



Use of platelet-rich plasma isolated or in combination in osteoarthritis of the temporomandibular joint: a systematic review

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DOI: <https://doi.org/10.54448/mdnt24S202>

Received: 01-18-2024; Revised: 03-06-2024; Accepted: 03-08-2024; Published: 03-11-2024; MedNEXT-id: e24S202

Abstract

Introduction: Temporomandibular joint osteoarthritis (TMJ-OA) is a common disease in the oral and maxillofacial regions and is the most serious type. Among temporomandibular disorders, TMJ-OA accounts for 18% to 85% of all cases. The use of platelet-rich plasma (PRP) has been highlighted, as well as in combination with other types of treatments such as hyaluronic acid, arthrocentesis, and corticosteroids.

Objective: to highlight the main clinical outcomes of the treatment of osteoarthritis of the temporomandibular joint through the injectable use of platelet-rich plasma, alone or in combination with other types of treatment. **Methods:** The research and development of the work were carried out from December 2023 to February 2024 in the databases Scopus, PubMed, Science Direct, and Scielo, using scientific articles from 2013 to 2023, following the PRISMA rules. The quality of the studies was based on the GRADE instrument and the risk of bias was based on the Cochrane instrument (Funnel Plot). **Results and**

Conclusion: A total of 178 studies were found that were subjected to eligibility analysis. The final sample had 45 eligible studies and 31 studies were described in the systematic review. Most studies showed homogeneity in their results, with $X^2 = 66.7\% > 50\%$, with $p < 0.05$. The symmetric funnel plot did not suggest a risk of bias among studies with a small sample size. The results showed that platelet-rich plasma performed better than hyaluronic acid in the treatment of osteoarthritis of the temporomandibular joint during

longterm follow-up in terms of reducing pain and increasing interincisal distance. Combined injection of hyaluronic acid and platelet-rich plasma after arthrocentesis is more effective than hyaluronic acid or platelet-rich plasma alone in the treatment of osteoarthritis of the temporomandibular joint, as well as platelet-rich plasma with hyaluronic acid after arthrocentesis showed significant clinical efficacy long-term concerning pain relief. Furthermore, it was found that intra-articular injections of platelet-rich plasma reduced pain on palpation of the temporomandibular joint more effectively compared to hyaluronic acid and corticosteroids. Platelet-rich plasma injection can significantly improve pain, mouth opening, abnormal joint sound, and jaw function in patients with temporomandibular joint osteoarthritis, and has a good repair effect on condylar bone defects. Furthermore, platelet-rich plasma injection combined with physical therapy can effectively control medium and long-term pain in patients.

Keywords: Osteoarthritis. Temporomandibular joint. Platelet-rich plasma. Hyaluronic acid. Corticosteroids.

Introduction

In the context of temporomandibular disorders (TMD), temporomandibular joint osteoarthritis (TMJ-OA) is a common disease in the oral and maxillofacial regions, as well as being the most serious type [1]. The incidence of TMD is high, affecting approximately 5%-12% of the population [2]. Among TMD, TMJ-OA accounts for 18% to 85% of all cases [3].

In this aspect, TMJ-OA is a chronic and progressive disease that causes degeneration of the cartilage of the temporomandibular joint [1,4], pathologically characterized by degeneration, destruction, loss of articular cartilage, osteosclerosis, formation of osteophytes, formation of sub osseous microcapsule, and varying degrees of synovial inflammation. The clinical symptoms of TMJ-OA include joint pain and joint clicking, which can eventually destroy the joint structure, severely affecting patients' quality of life [5,6].

Also, the temporomandibular joint (TMJ) is one of the most complex joints in the human body because of its anatomical shape and physiological perspectives. The TMJ is the only bilateral joint, where the right and left joints are fused and work together during mandibular movements [6]. The TMJ comprises ginglymoarthroid joint compounds between the mandibular condyles, articular discs, and glenoid fossae of the temporal bones [7]. The TMJ is the only ginglymoarthroid joint because it shows hinge and sliding movements. In this sense, TMDs have a considerable and direct impact on patients' quality of life [8,9]. There are inflammatory disorders in which various joint tissues become inflamed as a result of the degradation of articular cartilage (osteoarthritis) [10].

