

Dynamics of clinical parameters and indicators of quality of life in the course of long-term combined treatment with the drug Target T - orally and intramuscularly or periarticular

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SUMMARY

The purpose of the work is to determine the dynamics of clinical parameters and indicators of quality of life (QOL) according to the SF-36 and HAQ questionnaire in patients with osteoarthritis of the knee and hip joints with various long-term course combined treatment using the homeopathic drug Goal T in combination with NSAIDs.

Material and methods. Examined 37 patients with exacerbation of OA in a municipal clinic. Among the patients, women predominated (89%) aged 41 to 65 years, with stages I-III of OA according to Kellgren. Patients were prescribed a course of combined treatment using Target T (A - oral and periarticular; B - oral and intramuscular) in combination with NSAIDs. We studied the dynamics of clinical parameters (VAS at rest and movement, Lequesne indices, WOMAC) and QOL indicators according to the SF-36 and HAQ questionnaire.

Results. During two-year follow-up in patients who received various course combined treatment with Purpose T and NSAIDs, a wave-like course of the process was observed, which is characterized by improvement after the first and other courses of treatment, followed by deterioration after some time. Only when included in the complex treatment Target T for oral and periarticular most of the clinical parameters and QOL indicators, starting from 3 months and after 6, 12, 15, 21 and 24 months from the start of treatment, were statistically significantly better than when using Target T orally and intramuscularly in combination with NSAIDs.

Conclusion. The research results showed that the best results were when using Target T is oral and periarticular. With the second combination, the effect was short-lived and was observed only during the course of treatment.

Key words: osteoarthritis, quality of life, questionnaires SF-36, HAQ, Treatment Efficacy, Target T.

Introduction

The problem of osteoarthritis (OA) in recent decades has acquired great importance due to the widespread prevalence of the disease, the rapid development of functional disorders in the lesion of the bearing joints of the lower extremities - knee and hip [8].

Despite the large number of works devoted to the treatment of OA, more than 75% of patients do not receive adequate treatment, while their quality of life (QOL) remains unsatisfactory. As a rule, only NSAIDs are used for the treatment of OA, and preference is given to the cheapest (nonselective) drugs, the use of which is accompanied by the development of adverse reactions, primarily from the gastrointestinal tract [9]. Modern treatment of OA, recommended by leading foreign and Russian rheumatologists, is aimed at slowing down the progression and postponing for years difficult and expensive endoprosthetics, for example, of the hip joint [7, 10, 25]. In the treatment regimens for OA, according to the EULAR recommendations, it is recommended to include, in addition to NSAIDs, drugs that have a structurally modifying effect on cartilage, in our country they are called "chondroprotectors", although this term is dubious. One of these drugs is chondroitin sulfate (CS), which has a high level of IA evidence according to the data of controlled clinical trials and forms the basis of the basic therapy for OA [7, 25, 27]. On the national pharmaceutical market, CS is represented by Structum (Pierre Fabre, France) for oral administration and Chondrolone (Immunohimpreparat, Russia) for intramuscular administration [13]. Since these drugs are not included in the system of free supplementary drug provision (DLO), patients are forced to purchase them at their own expense. High prices for these drugs, especially Structum, and the need for long-term administration (up to 6 months) restrain their widespread use in patients with OA, especially the elderly, who often suffer from a number of chronic

diseases. The drug Chondrolone, although it costs patients a little cheaper, its use is limited by contraindications. So, this drug cannot be used for benign tumors, in particular of the female genital area, such as fibroids, mastopathy, etc., as well as for chronic varicose veins. Since the overwhelming majority of patients with OA are women of older age groups, these diseases are observed in them quite often - up to 50% of cases.

In this regard, the treatment of OA in these categories of patients presents great difficulties. The use of the homeopathic preparation Purpose T ("Heel", Germany), which has been widely used in practice, deserves interest. The drug contains, in addition to plant, components of the cartilage of the embryonic tissue of animals and can potentially have a chondroprotective direction of action [4, 5, 6, 13, 16, 23] and can also be used orally and parenterally (intramuscularly, intraarticularly, periarticularly). The advantage of this drug is the absence of side effects.

