month. Patients in G3, in addition to the standard therapy of GA and multimorbid pathology, received Rosuvastatin 20 mg/day for 3 months and Arginine hydrochloride 4.2 % 100 ml intravenously No. 10 with subsequent oral Arginine aspartate administration (5 ml) 4 times daily for 3 months. At the outpatient stage of treatment, patients with signs of significant joint functional impairment received compresses with Dimethyl sulfoxide solution in combination with Nimesulide gel for 2 weeks followed by the use of typical physiotherapeutic procedures, mainly of a thermal nature, for 1 month.

In order to normalize body weight, diet therapy was recommended: to exclude fat, smoked, salty foods with a predominance in the diet of dairy products, vegetable soups, cereals, compotes; to increase water intake (2.2–2.5 liters per day); to avoid alcohol consumption and limit salt intake. It was recommended to add dairy, fish products, vegetables and fruits enriched with vitamins E, C, D, and drink green tea. The patients were educated on lifestyle modification, nutrition, and weight loss.

Evaluation of the treatment effectiveness on the outpatient basis using the method proposed by us was carried out by analyzing the dynamics of the GA clinical picture, changes in pro-oxidant and antioxidant systems, C-reactive protein levels, blood serum cytokine profile and lipid spectrum.

The results obtained were processed statistically using a Microsoft Excel package and the Biostatistics 7.0 program.

Normality of distribution was assessed using the Shapiro–Wilk test. Differences between data that did not meet the criteria for a normal distribution were compared using non-parametric methods of statistical analysis. Significance of differences in qualitative characteristics was assessed using Pearson's chi-squared test, and Fisher's exact method was used to compare small studied groups.

Results

The frequency analysis of the arthralgic symptoms in GA patients with HTN and EBW in the treatment dynamics is presented in *Table 1*.

As can be seen from the obtained results, a significant decrease in the proportion of patients with pain during active and passive movements was found in all groups after treatment. The proportion of patients with a feeling of joint stiffness was significantly decreased in G2 (by 14.2 %), and the index of joint swelling was significantly lower in G2 and G3, where the number of patients with joint swelling was 13.8 % and 12.65 % reduced, respectively.

Table 1. The frequency of arthralgic symptoms in GA patients with HTN and EBW in the treatment dynamics, %

Arthralgic symptoms	G1		G3		G3	
	Before, n = 59	After, n = 36	Before, n = 74	After, n = 57	Before, n = 65	After, n = 41
Pain without exertion	15.25	13.88	18.92	15.78	20.01	19.51
Pain during active movements	74.57	58.33**	45.94	21.05**	47.69	21.95**
Pain during passive movements	8.47	2.77*	17.76	12.28*	24.61	12.19**
Pain on palpation	3.38	2.77	4.05	3.51	16.92	14.63
Movement restrictions	91.52	38.88**	97.29	35.08**	98.46	46.34**
A feeling of stiffness	8.47	5.56	22.97	8.77**	47.69	41.46*
Crepitation	10.17	8.33	86.48	77.19*	98.46	73.17**
Swelling	2.22	2.77	24.32	10.52**	49.23	36.58**
Deformation	91.52	86.11	95.94	92.98	98.46	90.24*

*: $p < 0.05$; **: $p < 0.001$.

Table 2. The results of the joint functional state assessment according to the WOMAC index in GA patients with HTN and EBW in the treatment dynamics

Indexes measurement WOMAC, mm	G1		G2		G3	
	Before, n = 59	After, n = 36	Before, n = 74	After, n = 57	Before, n = 65	After, n = 41
Pain	195.1 ± 18.1	158.6 ± 9.1*	212.5 ± 19.9	178.6 ± 9.3	256.5 ± 26.3	195.8 ± 13.2*
Stiffness	47.3 ± 5.3	38.2 ± 2.5	61.2 ± 3.7	34.6 ± 1.3*	90.7 ± 4.2	63.4 ± 2.1*
Functional insufficiency	712.2 ± 26.8	565.2 ± 9.4*	801.4 ± 25.9	656.8 ± 12.3*	916.9 ± 22.7	783.6 ± 11.4*

*: $p < 0.05$; **: $p < 0.001$.