As a corollary of this, TMJ-OA is a common chronic joint disorder that can be caused by micro- or macro-trauma to the TMJ, or by other pathological processes, causing progressive inflammatory degeneration of the TMJ articular cartilage [11]. Thus, patients with TMJ-OA generally present dysfunction and pain in the TMJ region [12].

In this context, treatment for TMJ-OA mainly includes non-surgical and minimally invasive options, e.g., therapies, dietary adjustments, occlusal splints, oral nonsteroidal anti-inflammatory drugs (NSAIDs), muscle relaxants, intra-articular drug therapies, and arthrocentesis [13-16]. Furthermore, the literature has highlighted platelet-rich plasma (PRP), which is a biological therapy that comprises an autologous concentrate of platelets acquired by blood centrifugation [17]. This concentrate has shown potential benefits due to the abundance of growth factors within it.

A systematic review in 2018 showed some evidence for the potential superiority of intra-articular PRP injections in patients with TMJ-OA [18]. Furthermore, additional injection of PRP at the end of arthrocentesis may provide better results than arthrocentesis alone [19]. However, there is still controversy regarding which minimally invasive method is most effective in TMJ-OA. Therefore, this study was conducted to compare the results of three treatment protocols, namely arthrocentesis, PRP injection, and a combination of both

in alleviating the symptoms of TMJ-OA.

Given the above, the present study aimed to highlight the main clinical outcomes of the treatment of osteoarthritis of the temporomandibular joint through the injectable use of platelet-rich plasma, alone or in combination with other types of treatment.

Methods

Study Design

The present study followed the international systematic review model, following the rules of PRISMA (preferred reporting items for systematic reviews and meta-analysis). Available at: <http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1>. Accessed on: 02/11/2024. The methodological quality standards of AMSTAR-2 (Assessing the methodological quality of systematic reviews) were also followed. Available at: <https://amstar.ca/>. Accessed on: 02/11/2024.

Quality of Studies, Eligibility Criteria, and Risk of Bias

Following GRADE recommendations, the quality of scientific evidence in the studies covered was classified as high, moderate, low, or very low, according to the risk of evidence bias, sample size, clarity of comparisons, precision, and consistency of effects. of the analyses. A high quality of evidence was assigned using four criteria: 1) Randomized or prospective controlled clinical trials; 2) Retrospective clinical trials; 3) Sample size greater than 15 participants; 4) Studies with statistically well-designed results; 5) Studies published in indexed journals and with a significant impact factor; 6) descriptive validity (identification of studies that show the TMJ surgical technique), interpretative (identification of the advantages and disadvantages of the customized prosthesis and the stock prosthesis), theoretical (credibility of the methods) and pragmatic (application of PRP in the surgeon's daily life).

As inclusion criteria, articles were selected that showed the use of injectable PRP in the temporomandibular joint as a regenerative and rehabilitative treatment for osteoarthritis. Articles that did not report the technique used and that did not meet the GRADE quality criteria were excluded. The Cochrane Instrument was adopted to evaluate the risk of bias of the chosen studies using the Cohen Test to calculate the effect size (Effect Size) versus the Inverse of the Standard Error (precision or sample size) to determine the Risk of Bias of the studies using the Funnel Plot graph. The Heterogeneity Test (Chi-square Test, $25\% < X < 50\%$, and high association = $> 50\%$).

Data Sources, Research Strategy, and Study Timing

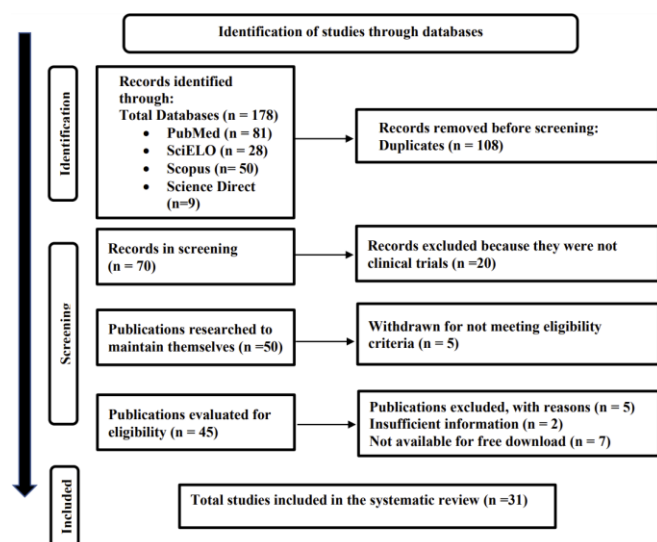
The search strategies for the present study were based on the keywords (MeSH Terms): *Osteoarthritis*. *Temporomandibular joint*. *Platelet-rich plasma*. *Hyaluronic acid*. *Corticosteroids*. Search filters designated as clinical studies were used. The research and development of the work was carried out from December 2023 to February 2024 in the Scopus, PubMed, OVID, Science Direct, LILACS, and EBSCO databases, using scientific articles from 2013 to 2023. In addition, a combination of the words- key with the booleans "OR", AND and the "NOT" operator were used to target scientific articles of interest. The title and abstracts were examined in all conditions.