The main criterion for the effectiveness of treatment is usually considered the severity of pain syndrome, the need to use NSAIDs, but it is more important to take into account the effect on joint function and quality of life [10, 11, 12]. The quality of life is an integral characteristic of the patient's physical, psychological, emotional and social functioning, based on his subjective perception [11, 12]. Over the past decade, dozens of clinical studies have been carried out in rheumatology, in which the effectiveness of various treatment methods using QOL questionnaires was assessed. To study the QOL of patients with OA, both general (SF-36, EQ-5D, etc.) and special techniques (KOOS, HAQ, NPB, AIMS-2) are used [1, 2, 12, 14, 15, 19, 21], which are combined with algo-functional indices (VASH, Lekena, WOMAC) [2, 13,

Literary data on the study of the clinical efficacy and quality of life of patients with OA during long-term combined treatment with the use of the drug Target T orally and parenterally (intramuscularly or periarticularly) in combination with NSAIDs are few. This problem is of interest due to the prevalence of these schemes in practice.

The purpose of the work is to determine the dynamics of clinical parameters and indicators of quality of life in long-term course combined treatment using the drug Target T orally and parenterally (intramuscularly or periarticularly) in combination with NSAIDs in patients with osteoarthritis.

Materials and methods

The study included 37 patients who applied to polyclinics in Orenburg (municipal polyclinics MMUZ No. 5 and No. 2 MMUZ named after NI Pirogov) with exacerbation of OA of the hip and knee joints. Among sick women there were more than men (89% and 11%, respectively). The age of the patients ranged from 45 to 65 years, persons from 51 to 60 years predominated. In most patients, the duration of OA did not exceed 10 years. The study included patients with a predominant lesion of the knee and hip joints, meeting the diagnostic criteria of the American College of Rheumatology (ACR, 1991) [18], with stages I-III according to Kellgren, with the severity of pain according to VAS ≥ 40 mm, the need to take NSAIDs. All patients gave informed consent to be included in the study. All patients underwent clinical and arthrological (general pain assessment according to the visual analogue scale (VAS), pain at rest and movement according to the VAS, range of motion in the knee and hip joints according to goniometry data, duration of stiffness, Lequesne indices for gonarthrosis and coxarthrosis, general WOMAC and its three subscales) examinations, as well as radiography and ultrasound of the joints. If the patient has several affected joints, the clinical data were assessed for the most affected joint. The X-ray stage of the process was determined according to the classification of I. Kellgren. Before the start of regular treatment, the patients did not take any medications for two weeks, if possible. Clinical data were supplemented by assessing the quality of life of patients using approved SF-36 and HAQ questionnaires.

Depending on the treatment, the patients were divided into 2 subgroups (A and B). Patients of both subgroups at the beginning of treatment (with exacerbation) received a course of NSAIDs (Nise) and the same physiotherapy - magnetotherapy or "Amplipulse". Nise was used for 14 days at a dose of 200 mg / day. In the future, NSAIDs were used as needed - in connection with the severity of pain

syndrome in various doses and with varying duration.

In addition to NSAIDs, combined treatment with the drug Target T was prescribed in accordance with the schemes recommended in the literature [4, 5, 6, 13, 16, 23]. In subgroup A (n = 20) - orally 1 tablet 3 times a day for 3 months and 2.2 ml periarticularly 2 times a week, for a course of 10 injections. The drug was injected at the points of maximum pain on palpation along the medial or lateral surface of the knee joint and in the projection area of the hip joint along the anterior surface [17]. In subgroup B (n = 17), Target T was administered orally and intramuscularly according to the same scheme. The combined treatment courses were repeated after 3 months.

The characteristics of the patients are presented in Table 1, from which it follows that the patients of both subgroups were comparable in terms of sex, age, stage and severity of the process, and the degree of functional insufficiency of the joints. In both subgroups, stage II-III patients prevailed (75%), and only a quarter of patients had stage I of the process. According to ultrasound of the joints in all patients, the exacerbation of OA was complicated by synovitis and tendinitis.

