TREATMENT OF GONARTHROSIS USING AUTOLOGOUS PLATELET-RICH PLASMA

Egiazaryan KA, Danilov MA ✉, Abdusalamov RM

Pirogov Russian National Research Medical University, Moscow, Russia

Injections of platelet-rich plasma are considered to be a promising treatment. Medicines acting on the subchondral bone can improve tissue's structure and slow down destruction of the articular cartilage. This study aimed to analyze the results of intraarticular and intraosseous administration of platelet-rich plasma (PRP) in gonarthrosis cases. One hundred and eighty-seven participants (gonarthrosis stages 1 through 3) were divided into three groups. Group 1 (treatment group) received intraarticular PRP injections, group 2 (comparison group) — intraosseous PRP injections. For assessment purposes, we used the SF-36 survey and visual analog scale. Three months after the treatment, initial pain level decreased in both groups 1 and 2. In group 1, the prevalence of synovitis went down after 3 months, in group 2 — after 6 months (21.9 and 31.3%, respectively; $p < 0.05$). Six months after the treatment, soft tissue swelling around the joint was registered less often in groups 1 and 2 (8.2 and 8.3%, respectively). As for the physical component of the quality of life, it improved in group 1 after 3 months (70.40%), in group 2 — after 6 months (69.80%); as for the mental component, the dynamics was acknowledged positive 3 months after the treatment in groups 1 and 2 (64.30 and 65.10%, respectively), and 6 months after the treatment (65.10 and 66.40%, respectively). Thus, administration of PRP in gonarthrosis cases attenuate pain and improves the quality of life. In terms of alleviation of the clinical symptoms and improvement of the physical component of patients' lives, intraosseous PRP injections performed significantly better.

Keywords: quality of life, pain, intraarticular injection, intraosseous injection

Author contribution: Egiazaryan KA, Danilov MA — study design development, analysis of results; Danilov MA, Abdusalamov RM — data collection, literature review, preparation administration, assessment of the results.

Compliance with ethical standards: the study was approved by the Ethics Committee of the N.I. Pirogov Russian National Research Medical University (Minutes #213 of December 13, 2021).

✉ **Correspondence should be addressed:** Maxim A. Danilov
Ostrovityanova, 1, Moscow, 117997, Russia; md.danilov@gmail.com

Received: 30.01.2024 **Accepted:** 02.03.2024 **Published online:** 19.04.2024

DOI: 10.24075/brsmu.2024.012

ЛЕЧЕНИЕ ГОНАРТРОЗА С ПРИМЕНЕНИЕМ АУТОЛОГИЧЕСКОЙ ОБОГАЩЕННОЙ ТРОМБОЦИТАМИ ПЛАЗМЫ

К. А. Егиазарян, М. А. Данилов ✉, Р. М. Абдусаламов

Российский национальный исследовательский медицинский университет имени Н. И. Пирогова, Москва, Россия

Инъекции плазмы с тромбоцитами рассматривают как перспективный метод лечения. Препараты, воздействующие на субхондральную кость, могут способствовать улучшению структуры ткани и замедлению разрушения суставного хряща. Целью работы было изучить результаты лечения пациентов с гонартрозом путем внутрисуставного и внутрикостного введения обогащенной тромбоцитами плазмы (ОТП). В исследование включены 187 пациентов с 1–3-й стадией, разделенные на три группы. В группе 1 (основная) осуществляли внутрисуставное введение ОТП, в группе 2 (сравнения) — внутрикостные инъекции ОТП. Для оценки использовали визуально-аналоговую шкалу и опросник «SF-36». В группе 1 и 2 было зарегистрировано снижение показателя стартовой боли уже через 3 месяца после проведенного лечения. Снижение частоты синовитов отмечено у пациентов группы 1 через 3 месяца; в группе 2 — через 6 месяцев (21,9 и 31,3% соответственно; $p < 0,05$). Частота регистрации отечности мягких тканей области сустава снижалась через 6 месяцев у пациентов группы 1 и группы 2 (8,2 и 8,3% соответственно). У пациентов группы 1 была выявлена положительная динамика через 3 месяца (70,40%), группы 2 — через 6 месяцев (69,80%) по физическому компоненту качества жизни; у пациентов группы 1 и группы 2 через 3 месяца (64,30 и 65,10% соответственно), через 6 месяцев (65,10 и 66,40% соответственно) — по психическому компоненту. Таким образом, использование ОТП при гонартрозе свидетельствует о снижении боли, улучшении параметров жизни. Внутрикостные инъекции ОТП значительно улучшают клинические симптомы и физическое качество жизни пациентов.

Ключевые слова: качество жизни, боль, внутрисуставное введение, внутрикостное введение

Вклад авторов: К. А. Егиазарян, М. А. Данилов — разработка дизайна исследования, анализ результатов; М. А. Данилов, Р. М. Абдусаламов — сбор данных, обзор литературы, проведение процедур введения, оценка результатов.