Results

Summary of Literary Findings

A total of 178 articles were found. Initially, duplicate articles were excluded. After this process, the abstracts were evaluated and a new exclusion was carried out, removing articles that did not include the topic of this article, resulting in 70 articles. A total of 45 articles were fully evaluated and included in this study and 31 were developed into the systematic review item (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 05 studies with a high risk of bias and 20 studies that did not meet GRADE. According to the GRADE instrument, the 31 studies that made up the systematic review presented homogeneity in their results about the effectiveness of the use of PRP in TMJ-OA, with $X^2 = 66.7\% > 50\%$, with $p < 0.05$. Due to limited literature, an open search strategy was performed to include a larger number of studies.

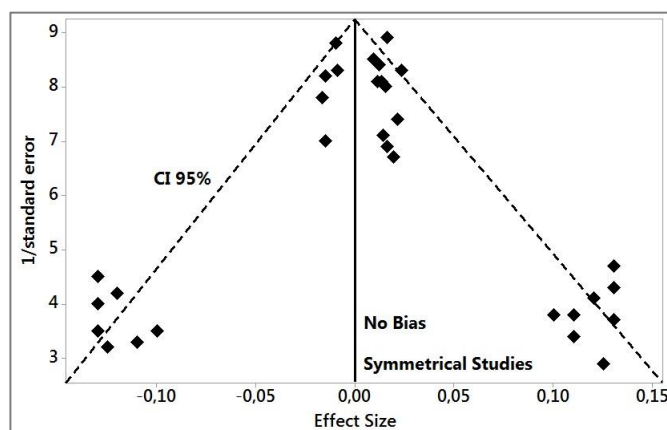
Figure 1. Flowchart showing the article selection process.



Source: Own Authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using the Cohen Test (d). The sample size was determined indirectly by the inverse of the standard error (1/Standard Error). This graph presented symmetrical behavior, not suggesting a significant risk of bias, both between studies with a small sample size (lower precision) that are shown at the base of the graph and in studies with a large sample size that are presented in the upper region.

Figure 2. The symmetric funnel plot suggests no risk of bias among the small sample size studies that are shown at the bottom of the plot. High confidence and high recommendation studies are shown above the graph (NTotal=31 clinical studies evaluated in full in the systematic review).



Source: Own Authorship.

Major Clinical Findings

Osteoarthritis is one of the most common disorders of the temporomandibular joint (TMJ). The complex etiopathogenesis of temporomandibular disorders (TMD) and the variability of symptoms make it difficult to adopt standardized therapeutic protocols [6]. Therefore, platelet-rich plasma (PRP) injections have been applied to the TMJ in patients with TMJ osteoarthritis. Furthermore, arthrocentesis has received wide acceptance as a minimally invasive surgical procedure for TMD [7].

Based on this, a randomized controlled clinical study carried out by the authors Abbadi, Kara, and Al-Khanati, 2022 [20], evaluated and compared the effect of each of these protocols (arthrocentesis, PRP injection, and their combination) in the management of TMJ-OA. A total of 33 participants with limited mouth opening, function pain, and joint sounds due to TMJ-OA. Participants were randomly divided into three groups: arthrocentesis with PRP group; PRP group; and Arthrocentesis group. Participants in all study groups showed statistically significant improvement in terms of

mouth opening and pain during the six-month postoperative period ($p < 0.05$) and did not show significant improvement in terms of joint noises ($p > 0.05$). Pain assessments showed better results in the arthrocentesis with PRP group compared to arthrocentesis or injectable PRP alone after six months of follow-up ($p < 0.05$). There were no significant differences in the results of mouth opening and joint sound assessments between the three groups after six months. Therefore, the three treatment protocols evaluated were effective in improving mouth opening limitation and pain in patients with TMJ-OA. A combination of TMJ arthrocentesis and intra-articular PRP injections showed the best results regarding pain symptoms.