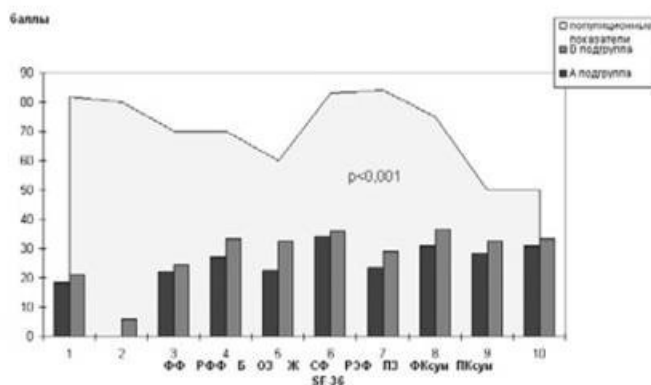
Both subgroups were also comparable in social characteristics and comorbidities, patients with an intellectual nature of work predominated, half were disabled and retired. Among the concomitant pathology prevailed were arterial hypertension, pathology of the thyroid gland and gastrointestinal tract, in women - gynecological pathology (mastopathy, fibroids, cysts, etc.).

Monitoring of the results of treatment of patients of all groups was carried out a month later and then every 3 months from the start of regular treatment for one or two years using all the listed research methods that were used before the start of regular treatment, except for X-ray examination of the joints; the latter was carried out only twice (one year later and two years later).

Statistical processing of the obtained indicators was carried out in the program "Statistica 5.5". Descriptive statistics methods were used - sample size, mean, standard deviation, standard error of the mean, minimum and maximum values, percentiles. The reliability of the indicators was determined using the Student's t-test, the Mann-Whitney tests were used, χ^2 , McNemara, Kruskal-Wallis ANOVA. When statistically evaluating the data, we were guided by the level of difference values $p < 0.05$.

Results and its discussion

Before treatment, in both subgroups, patients with OA with severe pain syndrome according to VAS and functional disorders according to Leken's indices for gonarthrosis and coxarthrosis, general WOMAC prevailed (Table 1). In all patients, the QoL indicators were studied using the SF-36 and HAQ questionnaires. In fig. 1 shows the baseline QoL indicators according to the SF-36 questionnaire in comparison with the population level. Before the start of the course of combined treatment with the drug Goal T in combination with NSAIDs, all patients showed the same pronounced decrease in QoL indicators in both subgroups on all SF-36 scales, which statistically significantly differed from the population ones. The most significant decrease was on the scales of Physical functioning, role (Role physical functioning and Role emotional functioning), Pain, Vital activity,



Rice. 1. Initial indicators of QoL by SF-36 in subgroups A and B.

Scales of the SF-36 questionnaire: FF - physical functioning; RFF - role-based physical functioning;

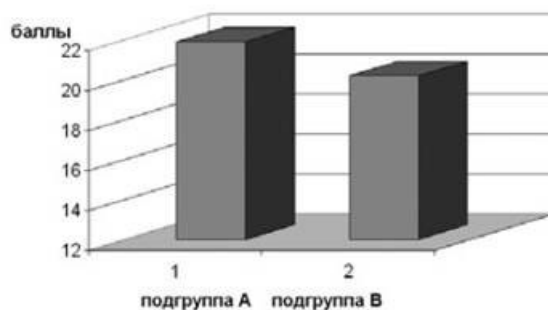
B - pain; OZ - general health; F - vitality; SF - social functioning; REF - role-playingemotional functioning; PZ - mental health; ФКсум - total physical component;

PCsum is a total mental component.

Note: $p < 0.001$ - Wilcoxon test;

From fig. 2 it follows that the values of the index of functional impairment according to the HAQ questionnaire were equally significantly increased in patients of both subgroups, which is obviously associated with pronounced restrictions in daily activities, caring for themselves, getting up, restriction of walking, including climbing and descending stairs in this category sick.

In the course of long-term course combined treatment Goal T in combination with NSAIDs, the following dynamics of changes in clinical parameters and also functional indices was observed in patients of both subgroups during two-year follow-up (Fig. 3-6). Prior to the start of regular treatment, in all patients with aggravated OA of the knee and hip joints, the main clinical parameters were increased, and the QOL indicators were decreased and statistically significantly different from the average population ($p < 0.05$).



Rice. 2. Indicators of QOL according to the questionnaire HAQ before treatment in subgroups A and B.