Соблюдение этических стандартов: исследование одобрено этическим комитетом ФГАОУ ВО РНИМУ им. Н. И. Пирогова (протокол № 213 от 13 декабря 2021 г.).

✉ **Для корреспонденции:** Максим Александрович Данилов
ул. Островитянова, д. 1, г. Москва, 117997, Россия; md.danilov@gmail.com

Статья получена: 30.01.2024 **Статья принята к печати:** 02.03.2024 **Опубликована онлайн:** 19.04.2024

DOI: 10.24075/vrgmu.2024.012

Osteoarthritis (OA) of the knee (gonarthrosis) is a degenerative progressing joint disease involving loss of articular cartilage [1].

About 13% of women and 10% of men aged 60 and above suffer from symptomatic knee OA. After 70, the prevalence of this pathology increases to 40%. Disregarding age as a factor, the frequency of symptomatic gonarthrosis is approximately 240 cases per 100,000 people per year [2].

Gonarthrosis is a progressive disease; as a rule, the specifics of its pathogenesis lead to a disability.

The causes of damage to the cartilage associated with osteoarthritis are not fully understood, but may stem from constitutional and genetic factors, trauma, overload disease, etc. Recently, pathological changes in the subchondral bone — ischemia and local necrosis — have been receiving

increasing attention as the disease's pathogenetic factors [3]. A history of knee injuries is also considered to be an important aspect [4].

Physical activity restrictions, pain and discomfort associated with movements undermine patients' daily routines and social life, which degrades their quality of life (QOL) [5].

In this connection, investigation of methods of treatment of knee OA is considered to be an important task. With varying efficacy, conservative approaches aim to eliminate clinical manifestations (pain) and partially improve the joint's functional state [6]. However, the respective therapeutic strategies have no effect on the OA pathogenesis and do not help to improve the patients' QOL.

Contemporary orthopedics sees promise in the development and introduction of the new OA treatment techniques that would not only address clinical symptoms but also prevent progression of the pathological process. Injections of platelet-rich plasma (PRP) is one of such techniques [7, 8]. The effects of PRP mainly depend on the platelet secretion products. In addition to organelles, platelet cytoplasm contains many granules carrying over 300 different biologically active substances. There are three types of platelet secretory granules: dense granules (or γ-granules), α-granules and lysosomes. The latter are commonly represented by various enzymes (acid hydrolases). Dense granules contain catecholamines, serotonin, ADP, ATP and calcium, which are involved in the activation of the coagulation cascade. Driven by the growth factors, fibroblasts, endothelial cells and epithelial cells migrate to the injury and multiply there. Subsequently, there forms an extracellular matrix, new vessels grow, and connective tissue matures and remodels. Mediators of α-granules HGF, TNFa, TGFß1, VEGF and EGF deliver the anti-inflammatory effect, and attenuation of inflammation also has an analgesic effect [9–12].

The prupose of this study is to analyze the results of intraarticular and intraosseous administration of platelet-rich plasma (PRP) in knee OA cases.

METHODS

From 2018 through 2022, we examined and treated 187 patients with knee OA, stages 1 through 3 (ages 40 through 70), and subsequently monitored the dynamics of the symptoms and signs of the disease. This part of the study was conducted at the premises of the N. I. Pirogov State Clinical Hospital #1, Moscow, and the Republican Clinical Hospital, Makhachkala (Republic of Dagestan).

The knee OA diagnosis was verified under the applicable regulations [13–15].

The inclusion criteria were: age from 40 to 70 years; knee AO confirmed by radiographic examination; disease stage 1 through 3 under Kellgren classification; walking-associated pain intensity ≥40 mm on the visual analog scale (VAS) over the past 2 weeks; no intake of systemic chondroprotectors and/or cartilage regeneration stimulating drugs within 2 months before the study; no intake of nonsteroidal anti-inflammatory drugs (NSAIDs) for 2 weeks before the study; voluntary consent to participate in the study and adequately cooperate in its context.

The exclusion criteria were: age under 40 and over 70; refusal to participate in the study and/or sign the informed consent form; walking-associated pain intensity <40 mm on VAS; stage 4 damage under Kellgren classification; surgical treatment of gonarthrosis during the previous 6 months; pronounced deformity of the knee joint; exacerbation lasting more than a month; pregnancy and/or lactation; serious or unstable somatic diseases (severe diseases of the liver, cardiovascular system, lungs or kidney, oncological, mental diseases), decompensated diabetes mellitus; intake of tissue regeneration drugs, systemic chondroprotectors withing 2 months before the study; intake of NSAIDs within 2 weeks before the study.