Furthermore, the authors Wu et al. 2022 [21] evaluated the effectiveness of splint combined with PRP for the treatment of TMJ-OA. A total of 31 patients with TMJ-OA treated with splints combined with PRP from January 2021 to June 2021 in the Department of Oral and Maxillofacial Surgery, School of Stomatology, China Medical University (Shenyang, China) were retrospectively reviewed. Visual analog scale (VAS) scores of all patients were recorded before and 6 months after treatment and maximum comfortable mouth opening was recorded. Treatment with combined splints + PRP was successful in 31 patients. The mean pretreatment VAS score was 6.1, and the mean VAS score 6 months after treatment was 4.1. The post-treatment VAS score was significantly lower than the pre-operative VAS score ($p < 0.05$). The mean maximum comfortable mouth opening pre-treatment was 27.6 mm, and the mean 6 months after treatment was 34.8 mm. Comfortable mouth opening increased significantly ($p < 0.05$).

Added to this, the authors Asadpour et al. 2022 [22] evaluated, through a randomized clinical study, the effectiveness of PRP and HA injection after arthrocentesis in individuals with TMJ-OA. Healthy adults diagnosed with TMJ-OA who were treated with nonsurgical methods initially but did not respond participated in this study. Subjects were randomly allocated to AH, PRP, or combined PRP+HA groups after arthrocentesis. A total of 30 consecutive patients (15 men and 15 women) with a mean age of 29.63 ± 8.34 years were followed for 6 months in this study. The mean pain reduction at 6 months was 4.1 ± 0.9 , 4.1 ± 1.1 , and 5.1 ± 1.0 for HA, PRP, and HA/PRP, respectively ($p < 0.05$). In all 3 treatment groups, mean VAS parameters significantly reduced after treatment and these postoperative values were significantly lower in the PRP+HA group ($p < 0.001$). The mean increase in mouth opening after 6 months was 8.0 ± 2.8 , 8.0 ± 3.0 , and 10.1 ± 3.3 for HA, PRP, and HA/PRP, respectively

($p < 0.05$). Mouth opening, lateral and protrusive mandibular movements improved significantly after treatment in all 3 groups ($p < 0.001$). TMJ noises were significantly reduced in all treatment groups ($p < 0.001$), with the PRP+HA group showing a greater reduction.

Authors Liu et al. 2022 [23] analyzed the effectiveness of PRP injection combined with individualized comprehensive physical therapy for the treatment of TMJ-OA through a prospective cohort study with 40 patients. Pain intensity, maximum mouth opening, temporomandibular joint sounds, and Jaw Functional Limitation Scale (JFLS) scores and imaging findings were compared before treatment and during follow-up. Pain intensity, maximum mouth opening, and temporomandibular joint sounds in both groups improved significantly with increasing treatment time ($p < 0.05$). The improvement in pain in the combined treatment group was greater than that in the PRP injection group at 3 and 6 months ($p < 0.05$). The improvement in mouth opening was better in the combined treatment group, while the improvement in joint sounds was better in the PRP injection group. The improvement in JFLS scores in the combined treatment group was greater than that in the PRP injection group at 6 months ($p < 0.05$). The image improvement rates of the two groups were similar.

Furthermore, authors Li et al. 2021 [24] observed, through a retrospective study, the effect of autologous PRP injected into the upper cavity versus chitosan for the treatment of TMJ-OA. Data from 27 patients with TMJ-OA treated at the Stomatology Hospital of China Medical University from September 2018 to September 2019 were analyzed. Maximum interincisal opening, pain intensity, and TMJ sounds were recorded and compared before treatment and at the 3rd and 6th months after treatment. Better results were observed in the group treated with PRP in terms of maximum interincisal opening and pain intensity than in the group treated with chitosan. Regarding TMJ sounds, relief was observed in both groups, with no significant difference.