During the two-year follow-up, patients who received various combined course therapy Target T in combination with NSAIDs, observed a wave-like course of the process, which is characterized by improvement after the first and other courses of treatment, followed by deterioration after some time. At the same time, significant differences were revealed in the course of the process, depending on whether, in addition to oral administration, the periarticular or intramuscular route of administration was used. The subsequent periods were statistically significantly better than the initial, but after 6, 12, 18 and 24 months from the start of treatment, most of the clinical parameters (walking in a straight line, up stairs, WOMAC index and its subscales, Lequin and HAQ indices) no longer significantly differed from the initial ones. The QOL analysis showed that, with this combination, all indicators of the SF-36 scales were statistically significantly better than the initial ones throughout the entire observation period, and only after 12 and 24 months there was a decrease in QOL according to 2-3 scales (Physical functioning, Pain, General health), and their values remained significantly better than the initial values.

When using the course combined oral and intramuscular administration of Goal T in combination with NSAIDs, most of the indicated indicators during this period were also significantly better than the initial ones, but after 6, 12, 18 and 24 months from the start of treatment, all clinical parameters did not differ significantly from the initial ones. All QOL indicators when using this combination of the Target T drug were also statistically significantly better than the initial ones throughout the entire observation period, and only after 12 and 24 months there was a decrease in QOL according to 5 scales of the SF-36 questionnaire (Physical functioning, Role physical functioning, Pain, General health, life) almost to their original values.

If at the end of each course of therapy, as well as before the start of the course of treatment, the clinical parameters and QOL indicators did not differ in the subgroups of patients taking different combinations of Goal T, then after 6, 12, 18 and 24 months most of the clinical indicators were significantly better in patients. who took a combination of oral and periarticular use Target T: after 6 months - VAS at rest, movement, total VAS and WOMAC, after 12 months - VAS in movement, total

VAS and WOMAC general and on the subscale of rigidity, after 18 months - VAS in motion, Leken's index for gonarthrosis and WOMAC for the same indicators, after 24 months - VAS at rest and in motion, and WOMAC (Fig. 3-6).

It was noted that the most pronounced significant positive dynamics of QoL in the course of treatment with the use of different combinations of administration of Goal T was noted on the scales of Physical functioning, Role physical functioning, Pain and Role emotional functioning, the values of which were initially significantly reduced, and the lowest dynamics was according to the scales of General health, Vital functions, Social functioning, Mental health.

In accordance with this, when using the course combined treatment with the drug Goal T, some of the clinical parameters reliably approached the normal values, and the QOL indicators - to the population values. At the same time, better results were obtained when using a combination of oral and periarticular administration than intramuscular and oral administration. The data of X-ray examination of patients remained stable over a two-year follow-up period in patients of both subgroups.

Such dynamics of the state of patients is confirmed by the need for the use of NSAIDs. So, by the end of the third month (after the first course of therapy) the majority of patients - 70% of subgroup A and 48% of subgroup B - refused to take NSAIDs and only 3-4 patients in each subgroup still used large doses. A similar trend was observed during the first and second years of observation. So, after the fourth course of Goal T, both subgroups of patients experienced improvement, which was more pronounced after using Goal T orally and periarticularly: over the past two-year follow-up period, 60% of patients in this subgroup refused high doses of NSAIDs, and in subgroup B only 28% ... Large doses of NSAIDs were taken by 20% and 44% of patients, respectively, in subgroups A and B.

Table 1

Clinical characteristics of patients before starting the course of combined treatment Purpose
T