Depending on the technique applied, the patients were divided into three groups. Treatment group (group 1) included 73 patients, 21 male and 52 female, mean age 57.4 ± 2.87 years; they received intraarticular injections of PRP. Comparison group (group 2) included 48 patients, 15 male and 33 female, mean age 56.9 ± 2.85 years; the received intraosseous injections of PRP. Control group (group 3) consisted of 66 people, 21 male and 45 female, means age 57.1 ± 2.86 years; their treatment plan included NSAIDs, a course of chondroprotectors, and a course of glucorticoids administared intraarticularly. In group 1, autologous PRP was injected intraarticularly in a single course, three injections once a week, once a year; in group 2, PRP was injected intraosseously, two injections every two weeks, once a year.

In all groups, the most common stage was 2nd: 37 (50.7%) patients in group 1, 22 patients (45.8%) in group 2, and in 27 (40.9%) patients in the control group. We found no statistically significant intergroup differences in the frequency stage-wise OA diagnosis within the sample.

All patients underwent a comprehensive examination, which included registration of complaints, study of the medical and life history, physical examination and analysis of the objective signs of joint pathology, and assessment of the severity of damage.

Radiography, ultrasonography, and magnetic resonance imaging (MRI) were also parts of the comprehensive primary examination.

The intensity of pain was recorded with the help of the visual analog scale (VAS), and QOL indicators registered with a non-specific SF-36 survey (before treatment, three and six months thereafter).

Statsoft's STATISTICA 10 and Microsoft Excel 2016 (USA) were used for statistical data analysis.

In case of normal distribution of indicators, we applied the Student's test to compare groups, and used the Mann–Whitney test when distribution was nonparametric. Normality of distribution was assessed with the help of the Shapiro-Wilk test. The null hypothesis (α) was considered significant at $p = 0.05$ (all intergroup comparisons).

RESULTS

Figure 1 shows the initial pain intensity dynamics after over 30 minutes of rest.

These data indicate that before the treatment, all patients (100%) experienced pain after resting for more than 30 minutes.

Three months after treatment, in groups 1 and 2, initial pain after over 30 minutes of rest decreased to 64.4 and 47.90%, respectively, from 100%.

After six and twelve months, the intensity of pain in the treatment group increased to 72.60 and 79.50%, respectively, that in the comparison group — to 62.50 and 68.80%, respectively.

In the control group, the dynamics of the initial pain was not significant; it amounted to 92.40% after three months, 93.90% after six months, and 97.0% after twelve months.

Figure 2 shows the dynamics of indicators of morning joint stiffness in the entire sample.

Compared to the control group, both group 1 and group 2 exhibited a significant decrease in the number of complaints about morning joint stiffness.

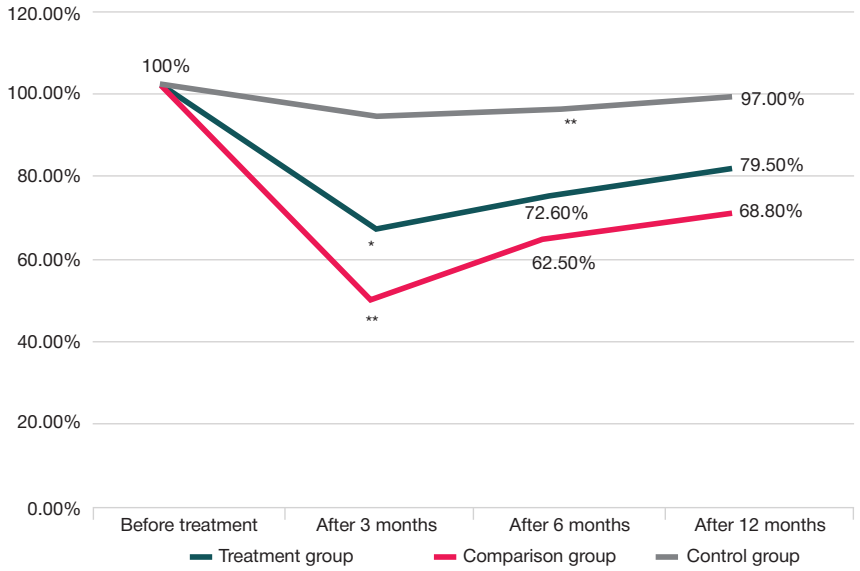

Fig. 1. Initial pain intensity dynamics after over 30 minutes of rest, all groups, percentages. * — significance of differences ($p < 0.05$) between indicators of the control group and those registered for groups 1 and 2; ** — significance of differences ($p < 0.001$) between indicators of the control group and group 2

Table presents the knee OA parameters as registered with ultrasonography.

