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A COMPARATIVE EVALUATION OF OZONE AND PLATELET RICH FIBRIN INJECTION IN MANAGEMENT OF UNILATERAL ANTERIOR DISC DISPLACEMENT WITH REDUCTION IN TEMPOROMANDIBULAR JOINT: A RANDOMIZED CONTROL TRIAL

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ABSTRACT

Background: Temporomandibular disorders (TMDs), particularly anterior disc displacement with reduction (ADDwR), are common intra-articular disorders associated with pain, joint sounds, and functional limitation of the temporomandibular joint (TMJ). Conventional treatment modalities often provide variable outcomes, creating a need for minimally invasive regenerative approaches. Injectable platelet-rich fibrin (i-PRF) and ozone therapy have gained attention due to their anti-inflammatory, analgesic, and regenerative properties.

Aim: To compare the efficacy of intra-articular injectable platelet-rich fibrin and ozone injections in the management of unilateral anterior disc displacement with reduction of the temporomandibular joint.

Materials and Methods: This prospective randomized controlled clinical trial included 80 patients diagnosed with unilateral anterior disc displacement with reduction who were randomly divided into two groups of 40 patients each. Group I received a single intra-articular i-PRF injection, while Group II received intra-articular ozone injections (10 µg/mL) twice weekly for three weeks. All patients received occlusal splint therapy before intervention. Clinical parameters including pain intensity assessed using Visual Analog Scale (VAS), maximum inter-incisal opening, and lateral mandibular excursion were evaluated at baseline, 2 weeks, 3 months, and 6 months. Magnetic resonance imaging (MRI) was performed at baseline and after 12 months to evaluate regenerative changes.

Results: Both treatment modalities demonstrated significant improvements in pain reduction and mandibular function during follow-up. Ozone therapy showed significantly greater pain reduction at 3 and 6 months and demonstrated superior regenerative changes on MRI evaluation compared with i-PRF. Improvement in maximum inter-incisal opening and lateral mandibular excursion was observed in both groups without statistically significant intergroup differences.

Conclusion: Both i-PRF and ozone therapy were effective in managing unilateral ADDwR; however, ozone therapy demonstrated comparatively superior clinical and regenerative outcomes.

KEYWORDS: Anterior disc displacement; Injectable platelet-rich fibrin; Intra-articular injection; Ozone therapy; Regenerative medicine; Temporomandibular joint disorder.

INTRODUCTION

The temporomandibular joint (TMJ) is one of the most complex and frequently utilized synovial joints in the human body, responsible for coordinating essential functions such as mastication, speech, swallowing, and facial expressions [1]. Anatomically, it is a bilateral diarthrodial articulation formed by the mandibular condyle and the mandibular fossa of the temporal bone, separated by a fibrocartilaginous articular disc. Unlike most synovial joints, whose articulating surfaces are covered by hyaline cartilage, the TMJ is lined with fibrocartilage that demonstrates superior resistance to mechanical stress and a greater capacity for remodeling [2]. The articular disc divides the joint cavity into superior and inferior compartments and plays a vital role in load distribution, lubrication, shock absorption, and smooth mandibular movements [3]. The synchronized movement of both temporomandibular joints permits rotational and translational movements of the mandible, allowing normal oral functions [3]. Temporomandibular disorders (TMDs) comprise a heterogeneous group of musculoskeletal and neuromuscular conditions affecting the temporomandibular joint, masticatory muscles, and associated structures [4]. These disorders are among the most common causes of non-dental orofacial pain and are

frequently associated with significant impairment in quality of life. The prevalence of TMD has been reported to range from 5% to 12% in the general population, with clinical signs and symptoms observed in approximately 40–60% of individuals [5]. Women are more commonly affected than men, especially during the second to fourth decades of life, suggesting possible hormonal and psychosocial influences in disease pathogenesis [6].

The etiology of TMD is multifactorial and includes structural, functional, psychological, and behavioral factors [7]. Occlusal discrepancies, trauma, parafunctional habits such as bruxism, psychological stress, inflammatory changes, and degenerative alterations have all been implicated in the initiation and progression of these disorders [7]. Clinically, TMD may manifest as pain in the preauricular region, restricted mouth opening, joint sounds, mandibular deviation during movement, headache, facial muscle tenderness, and functional limitations that interfere with daily activities [8].