Признак	Подгруппа А (n = 20) (Цель Т перорально+ периартикулярно)	Подгруппа В (n = 17) (Цель Т перорально+ внутримышечно)	p
Пол:			
Женщины, n,%	18 (90%)	15 (88,5%)	>0,05
Мужчины, n,%	2 (10%)	2 (11,5%)	>0,05
Возраст, лет	54,3±5,86 [52-57]	52,8±5,36 [50-58]	>0,05
Индекс массы тела, кг/м ²	32,3±5,28 [30-35]	32,9±7,66 [29-38]	>0,05
Длительность ОА, лет	8,0±5,4 [4-11]	6,6±4,7 [4-10]	>0,05
Длительность обострения ОА, месяцы	2,6 ±1,86 [1-3,5]	1,9 ±1,6 [1-2,5]	>0,05
Гонартроз, n,%	14 (70%)	13 (76%)	>0,05
Коксартроз, n,%	6 (30%)	4 (24%)	>0,05
Рентгенологическая стадия гонартроза по Келлгрену и Лоуренс, n,%	(n = 14)	(n = 13)	
I стадия	5 (25)	5 (29)	>0,05
II стадия	5 (25)	5 (29)	>0,05
III стадия	4 (20)	3 (18)	>0,05
Рентгенологическая стадия коксартроза по Келлгрену и Лоуренс, n,%	(n = 6)	(n = 4)	
I стадия	-	-	>0,05
II стадия	2 (10)	1 (6)	>0,05
III стадия	4 (20)	3 (18)	>0,05
Функциональная недостаточность суставов, n,%:			
I степень	4 (20)	3 (18)	>0,05
II степень	10 (50)	9 (53)	>0,05
III степень	6 (30)	5 (29)	>0,05
Оценка показателя боли по ВАШ в покое, мм	52,25 (13,6) [40-60]	54,7 (18,75) [30-50]	>0,05
Оценка показателя ВАШ в движении, мм	93,1 (11,38) [90-100]	89,41 (22,7) [60-100]	>0,05
Оценка показателя Лекена при гонартрозе, баллы	19,35 (2,4) [18-21]	19,13 (3,46) [18-21]	>0,05
Оценка показателя Лекена при коксартрозе, баллы	19,44 (1,94) [18-21]	18,62(2,92) [16-20]	>0,05
Оценка по WOMAC, баллы			
Общая	189,35 (29,37) [178-207]	183,68 (48,94) [117-179]	>0,05
Боль	36,5 (8,0) [33-44]	29,26 (12,1) [20-38]	>0,05
Скованность	16,82 (3,94) [16-20]	14,12 (5,27) [10-20]	>0,05
Функциональность	132,94 (22,33) [119-147]	128,65 (32,97) [91-131]	>0,05
Оценка по шкале NAQ, баллы	1,16(0,37) [0,9-1,55]	1,1 (0,44) [0,55-1,3]	>0,05

Note: data are presented as mean (standard deviation), [25% -75%] - interquartile range.

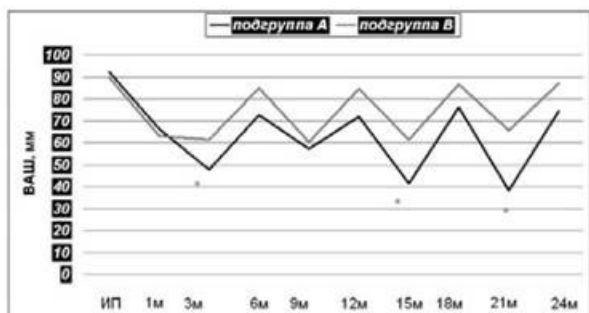
By the end of the second year (3 months after the fourth course of therapy), some deterioration was again noted, equally expressed in both subgroups (60% and 57%, respectively, in subgroups A and B). Thus, taking into account the use as a result of four courses of a combination of oral and periarticular administration of Goal T, the result turned out to be somewhat better: in subgroup A, 80% of patients received large doses of NSAIDs, and in subgroup B - all patients. Not a single patient in subgroup B did without NSAIDs, and in subgroup A, only 20% of patients took small doses.

The need to take NSAIDs at different periods of observation was associated with the dynamics of fluctuations in clinical parameters and indicators of quality of life. This dynamics confirms the slightly greater effect of the first combination both in the first and second years of treatment.