It should be noted that before treatment, the prevalence of synovitis, soft tissue edema, osteophytes, and subchondral sclerosis was comparable between the groups. In the treatment group, the differences in the prevalence of synovitis became significant (compared to baseline) after three months (27.4%); in the treatment and comparison groups — after six months (21.9 and 31.3%, respectively). As for the prevalence of swelling around the joint, the differences in prevalence thereof became significant after 6 months (treatment and comparison groups, 8.2 and 8.3%, respectively). After 12 months, the differences registered between groups have lost significance, but the lowest values were recorded (ultrasonography) in the treatment group.

Figures 3 and 4 show the results of a comparative analysis of physical and mental components of QOL, as registered with the SF-36 survey; time points — before treatment, 3 and 6 months after treatment.

With treatment in the background, groups 1 and 2 exhibited significant positive dynamics: groups 1 after three months (70.40%), group 2 after six months (69.80%).

Six months after treatment, values of the indicators were above baseline in both group 1 and group 2, with group 2 performing better. In control group, the physical component of QOL, according to the SF-36 survey, did not change throughout the study (51.20% — before treatment; 53.50% — after 3 months; 54.0% — after 6 months).

As registered with the SF-36, against the background of treatment, both group 1 and group 2 have shown positive dynamics of the mental component of QOL after 3 months (64.30 and 65.10%, respectively), and after 6 months (65.10% and 66.40%, respectively). In control group, the situation remained largely unchanged (42.20% before treatment, 44.30% after 3 months, and 44.60% after 6 months).

Figure 5 shows pain intensity as recorded with the help of VAS.

Against the background of treatment, groups 1 and 2 exhibited significant ($p < 0.05$) positive dynamics after 3 and 6 months; after 3 months, the values were better in group 1 (2.80 ± 0.14 and 3.90 ± 0.19, respectively), and after 6 months — in group 2 (3.40 ± 0.17 and 3.0 ± 0.15, respectively). In the control group, therapy failed to relief the pain, and the values remained on the same level throughout the study (before treatment —

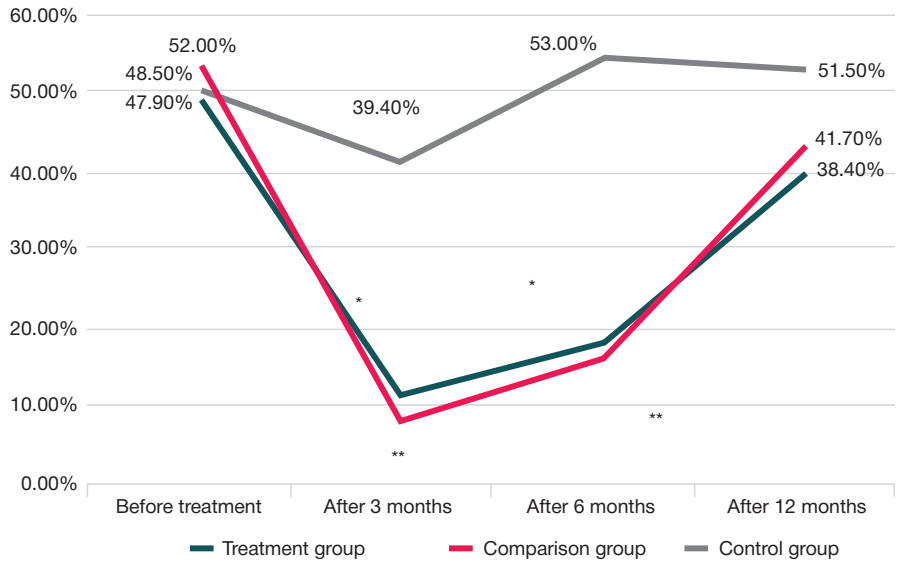

Fig. 2. Morning joint stiffness dynamics, all participants, percentages. * — significance of differences ($p < 0.05$) between indicators of the control group and those registered for groups 1 and 2; ** — significance of differences ($p < 0.001$) between indicators of the control group and groups 1 and 2

Table. Dynamics of ultrasonography indicators of the knee OA against the background of treatment, all patients

Indicators	Treatment group (n = 73)		Comparison group (n = 48)		Control group (n = 66)	
	Abs.	%	Abs.	%	Abs.	%
Before treatment						
Synovitis	55	75.3	37	77.0	49	74.2
Swelling of soft tissues in the joint area	11	15.1	8	16.7	12	18.1
Osteophytes	59	80.8	40	83.3	54	81.8
Subchondral sclerosis	61	83.6	41	85.4	56	84.8
3 months after treatment						
Synovitis	20	27.4*	30	62.5	47	71.2
Swelling of soft tissues in the joint area	8	10.9	6	12.5	5	4.5*
Osteophytes	59	80.8	40	83.3	54	81.8
Subchondral sclerosis	61	83.6	41	85.4	56	84.8
6 months after treatment						
Synovitis	16	21.9*	15	31.3*	45	68.2
Swelling of soft tissues in the joint area	6	8.2*	4	8.3*	5	7.5*
Osteophytes	57	78.1	39	81.3	54	81.8
Subchondral sclerosis	59	80.8	40	83.3	56	84.8
12 months after treatment						
Synovitis	24	32.9	22	45.8	48	72.7
Swelling of soft tissues in the joint area	10	13.7	8	16.7	11	16.7
Osteophytes	57	78.1	39	81.3	54	81.8
Subchondral sclerosis	59	80.8	40	83.3	56	84.8

Note: * — significance of differences ($p < 0.05$) of the indicator values before and after treatment, intragroup.