A randomized clinical study carried out by authors Hegab et al. 2015 [25] compared the use of PRP and HA in the treatment of TMJ-OA with long-term follow-up data. A total of 50 patients with TMJ-OA were included in the study (29 women and 21 men, age range 31 to 49 years, mean age 38.6). In group I, 25 patients received 3 injections of 1 mL of PRP. In group II, 25 patients received 3 injections of 1 mL of low molecular weight HA. Between-group comparisons of outcome variables over time revealed significant improvements in group II at 1 and 3 months. At 6 and 12 months, the PRP group performed better compared to the HA group in terms of recurrence of pain and joint noises. The improvements obtained with PRP injections in group I

were maintained during the follow-up period. At the end of the follow-up period, the median mouth opening in group I was 41.0 mm. In group II, the median mouth opening was 39.0 mm. Therefore, PRP performed better than HA in the treatment of TMJ-OA during long-term follow-up in terms of reducing pain and increasing interincisal distance.

The authors Gokçe et al. 2019 [26] compared the clinical results of intra-articular injections of Corticosteroid (CS), HA, and PRP in patients with TMJ pain and clinically diagnosed with TMJ-OA. Patients were evaluated in 2 groups as patients who felt pain on lateral (n=31) and posterior (n=43) palpation. The patients evaluated in the study were randomly distributed into 3 different treatment groups Group 1 (PRP), Group 2 (HA), and Group 3 (CS). Pain felt in the TMJ on lateral and posterior palpation was assessed before treatment and every month for 3 months using a 5-point pain scale. The presence of crepitus, loss of function, and loss of strength were assessed before treatment and every month for 3 months. Significant changes were observed in the PRP and HA groups when patients were evaluated according to VAS scores assessed at different follow-up times for TMJ pain on lateral palpation.

Furthermore, a retrospective cohort study developed by authors Lin et al. 2018 [19] compared the effectiveness of 2 TMJ-OA treatment approaches, arthrocentesis plus platelet-rich plasma (A+PRP) and PRP alone, and attempted to provide another potential treatment option with a single high-concentration 2 mL injection and high purity PRP. A total of 208 patients were treated for TMD in the Department of Oral and Maxillofacial Surgery of Tainan Sin-Lau Hospital between August 2013 and January 2016, of which 90 patients were selected for the final analysis. Among the 90 patients, 30 were assigned to the A+PRP group and 60 were assigned to the PRP group. After treatment, the A+PRP and PRP groups showed improvements in TMJ-OA. The 2 treatment groups showed no statistically significant differences in rates of improvement in symptoms of joint crepitus sounds, reparative remodeling, and TMJ arthralgia. However, compared to PRP alone, A+PRP treatment demonstrated superior performance in improving TMD-associated headache, jaw range of motion <6 mm, myofascial pain with referral, and pain when chewing most foods. Both A+PRP and PRP treatments can effectively improve various symptoms of TMJ-OA. A single injection with 2 mL of high-concentration, high-purity PRP is recommended for the treatment of TMJ-OA.

Linked to this, a randomized clinical trial in adult patients with TMJ-OA compared the long-term clinical and cone-beam computed tomography (CBCT)

outcomes of TMJ-OA treated with arthrocentesis plus platelet-rich plasma (PRP) versus arthrocentesis alone. The sample consisted of 30 consecutive patients with TMJ-OA randomly treated with arthrocentesis alone (control group) or initial arthrocentesis plus PRP injection and then 4 consecutive PRP injections (study group). The outcome variables were visual analog scale assessments (masticatory efficiency, joint sounds, and pain complaints), maximum interincisal opening, and CBCT findings. Outcome variables were recorded preoperatively and 12 months after surgery. The sample consisted of 47 joints from 30 patients with OA (control group: 15 joints from 12 patients; mean age, 35.08 ± 14.84 years; study group: 32 joints from 18 patients; mean age, 32.22 ± 14.32 years). Joint sounds and general complaints of pain statistically decreased in both groups, while chewing efficiency, painless interincisal opening, and lateral movement statistically increased only in the study group. However, only chewing efficiency showed a statistically greater improvement in the study group compared to the control group. CBCT assessments showed that reparative remodeling of bone abnormalities occurred at rates of 87.5 and 46.6% in the study and control groups, respectively. Therefore, arthrocentesis and PRP injections constitute a safe and promising method for the treatment of TMJ-OA that is superior to arthrocentesis alone [27].