Table 3. Indicators of the Lequesne index in GA women with HTN and EBW in the treatment dynamics, %

Lequesne index	G1		G2		G3	
	Before, n = 59	After, n = 36	Before, n = 74	After, n = 57	Before, n = 65	After, n = 41
Mild, 1–4	–	30.56**	–	33.33**	–	–
Moderate, 5–7	76.27	58.33**	48.64	35.08**	12.3	29.26**
Severe, 8–10	15.25	8.33*	32.43	21.05**	43.07	36.58*
Very severe, 11–13	8.47	2.77*	18.91	10.52*	24.61	19.51
Extremely severe, ≥14	–	–	–	–	20.0	14.63

*: $p < 0.05$; **: $p < 0.001$.

Table 4. The serum levels of IL-6, IL-10 and CRP in GA women with HTN and EBW in the treatment dynamics

Parameter, units of measurement	Reference values	G1		G2		G3	
		Before, n = 59	After, n = 36	Before, n = 74	After, n = 57	Before, n = 65	After, n = 41
IL-6, pg/ml	<9.1 pg/ml	22.12 ± 2.47	18.67 ± 1.62	29.35 ± 1.11	8.05 ± 1.60**	34.19 ± 0.79	25.13± 3.19*
IL-10, pg/ml	<9.1 pg/ml	8.53 ± 1.29	11.26 ± 2.06*	7.54 ± 1.61	14.87 ± 1.39*	9.85 ± 2.46	10.02 ± 1.64*
CRP, mg/l	<0.4 mg/l	5.20 ± 0.21	1.44 ± 0.15*	8.11 ± 0.48	2.27 ± 0.76*	20.00 ± 1.00	12.34 ± 1.25*

*: $p < 0.05$; **: $p < 0.001$.

According to the survey and examination of female patients in the treatment dynamics, the percentage of patients with limitation of joint movements was decreased by 62.21 % in G2 and by 52.12 % in G3 indicating the effectiveness of adding Rosuvastatin and Arginine to the basic therapy for GA women with HTN and EBW.

Positive dynamics have also been revealed regarding pain and limitation of mobility. It was important for improving well-being during the night hours. The sleep of most patients was becoming more stable. At the end of the treatment course, women with initial EBW reported an average weight loss of 0.5–1.5 kg every 3 months. BMI was decreased by an average of 11.70 % in 23.88 % of patients.

The analysis of joint functional state assessment findings according to the WOMAC index after treatment has shown a significant decrease in all indicators in all patients. In particular, a decrease in pain sensations was documented in G1 patients by 1.23 times, G2 – by 1.19 times, G3 – by 1.31 times in comparison with the corresponding indicator before the treatment (*Table 2*).

A significant improvement in the joint functional capacity was revealed in G1 patients by 1.26 times, G2 – by 1.22 times, G3 – by 1.17 times, and stiffness reduction in G2 by 1.76 times, in G3 – by 1.43 times compared to these indicators before the treatment.

The GA course severity in the treatment dynamics was also determined according to the Lequesne index. The examination findings of women are presented in *Table 3*.

The analysis of the Lequesne index has shown that a mild course of GA was not observed in all examined groups of patients at the beginning of treatment. A moderate course, according to the methodology, was found in 76.27 % of G1 patients, 48.64 % of G2 patients, and 12.30 % of G3 patients. A very severe course of GA was observed in 8.47 % of G1 patients, 18.91 % of G2 patients, and 24.61 % of G3 patients. An extremely severe course

was assessed only in G3 patients in 20.0 % of cases. In the treatment course, significantly ($p < 0.001$) improved indicators were documented in all groups, both due to an increase in cases of mild course in G1 and G2 and an increase in moderate course in G3.