Internal derangement of the temporomandibular joint represents one of the most common intra-articular disorders and refers to an abnormal positional relationship between the articular disc, condyle, and articular eminence [9]. Among the various forms of internal derangement, anterior disc displacement with reduction (ADDwR) is considered the most frequently encountered condition. In ADDwR, the articular disc assumes an anterior position relative to the condylar head when the mouth is closed but returns to its normal position during mouth opening [9]. This reduction of the displaced disc often produces a characteristic clicking or popping sound during mandibular movements. Although early stages may remain asymptomatic, progressive disc displacement can eventually result in pain, inflammation, mechanical dysfunction, and degenerative changes within the joint structures [10].

The pathophysiology of anterior disc displacement with reduction involves alterations in disc morphology, ligamentous laxity, biomechanical imbalance, and degenerative changes affecting surrounding structures [11]. Repetitive microtrauma and increased intra-articular loading may lead to progressive deterioration of joint components and initiate inflammatory pathways responsible for pain and dysfunction [12]. Persistent inflammation may induce synovitis, cartilage degeneration, and fibrosis, thereby reducing the functional efficiency of the joint. Consequently, patients often experience pain during mastication, limited mouth opening, joint sounds, and reduced mandibular movements [12].

The management of temporomandibular disorders generally follows a conservative approach as the first line of treatment [11]. Therapeutic modalities include patient education, behavioral modifications, pharmacotherapy, physical therapy, occlusal splints, exercises, and psychological interventions [12]. Although these methods are effective in many cases, certain patients continue to exhibit persistent symptoms despite conservative treatment. In such situations, minimally invasive procedures including arthrocentesis and intra-articular injections have gained considerable attention due to their ability to directly target intra-articular pathology while minimizing surgical morbidity [13].

Recently, regenerative medicine has emerged as a promising field in musculoskeletal and joint disorders by promoting tissue repair and reducing inflammation through biological mechanisms. Injectable platelet-rich fibrin (i-PRF) and ozone therapy have demonstrated encouraging results in various orthopedic and dental applications owing to their regenerative and anti-inflammatory properties [12-14].

Injectable platelet-rich fibrin is a second-generation autologous platelet concentrate prepared without anticoagulants [11]. It contains a high concentration of platelets, leukocytes, growth factors, and fibrin matrix proteins that contribute to tissue regeneration and healing [11]. Growth factors released from i-PRF, including platelet-derived growth factor, transforming growth factor-beta, vascular endothelial growth factor, and insulin-like growth factor, stimulate angiogenesis, enhance cellular proliferation, promote collagen synthesis, and facilitate cartilage repair. Furthermore, i-PRF acts as a biological scaffold supporting migration and differentiation of mesenchymal stem cells, thereby improving tissue regeneration and functional recovery [15].

Ozone therapy has gained increasing interest as a minimally invasive treatment modality because of its analgesic, anti-inflammatory, antimicrobial, and regenerative properties [12]. Medical ozone consists of a controlled mixture of ozone and oxygen gases administered at specific therapeutic concentrations [13]. Ozone induces controlled oxidative stress that activates antioxidant defense mechanisms, improves oxygen metabolism, stimulates cellular activity, and promotes tissue repair processes. Additionally, ozone has been shown to reduce inflammatory mediators and enhance local blood circulation, thereby contributing to pain reduction and improved joint function [14].

Although both injectable platelet-rich fibrin and ozone therapy demonstrate promising therapeutic potential in temporomandibular joint disorders, direct comparative evidence regarding their effectiveness in managing unilateral anterior disc displacement with reduction remains limited [13]. Establishing the relative efficacy of these treatment modalities is essential for developing evidence-based treatment protocols and improving patient outcomes [14].