6.0 ± 0.3; after 3 months — 5.60 ± 0.28; after 6 months — 5.80 ± 0.29; after 12 months — 5.90 ± 0.30).

DISCUSSION

Knee OA is a pathology that grows more prevalent as the life expectancy of the population increases. This diseases poses a significant social, economic and medical problem, the solution of which should employ non-pharmacological, pharmacological, and surgical methods of treatment at different stages. Surgery, in the form of partial or complete knee replacement, is most often resorted to at late stages of knee OA [16–17]. Regenerative approaches, such as those involving PRP and cell therapy, aim to expand the therapeutic arsenal to prevent or delay surgery. While cell therapy is still in its infancy and has to overcome a number of problems, PRP has been used for more than 15 years, and there is a consolidated position about it in the context of treatment of this disease. An increasing number of randomized clinical trials are being conducted to obtain convincing conclusions about the effectiveness and safety of PRP. Despite the fact that intraarticular injection of PRP as knee OA treatment shows promising results, this method, according to a number of authors, affects only the articular cartilage and the synovial membrane, without affecting the subchondral bone. Intraosseous injections to the subchondral bone can make the protocol more comprehensive [18, 19].

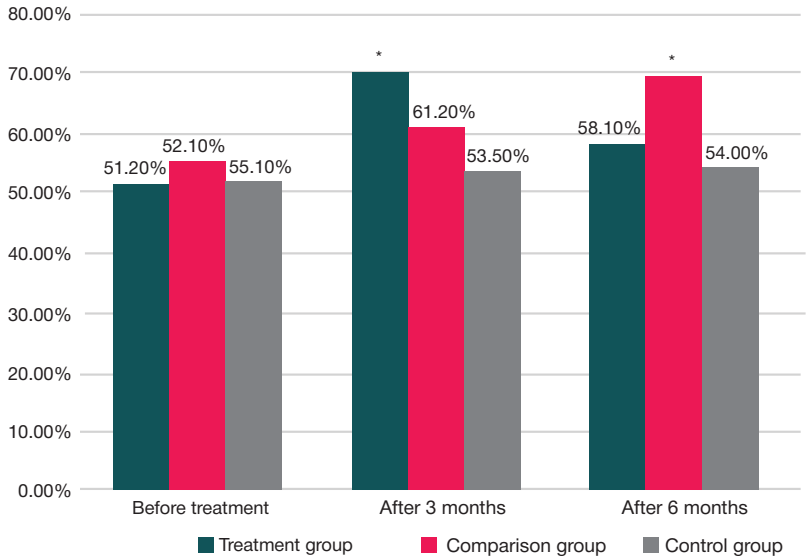

Fig. 3. Dynamics of the physical indicators of QOL, as registered with a SF-36 survey before treatment, 3 and 6 months thereafter. * — significance of differences ($p < 0.05$), indicator's value before and after treatment, intragroup; ** — significance of differences ($p < 0.001$), indicator's values, treatment group and comparison group, 3 and 6 months after treatment