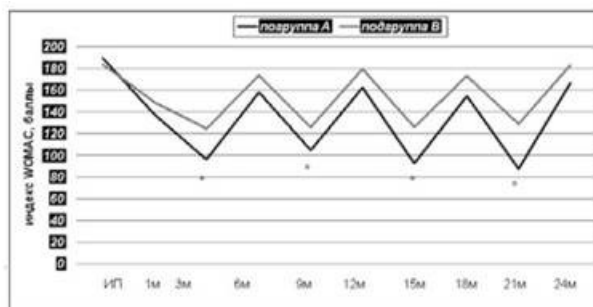
Our results are consistent with the data of other researchers [13, 14, 15], which show that QOL is significantly impaired in patients with OA. So, in the work of Tsapina T.N. and Erdes S.F. [10] conducted a study of QoL in patients with OA, mainly stage II-III (85 patients) using the SF-36 questionnaire, which revealed a decrease in QoL indicators in OA patients on all scales of this questionnaire, on average, 30% lower than in the population. So, the most reduced indicators of physical health: physical functioning (FF) by 46%, pain intensity (B) and role scales (P of physical and emotional functioning) - by 50%. Social functioning (SF) was quite high, but there was a 15% decrease in comparison with the population value. QOL on all scales SF-36 significantly decreased as the stage of OA increased [14, 15]. QOL studies by M. Hopman-Rock et al. [22] confirm these results. In numerous domestic and foreign studies, including in

placebo-controlled, high clinical efficacy of the drug Target T in patients with gonarthrosis has been shown [4, 6, 16, 23]. A study of the clinical efficacy of Goal T in coxarthrosis is not known to us. Dynamics of QoL indicators under the influence of course treatment Goal T in combination with NSAIDs has been studied only in a few studies [13] and also requires further clarification. Our data are consistent with the results of this QOL study, in which there was a positive trend in both clinical indicators and QOL parameters during the course of oral administration of Goal T in patients with gonarthrosis. The greatest influence of therapy was noted on the scales of Physical functioning and role scales (Physical and Emotional role functioning), which indicates a decrease in depression and negative emotions,

Thus, the study of QOL allows one to obtain a more complete description of the pain syndrome, functional disorders and to establish a relationship between the severity of pain and the violation of the physical and psychological state of patients with joint pathology.



Rice. 3



Rice. 5

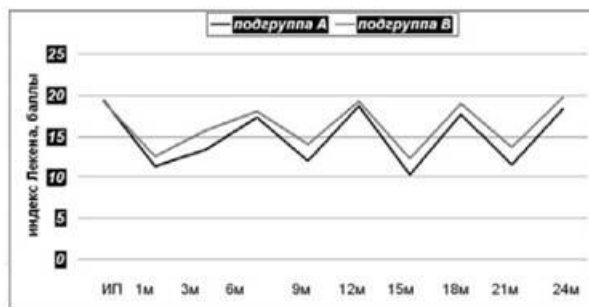
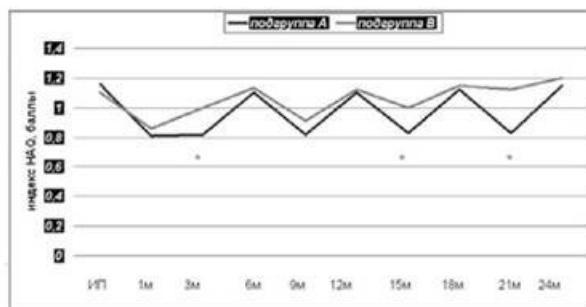


Fig. 4



Rice. 6

Rice. 3. Dynamics of pain in movement according to VAS in patients with OA.

Rice. 4. Dynamics of the Lequesne index in patients with OA.

Rice. 5. Index dynamics WOMAC in patients with OA.

Rice. 6. Index dynamics HAQ in patients with OA. * - p < 0.05 Mann-Whitney test

conclusions

1. According to the study, it can be concluded that in patients with exacerbation osteoarthritis of the knee and hip joints, predominantly II-III radiological stages, a deterioration of the main clinical parameters and a decrease in the quality of life indicators are revealed, while the physical and emotional component of health suffers more.

2. Long-term combined course combined treatment using the drug Target T orally and periarticular showed a more pronounced and lasting clinical effect in the treatment of patients with osteoarthritis complicated by synovitis and tendinitis compared with the combination of parenteral and intramuscular administration of this drug in terms of the effect on the severity of pain, joint function and QoL indicators, the need for the use of NSAIDs.

3. Positive clinical effect and improvement of QOL parameters with a combined course combined use Target T orally and intramuscularly turned out to be unstable and manifested

only in the course of treatment.

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