Therefore, the present randomized controlled trial was undertaken to comparatively evaluate the efficacy of ozone and platelet-rich fibrin injections in the management of unilateral anterior disc displacement with reduction in the temporomandibular joint by assessing pain reduction, improvement in maximum inter-incisal opening, lateral mandibular excursion, and regenerative changes within the articular disc.

MATERIALS AND METHOD

Study Design

The present study was designed as a prospective randomized controlled clinical trial to comparatively evaluate the effectiveness of intra-articular ozone and injectable platelet-rich fibrin (i-PRF) injections in the management of unilateral anterior disc displacement with reduction (ADDwR) of the temporomandibular joint (TMJ). The study aimed to assess changes in pain intensity, maximum inter-incisal opening (MIO), lateral mandibular excursion, and regenerative alterations within the articular disc following treatment. The study was conducted in the Department of Prosthodontics and Crown and Bridge in collaboration with the Department of Oral and Maxillofacial Surgery at Sardar Patel Post Graduate Institute of Dental and Medical Sciences, Lucknow.

Ethical Approval
The study protocol was reviewed and approved by the Institutional Scientific Review Board and Institutional Ethics Committee before commencement of the study. All procedures were carried out according to the ethical principles of the Declaration of Helsinki for research involving human participants. Written informed consent was obtained from all participants prior to enrollment after explaining the objectives, benefits, procedures, and possible risks associated with the study.

Study Population and Sample Size
The study included a total of 80 participants diagnosed with unilateral anterior disc displacement with reduction according to clinical and radiographic criteria. Participants were selected from patients reporting to the outpatient department with symptoms suggestive of temporomandibular joint dysfunction.
Sample size calculation was performed using the formula proposed by Wang and Fan for pilot and experimental studies:
n≥C×2V2d2n \geq \frac{C \times 2V^2}{d^2}n≥d2C×2V2
where:
- **V** = assumed variability between groups (15%)
- **C** = constant at 95% confidence interval and 80% study power (7.84)
- **d** = effect size (10%)

The calculated sample size was approximately 36 subjects per group. Considering a potential dropout rate of 10%, the sample size was rounded to 40 subjects per group, resulting in a total sample size of 80 participants.
Inclusion Criteria: participants fulfilling the following criteria were included:
Patients included in the present study were individuals aged between 20 and 60 years who were clinically and radiographically diagnosed with unilateral anterior disc displacement with reduction of the temporomandibular joint. Participants experiencing moderately severe chronic temporomandibular joint pain persisting for more than three months and presenting with compromised mouth opening were considered eligible for inclusion. Only patients classified as American Society of Anesthesiologists (ASA) physical status I or II, indicating good general systemic health, were enrolled. Furthermore, participants were required to possess adequate physical and mental health status and provide written informed consent after receiving a detailed explanation regarding the study protocol, procedures, benefits, and potential risks. Patients who had not received previous treatment for temporomandibular disorders and were willing to comply with follow-up protocols were included in the study.
Exclusion Criteria: participants presenting with the following conditions were excluded:
Patients were excluded from the study if they had conditions that could potentially influence treatment outcomes or interfere with the study protocol. These included immunocompromised individuals, psychologically compromised patients, and patients with a known history of hypersensitivity or allergy to local anesthetic agents. Patients presenting with active rheumatologic diseases, facial pain associated with infection, or dental pathologies such as extensive carious lesions or sinus pathology contributing to orofacial pain were also excluded. Additionally, pregnant or lactating women, patients with anemia, and individuals diagnosed with glucose-6-phosphate dehydrogenase (G6PD) deficiency were not considered eligible. Patients with systemic conditions that could alter tissue healing responses or those unable to comply with follow-up evaluations were also excluded from participation in the study.

Randomization and Allocation
The recruited participants were randomly allocated into two equal treatment groups using a computer-generated randomization sequence.
Group I (n = 40): Patients received intra-articular injectable platelet-rich fibrin (i-PRF).
Group II (n = 40): Patients received intra-articular ozone injections.
Randomization was performed to minimize selection bias and ensure equal distribution of demographic variables among study groups.