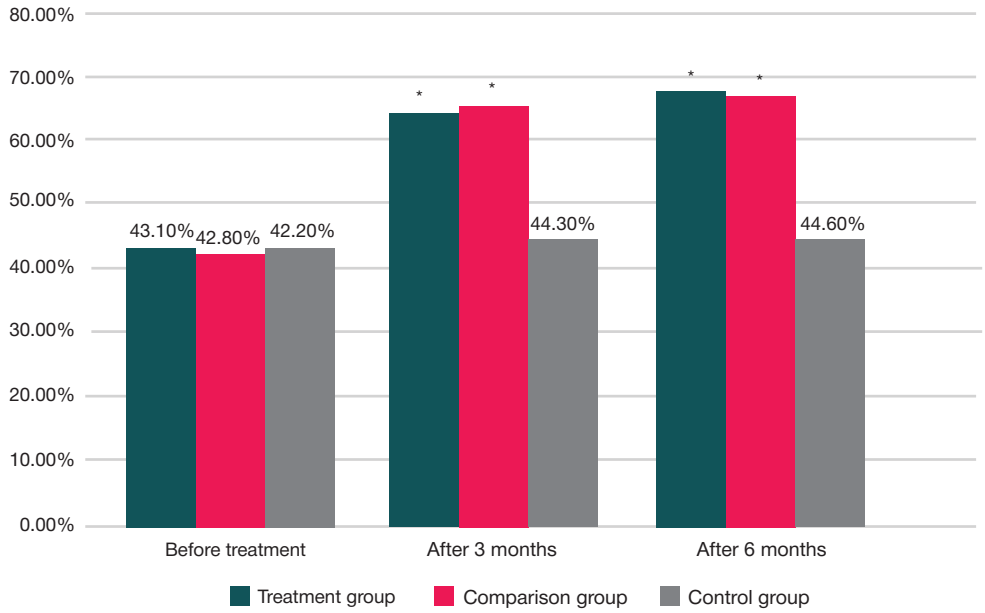

Fig. 4. Dynamics of the mental indicators of QOL, as registered with a SF-36 survey before treatment, 3 and 6 months thereafter. * — significance of differences ($p < 0.05$) of the indicator values before and after treatment.

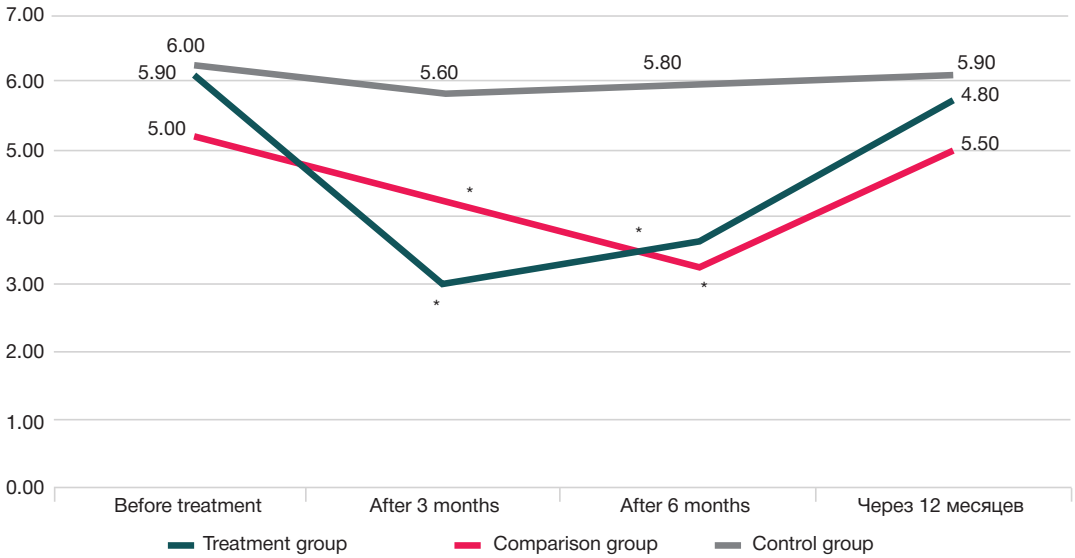

Fig. 5. Pain intensity, VAS registration, all patients (points). * — significance of differences ($p < 0.05$), indicator's value compared to control group; ** — significance of differences ($p < 0.001$), indicator's values, treatment group and comparison group compared

Currently, clinical studies of intraosseous administration of PRP in treatment of knee OA are in the early stages. The rationale for this method largely depends on the growing knowledge about the role of the bone-cartilaginous functional unit in the development of knee OA, as well as on growth of the number of preclinical studies and intraosseous methods of treatment of other bone pathologies [20, 21]. Further research is needed in this area to better understand cellular processes underlying the mechanism of action and to plan further pathways of intraosseous injections.

CONCLUSIONS

Compared to standard therapy, which relies on NSAIDs, chondroprotectors, and intraarticular administration of glucocorticoids, administration of PRP in OA cases yields significantly better results in terms of pain intensity and QOL parameters. Intraosseous injection of PRP allows achieving significantly better results in terms of clinical symptoms and physical component of the patients' QOL.

References

1. Hsu H, Siwiec RM. Knee Osteoarthritis. [Updated 2023 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507884/.
2. Magnusson K, Turkiewicz A, Englund M. Nature vs nurture in knee osteoarthritis — the importance of age, sex and body mass index. Osteoarthritis Cartilage. 2019; 27 (4): 586–92.
3. Egiazaryan KA, Lazishvili GD, et al. Knee osteochondritis desiccans: surgery algorithm. Bulletin of RSMU. 2018; 2: 73–78.
4. Egiazaryan KA, Cherkasov SN, Attaeva LZh. Analiz struktury pervichnoj zabolevaemosti po klassu travmy, otravlenija i nekotorye drugie posledstvija vozdejstvija vneshnih prichin vzroslogo naselenija Rossijskoj Federacii. Kafedra travmatologii i