Another randomized clinical study was implemented in adult patients with TMJ-OA. The sample comprised 49 osteoarthritic joints in 31 consecutive patients. Patients in the platelet-rich plasma (PRP) group underwent initial arthrocentesis plus PRP injection and then four consecutive PRP injections. Patients in the hyaluronic acid (HA) group underwent one session of arthrocentesis plus HA injection. The predictor variable was the treatment technique. Outcome variables included visual analog scale (VAS) assessments and maximum interincisal opening (MIO) measurements. Outcome variables were recorded preoperatively and 12 months postoperatively. The PRP group included 32 joints in 18 subjects, and the AH group included 17 joints in 13 subjects. No statistically significant differences were observed between groups for any of the changes in VAS parameters or MIO measurements. Both treatment techniques resulted in significant clinical improvements in all painless VAS and MIO parameters [28].

A clinical trial with one year of follow-up, conducted by the authors Giacomello et al. 2019 [29], investigated the effectiveness of injections of platelet-derived growth factors (PRGF-Endoret®) for the treatment of TMJ-OA. A total of 52 patients diagnosed with osteoarthritis according to the American Society of Temporomandibular Joint Surgeons guidelines

underwent a course of 3 injections (1 per month) PRGF. Two clinical parameters, pain at rest and maximum unassisted mouth opening, were assessed by the same blinded operator at the time of diagnosis (baseline), at each visit during treatment, and a 1-year follow-up visit. Both parameters showed improvements that were maintained over time. Statistical analyses showed significant changes in the first two injections. Data from the current investigation support findings from studies in other joints, which show the effectiveness of PRGF-Endoret injections in reducing osteoarthritis symptoms and maintaining improvements over time.

Furthermore, a recent randomized and prospective clinical study analyzed whether the injection of PRP+HA after arthrocentesis reduces pain and improves maximum incisal opening in patients with TMJ-OA. Patients were selected based on the Hegab classification: Group I: patients treated with arthrocentesis followed by a single injection of PRP; Group II (Control): patients treated with arthrocentesis followed by a single HA injection; and Group III: patients treated with arthrocentesis followed by a single injection of the PRP+HA combination. The primary predictor variable was the medication used for injection. The primary outcome variables were maximum voluntary mouth opening and pain index scores. The secondary outcome variable was joint sounds. All outcome variables were assessed and compared between the three groups at baseline and at 1-, 3-, 6-, and 12-month intervals. Other variables, including patient age and sex, were evaluated about patient outcomes. PRP+HA injection showed statistically significant improvement in primary and secondary treatment outcomes compared to PRP or HA injection throughout the study period ($p < 0.005$). PRP+HA injection after arthrocentesis had significant long-term clinical efficacy in terms of pain relief, considered the main concern of the patient and clinician [30].

Finally, a study carried out by the authors Fernández-Ferro et al. 2017 [31] evaluated the efficacy of PRP injection versus HA after arthroscopic surgery in patients diagnosed with internal TMJ-OA derangement. A total of 100 patients were randomized into two study groups. Group A ($n = 50$) received a PRGF injection and Group B ($n = 50$) received an HA injection. The mean age was 35.5 years (range 18 to 77 years) and 88% of patients were women. The best results were observed in the group treated with PRP, with a significant reduction in pain at 18 months, compared to treatment with HA. Regarding mouth opening, an increase was observed in both groups, without significant differences. PRP injection after arthroscopy is more effective than HA injection regarding pain in patients with advanced internal TMJ derangement.

Conclusion

It was concluded that platelet-rich plasma performed better than hyaluronic acid in the treatment of temporomandibular joint osteoarthritis during long-term follow-up in terms of reducing pain and increasing interincisal distance. Combined injection of hyaluronic acid and platelet-rich plasma after arthrocentesis is more effective than hyaluronic acid or platelet-rich plasma alone in the treatment of osteoarthritis of the temporomandibular joint, as well as platelet-rich plasma with hyaluronic acid after arthrocentesis showed significant clinical efficacy long-term about pain relief. Furthermore, it was found that intra-articular injections of platelet-rich plasma reduced pain on palpation of the temporomandibular joint more effectively compared to hyaluronic acid and corticosteroids. Platelet-rich plasma injection can significantly improve pain, mouth opening, abnormal joint sound, and jaw function in patients with temporomandibular joint osteoarthritis, and has a good repair effect on condylar bone defects. Furthermore, platelet-rich plasma injection combined with physical therapy can effectively control medium and long-term pain in patients.

Acknowledgement

Not applicable.

Ethical Approval

Not applicable.

Informed consent

Not applicable.

Funding

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate®.

Peer Review Process

It was performed.

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