Preoperative Clinical Evaluation
All participants underwent comprehensive clinical examination before initiation of treatment. Detailed medical and dental histories were recorded. Clinical assessment included evaluation of pain intensity, mandibular movements, and TMJ sounds.
Pain intensity was assessed using a 10-cm Visual Analog Scale (VAS), where 0 represented absence of pain and 10 represented severe pain.
Maximum inter-incisal opening was measured in millimeters using a digital vernier caliper by recording the distance between the incisal edges of the maxillary and mandibular central incisors during maximum mouth opening.
Lateral mandibular excursion was assessed by asking participants to move the mandible laterally from maximum intercuspation and measuring the distance traveled using a calibrated divider and digital caliper.
TMJ clicking and joint sounds were assessed through bilateral palpation during mandibular opening and closing movements.

Radiographic Assessment
Magnetic resonance imaging (MRI) of the temporomandibular joint was performed in both open-mouth and closed-mouth positions to determine disc position and evaluate degenerative changes.

The MRI protocol included:
- T1-weighted imaging
- T2-weighted imaging
- Proton density-weighted sequences

Baseline MRI was obtained before treatment and repeated at 12 months after intervention to assess regenerative changes and alterations in disc morphology.

Fabrication of Customized Positional Stent

A customized positional guide was fabricated for each participant to facilitate accurate and reproducible intra-articular injection placement. Cone beam computed tomography (CBCT) images and digital surface scans obtained using Candipro software were superimposed to create three-dimensional virtual models. The stents were fabricated using ultraviolet resin through three-dimensional printing technology.

The customized guide assisted in achieving precise needle positioning within the superior joint space and improved standardization of injection procedures.

Preparation of Injectable Platelet-Rich Fibrin (i-PRF)

Injectable platelet-rich fibrin (i-PRF) was prepared using the low-speed centrifugation concept described by Choukroun to obtain a liquid autologous concentrate rich in platelets, leukocytes, and growth factors. Approximately 5 mL of peripheral venous blood was collected from the antecubital vein of each participant under aseptic conditions using sterile vacutainer tubes without the addition of anticoagulants. The blood sample was immediately transferred to a centrifugation machine to prevent premature coagulation and centrifuged at 700 rpm for 3 minutes with a relative centrifugal force of approximately 60 g. Following centrifugation, three distinct layers were obtained within the tube: an upper straw-colored plasma layer, an intermediate fibrin-rich layer, and a lower red blood cell layer. The upper plasma layer together with the fibrin-rich portion containing injectable platelet-rich fibrin was carefully aspirated under sterile conditions and prepared for immediate clinical use. Owing to the absence of anticoagulants, i-PRF remains in a liquid state for a limited duration before fibrin polymerization occurs, allowing its intra-articular administration immediately after preparation. The obtained i-PRF contains a high concentration of platelets, leukocytes, and biologically active growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF), which collectively contribute to tissue regeneration, angiogenesis, anti-inflammatory effects, and enhancement of the healing process.

Preparation of Ozone

Medical-grade ozone was generated using a corona discharge ozone generator connected to an oxygen source. Pure oxygen molecules exposed to controlled electrical discharge resulted in the formation of an oxygen–ozone gaseous mixture. For intra-articular administration, ozone concentration was standardized at **10 µg/mL**

The concentration was selected according to previously reported therapeutic ranges demonstrating anti-inflammatory and analgesic effects while maintaining biological safety.

Injection Procedure

All procedures were performed under aseptic conditions by a single experienced operator.

The skin overlying the temporomandibular joint region was disinfected using antiseptic solution, followed by administration of local anesthesia targeting the auriculotemporal nerve.

The customized positional guide was then positioned to facilitate precise needle placement.

In **Group I**, approximately **2 mL of injectable platelet-rich fibrin** was administered into the superior joint space using an 18-gauge needle (**figure 1)**

In **Group II**, approximately **2 mL of oxygen–ozone mixture (10 µg/mL)** was injected intra-articularly using the same technique **(figure 2)**.

Patients in the ozone group received injections twice weekly for three weeks, whereas patients in the i-PRF group received a single intra-articular injection.

Following completion of treatment, patients were instructed to consume a soft diet for 24 hours and avoid excessive mandibular movements.