ortopedii. 2017; 1: 25–27. Russian.
5. Li JS, Tsai TY, Clancy MM, Li G, Lewis CL, Felson DT. Weight loss changed gait kinematics in individuals with obesity and knee pain. Gait Posture. 2019; 68: 461–5.
6. Vasileva LV, Lahin DI. Vlijanie metabolicheskogo sindroma na klinicheskuju kartinu osteoartroza. Medicinskij Vestnik Severnogo Kavkaza. 2017; 12 (1): 8–11. Russian.
7. Guseva AI, Tagilceva YuS. Primenenie obogashhennoj trombocitami plazmy v lechenii zabolevanij oporno-dvigatel'nogo apparata. Alleja nauki. 2018; 6 (5): 148–51. Russian.
8. Cui Y, Lin L, Wang Z, Wang K, Xiao L, Lin W, et al. Research trends of platelet-rich plasma therapy on knee osteoarthritis from 2011 to 2021: A review. Medicine (Baltimore). 2023; 102 (2): e32434.
9. Wang L, et al. Comparison of the effects of autologous and allogeneic purified platelet-rich plasma on cartilage damage in a rabbit model of knee osteoarthritis. Front Surg. 2022; 9: 911468.
10. Wang Y, et al. Clinical efficacy of platelet-rich plasma as adjuvant therapy in patients undergoing arthroscopic repair of meniscal injury. J Int Med Res. 2020; 48 (9): 300060520955059.
11. Sheean AJ, Anz AW, Bradley JP. Platelet-rich plasma: fundamentals and clinical applications. Arthroscopy. 2021; 37 (9): 2732–4.
12. dos Santos RG; et al. The regenerative mechanisms of platelet-rich plasma: A review. Cytokine. 2021; 144: 155560.
13. Ob utverzhdenii standarta pervichnoj mediko-sanitarnoj pomoshhi pri gonartroze i shodnyh s nim klinicheskih sostojanijah. Prikaz Ministerstva zdravoohranenija RF ot 24 dekabrja 2012 g. # 1498n. M., 2012. Russian.
14. Nasonov EL, redaktor. Rossijskie klinicheskie rekomendacii. Revmatologija pod red. M.: GJeOTAR-Media, 2017; 464 s. Russian.
15. Bruyère O, et al. A consensus statement on the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) algorithm for the management of knee osteoarthritis — from evidence-based medicine to the real-life setting. Seminars in arthritis and rheumatism. WB Saunders. 2016; 45 (4): S3-S11.
16. Moretti L, Maccagnano G, Coviello M, Cassano GD, Franchini A, Laneve A, et al. Platelet rich plasma injections for knee osteoarthritis treatment: A prospective clinical study. J Clin Med. 2022; 11 (9): 2640.
17. Cui Yubo, Lin Liqiong, Wang Zhiwei, Wang Kai, Xiao Lili, Lin Wentao, et al. Research trends of platelet-rich plasma therapy on knee osteoarthritis from 2011 to 2021: A review. Medicine. 2023; 102 (2): e32434.
18. Patel S, Rajnish RK, Baburaj V, Kumar P, Sharma S, Kumar V. Intraosseous infiltration of platelet-rich plasma for knee osteoarthritis: A systematic review of literature and limited meta-analysis. Indian J Orthop. 2022; 56 (11): 1847–57. DOI: 10.1007/s43465-022-00737-x. PMID: 36310547; PMCID: PMC9561501.
19. Sánchez M, Jorquera C, de Dicastillo LL, et al. Real-world evidence to assess the effectiveness of platelet-rich plasma in the treatment of knee degenerative pathology: a prospective observational study. Therapeutic Advances in Musculoskeletal Disease. 2022; 14. DOI: 10.1177/1759720X221100304.
20. Torres-Torrillas M, Damia E, Romero Ad, Pelaez P, Miguel-Pastor L, Chicharro D, et al. Intra-osseous plasma rich in growth factors enhances cartilage and subchondral bone regeneration in rabbits with acute full thickness chondral defects: Histological assessment. Front Vet Sci. 2023; 10: 1131666. DOI: 10.3389/fvets.2023.1131666.
21. Torres-Torrillas M, Damiá E, Peláez P, Miguel-Pastor L, Cuervo B, Cerón JJ, et al. Intra-osseous infiltration of adipose mesenchymal stromal cells and plasma rich in growth factors to treat acute full depth cartilage defects in a rabbit model: serum osteoarthritis biomarkers and macroscopical assessment. Front Vet Sci. 2022; 9: 1057079. DOI: 10.3389/fvets.2022.1057079.