It is well known that the progression of GA, especially when it is combined with HTN and EBW, depends on the intensity of immune response to damage, which involves pro-inflammatory cytokines and is accompanied by an increase in the content of C-reactive protein (CRP). Therefore, we examined changes in the CRP level as an indicator of degenerative cartilage alterations depending on the treatment by the proposed method. The study results on the serum concentrations of CRP, interleukin-6 (IL-6) and interleukin-10 (IL-10) in women with GA of the studied groups are presented in *Table 4*.

The analysis of on-treatment changes in serum IL-6 concentration has shown a general downward trend, significantly expressed in G2 and G3 (by 1.36 and 1.25 times, respectively). At the same time, on-treatment serum IL-10 concentrations were increased by 25.3 % ($p > 0.05$) – in G1, by 49.3 % ($p < 0.05$) – in G2, by 3.6 % ($p > 0.05$) – in G3.

The level of CRP was significantly decreased in all groups of patients (G1 – 3.65 times, G2 – 3.57 times, G3 – 1.62 times). There was no intergroup difference between CRP levels in G1 and G2 after the treatment. At the same time, the difference between these indicators in G1 and G3 was significant indicating the effectiveness of adding Rosuvastatin and Arginine to the standard treatment method, which led to a decrease in the inflammatory process intensity in GA women with comorbid pathology.

It should also be noted that determining the serum level of CRP had a greater diagnostic value due to its long half-life, the absence of fluctuations in the level throughout the day, as well as long-term stability in samples during storage. In this regard, CRP is a more reliable marker of inflammation than other pro-inflammatory cytokines.

Discussion

First of all, it is worth noting that the obtained results do not contradict the conclusions of earlier studies of national and foreign scientists, and once again confirm that the polymorbidity of these diseases significantly complicates the course of GA, which is burdened by HTN and EBW in women. Therefore, standard treatment does not achieve a positive result in normalizing the mechanisms of the cytokine link of chronic inflammation and requires further correction [4,5].

The researchers agree that the search for new ways of complex treatment of severe variants of GA, which positively affect the activation of the glutathione link of antioxidant protection and contribute to the control of the intensity of lipid peroxidation, as those used in our study, is completely justified and promising [1,2,7].

Conclusions

1. The peculiarities of the GA clinical manifestations in women with HTN and EBW under the influence of complex therapy were dynamically studied. The combination of Rosuvastatin 20 mg per day for the 3-month course and Arginine 100 ml intravenously No. 10 with subsequent oral administration of 5 ml 4 times daily for 1 month has been found to increase the effectiveness of treatment for patients with GA combined with hypertension and overweight, reduce the intensity and duration of joint pain syndrome and significantly improve the functional capacity of joints.
2. The use of the proposed treatment option in the complex therapy for GA women in combination with HTN and EBW resulted in a significant reduction in the proportion of patients with movement restriction in G2 and G3 by 62.21 % and 52.12 %, pain on active movement by 24.89 % and 52.12 % and swelling of the joints by 13.80 % and 12.65 %, respectively, indicating the effectiveness of adding the proposed type of drugs to the basic therapy.
3. The prescription of the proposed treatment complex led to a decrease in the content of IL-6 in G2 and G3 by 3.64 and 1.36 times, CRP by 1.97 and 1.12 times, and an increase in IL-10 by 3.57 and 1.62 times, respectively.
4. According to the WOMAC indicator, the proposed treatment method caused improvements in indicators of all studied groups, however, a significant increase occurred in G2 and G3, proving the need for the use of combined therapy for GA women with HTN and EBW as components of the metabolic syndrome.
5. On the treatment, according to the Lequesne index analysis, significantly improved indicators were revealed during the disease course in all groups, both due to the increase in the cases of mild severity in G1 and G2 and the increase in the moderate one in G3.

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