Occlusal Splint Therapy

All patients received customized occlusal splints for four weeks prior to intervention to standardize conservative treatment and reduce functional discrepancies among participants.

Follow-up Evaluation

Participants were recalled at: 2 weeks, 3 months, 6 months

Clinical parameters including pain intensity, maximum inter-incisal opening, and lateral mandibular excursion were reassessed at each interval. MRI evaluation for regenerative changes was performed at 12 months post-treatment.

Outcome Measures

The clinical outcomes of the study were categorized into primary and secondary outcome measures to comprehensively evaluate the therapeutic effectiveness of intra-articular injectable platelet-rich fibrin (i-PRF) and ozone injections in the

management of unilateral anterior disc displacement with reduction of the temporomandibular joint. The primary outcome measures included assessment of reduction in pain intensity and improvement in maximum inter-incisal opening. Pain intensity was evaluated using the Visual Analog Scale (VAS), a validated subjective measurement tool in which patients rated their pain on a scale ranging from 0 to 10, where 0 represented absence of pain and 10 represented the most severe pain imaginable. Maximum inter-incisal opening was measured in millimeters using a digital vernier caliper by recording the distance between the incisal edges of the maxillary and mandibular central incisors during maximum mouth opening. The secondary outcome measures included assessment of lateral mandibular excursion and regenerative changes within the articular disc. Lateral mandibular excursion was evaluated by instructing patients to perform maximum lateral movements of the mandible from the intercuspal position, and the movement distance was measured using standardized techniques with a calibrated measuring instrument. Regenerative changes in the temporomandibular joint structures, particularly the articular disc, were assessed radiographically using magnetic resonance imaging (MRI). MRI examinations performed at baseline and during follow-up enabled evaluation of disc morphology, position, tissue integrity, and any regenerative or reparative changes occurring after treatment. Collectively, these outcome measures provided a comprehensive assessment of functional improvement, symptom relief, and biological tissue response following therapeutic intervention.

Statistical Analysis

The collected data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 21.0. Descriptive statistics were expressed as mean ± standard deviation (SD) and percentages wherever appropriate. Intergroup comparisons were performed using Student's independent *t*-test for normally distributed variables and Mann–Whitney U test for non-parametric data, whereas intragroup comparisons were analyzed using paired *t*-test and Wilcoxon signed-rank test. Categorical variables were compared using the Chi-square test. Statistical significance was considered at $p < 0.05$, with $p > 0.05$ regarded as not significant, $p < 0.01$ as highly significant, and $p < 0.001$ as very highly significant.

RESULTS

A total of 80 patients diagnosed with unilateral anterior disc displacement with reduction of the temporomandibular joint were included in the study and randomly allocated into two equal treatment groups: Group I (i-PRF injection; n=40) and Group II (Ozone injection; n=40). Both groups were comparable in terms of demographic and baseline characteristics, thereby minimizing selection bias and allowing valid comparison of therapeutic outcomes (**table 1)**.

The age of the study population ranged between 21 and 47 years, with a mean age of 33.98 ± 7.64 years. The majority of participants belonged to the 31–40 years age group (42.5%). Mean age was 34.18 ± 7.62 years in Group I and 33.78 ± 7.76 years in Group II, with no statistically significant difference between groups (p=0.817). Gender distribution also showed no statistically significant difference, indicating successful randomization.

Pain Assessment

Pain intensity assessed using VAS showed progressive reduction in both treatment groups over time. However, ozone therapy demonstrated significantly greater pain reduction at later follow-up intervals **(table 2)**.

There was no significant difference in pain immediately after treatment; however, pain scores were significantly lower in the ozone group at both 3 and 6 months. Ozone therapy produced greater reduction in pain compared with i-PRF. Intragroup analysis showed statistically significant reductions in pain at both follow-up intervals in each treatment group (p<0.001). The percentage reduction in pain at 6 months was 46.36% in Group I and 57.62% in Group II.

Maximum Inter-incisal Opening

Maximum inter-incisal opening increased progressively in both groups throughout the follow-up period **(table 3)**.