Литература

1. Hsu H, Siwiec RM. Knee Osteoarthritis. [Updated 2023 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507884/.
2. Magnusson K, Turkiewicz A, Englund M. Nature vs nurture in knee osteoarthritis — the importance of age, sex and body mass index. Osteoarthritis Cartilage. 2019; 27 (4): 586–92.
3. Егиазарян К. А., Лазишвили Г. Д. и др. Алгоритм хирургического лечения больных с рассекающим остеохондритом коленного сустава. Вестник Российского государственного медицинского университета. 2018; 2: 77–83.
4. Егиазарян К. А., Черкасов С. Н., Аттаева Л. Ж. Анализ структуры первичной заболеваемости по классу травмы, отравления и некоторые другие последствия воздействия внешних причин взрослого населения Российской Федерации. Кафедра травматологии и ортопедии. 2017; 1: 25–27.
5. Li JS, Tsai TY, Clancy MM, Li G, Lewis CL, Felson DT. Weight loss changed gait kinematics in individuals with obesity and knee pain. Gait Posture. 2019; 68: 461–5.
6. Васильева Л. В., Лахин Д. И. Влияние метаболического синдрома на клиническую картину остеоартроза. Медицинский Вестник Северного Кавказа. 2017; 12 (1): 8–11.
7. Гусева А. И., Тагильцева Ю. С. Применение обогащенной тромбоцитами плазмы в лечении заболеваний опорно-двигательного аппарата. Аллея науки. 2018; 6 (5): 148–51.
8. Cui Y, Lin L, Wang Z, Wang K, Xiao L, Lin W, et al. Research trends of platelet-rich plasma therapy on knee osteoarthritis from 2011 to 2021: A review. Medicine (Baltimore). 2023; 102 (2): e32434.
9. Wang L, et al. Comparison of the effects of autologous and allogeneic purified platelet-rich plasma on cartilage damage in a rabbit model of knee osteoarthritis. Front Surg. 2022; 9: 911468.
10. Wang Y, et al. Clinical efficacy of platelet-rich plasma as adjuvant therapy in patients undergoing arthroscopic repair of meniscal injury. J Int Med Res. 2020; 48 (9): 300060520955059.
11. Sheean AJ, Anz AW, Bradley JP. Platelet-rich plasma: fundamentals and clinical applications. Arthroscopy. 2021; 37 (9): 2732–4.
12. dos Santos RG; et al. The regenerative mechanisms of platelet-rich plasma: A review. Cytokine. 2021; 144: 155560.
13. Об утверждении стандарта первичной медико-санитарной помощи при гонартрозе и сходных с ним клинических состояниях. Приказ Министерства здравоохранения РФ от 24 декабря 2012 г. № 1498н. М., 2012.
14. Насонов Е. Л., редактор. Российские клинические рекомендации. Ревматология под ред. М.: ГЭОТАР-Медиа, 2017; 464 с.
15. Bruyère O, et al. A consensus statement on the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) algorithm for the management of knee osteoarthritis — from evidence-based medicine to the real-life setting. Seminars in arthritis and rheumatism. WB Saunders. 2016; 45 (4): S3-S11.
16. Moretti L, Maccagnano G, Coviello M, Cassano GD, Franchini A, Laneve A, et al. Platelet rich plasma injections for knee osteoarthritis treatment: A prospective clinical study. J Clin Med. 2022; 11 (9): 2640.
17. Cui Yubo, Lin Liqiong, Wang Zhiwei, Wang Kai, Xiao Lili, Lin Wentao, et al. Research trends of platelet-rich plasma therapy on knee osteoarthritis from 2011 to 2021: A review. Medicine. 2023; 102 (2): e32434.
18. Patel S, Rajnish RK, Baburaj V, Kumar P, Sharma S, Kumar V. Intraosseous infiltration of platelet-rich plasma for knee osteoarthritis: A systematic review of literature and limited meta-analysis. Indian J Orthop. 2022; 56 (11): 1847–57. DOI: 10.1007/s43465-022-00737-x. PMID: 36310547; PMCID: PMC9561501.
19. Sánchez M, Jorquera C, de Dicastillo LL, et al. Real-world evidence to assess the effectiveness of platelet-rich plasma in the treatment of knee degenerative pathology: a prospective observational study. Therapeutic Advances in Musculoskeletal Disease. 2022; 14. DOI: 10.1177/1759720X221100304.
20. Torres-Torrillas M, Damia E, Romero Ad, Pelaez P, Miguel-Pastor L, Chicharro D, et al. Intra-osseous plasma rich in growth factors enhances cartilage and subchondral bone regeneration in rabbits with acute full thickness chondral defects: Histological

assessment. Front Vet Sci. 2023; 10: 1131666. DOI: 10.3389/fvets.2023.1131666.
21. Torres-Torrillas M, Damiá E, Peláez P, Miguel-Pastor L, Cuervo B, Cerón JJ, et al. Intra-osseous infiltration of adipose mesenchymal stromal cells and plasma rich in growth factors to treat acute full depth cartilage defects in a rabbit model: serum osteoarthritis biomarkers and macroscopical assessment. Front Vet Sci. 2022; 9: 1057079. DOI: 10.3389/fvets.2022.1057079.