No statistically significant intergroup differences were identified at any follow-up period (p>0.05). Nevertheless, both groups demonstrated significant improvement from baseline values. At 6 months, percentage improvement in mouth opening was 7.51% in Group I and 8.55% in Group II (p<0.001 for intragroup comparison) (**figure 3 (a).**

Lateral Mandibular Excursion

Lateral mandibular excursion improved progressively in both groups with increasing follow-up duration.

No statistically significant difference was observed between groups at any follow-up interval (p>0.05). Intragroup comparison revealed statistically significant increases in lateral excursion at 3 and 6 months in both groups (p<0.001). At 6 months, improvement was 35.06% for Group I and 37.50% for Group II (**figure 3 (b).**

MRI Evaluation of Regenerative Changes

Immediately after injection, all patients in both groups demonstrated subluxation with reduction. At 12 months, MRI findings demonstrated significant differences between the two treatment groups **figure 4 (a) and (b).**.

A significantly greater degree of marked regeneration was observed in the ozone group (65%) compared with the i-PRF group (17.5%). Most patients treated with i-PRF demonstrated only slight regeneration, whereas the majority of ozone-treated patients exhibited marked regenerative changes. Overall, both treatment modalities resulted in significant improvements in clinical and functional parameters; however, ozone therapy demonstrated superior pain reduction and significantly greater regenerative changes on MRI evaluation.

DISCUSSION

Temporomandibular disorders constitute one of the most prevalent causes of chronic non-odontogenic orofacial pain and functional impairment [16]. Internal derangement, specifically anterior disc displacement with reduction (ADDwR), is characterized by an altered relationship between the condyle and articular disc resulting in pain, clicking, and restriction of mandibular movements [16]. Management of such conditions aims primarily at reducing pain, restoring functional movements, and preventing progressive degenerative changes [16]. Conservative treatment remains the first therapeutic approach; however, persistent symptoms often necessitate minimally invasive interventions capable of directly influencing intra-articular pathology. Consequently, regenerative modalities such as injectable platelet-rich fibrin (i-PRF) and ozone therapy have attracted increasing attention because of their analgesic, anti-inflammatory, and tissue-healing properties [17].

The present randomized clinical study compared intra-articular i-PRF and ozone injections in patients with unilateral ADDwR and assessed treatment outcomes through pain intensity, maximum inter-incisal opening, lateral mandibular excursion, and MRI evidence of regenerative changes. The findings demonstrated that both treatment modalities significantly improved clinical outcomes; however, ozone therapy exhibited superior pain reduction and more pronounced regenerative changes.

Pain reduction

Pain is generally considered the principal symptom leading patients with temporomandibular disorders to seek treatment and therefore represents an important indicator of therapeutic success. In the present study, both i-PRF and ozone therapy significantly reduced pain during follow-up periods; however, ozone therapy demonstrated significantly lower VAS scores at three and six months.

The observed reduction in pain following ozone therapy may be attributed to several biological mechanisms. Ozone induces mild controlled oxidative stress, which activates antioxidant defense pathways and modulates inflammatory mediator production. Previous investigations [16-19] have shown that ozone reduces concentrations of inflammatory cytokines including interleukin-6, tumor necrosis factor-α, and prostaglandins while simultaneously improving local oxygen metabolism and tissue perfusion. Reduction of inflammatory mediators may consequently decrease nociceptor sensitization and improve patient comfort.

These findings are consistent with observations by Emad T. Daif, [17] who reported significant improvement in pain among patients with TMJ internal derangement following ozone therapy. Similarly, Sheila Haghighat [18] observed superior pain reduction with ozone therapy compared with conventional pharmacologic management.

The beneficial effects observed with i-PRF may be explained by its high concentration of platelets and growth factors such as platelet-derived growth factor, transforming growth factor-β, vascular endothelial growth factor, and insulin-like growth factor. These molecules contribute to tissue healing by stimulating angiogenesis and reducing inflammatory responses. However, although pain reduction was significant with i-PRF, its effects were comparatively less pronounced than ozone therapy in the current study.

Previous studies [12,13] demonstrated significant reductions in pain and articular symptoms after i-PRF administration. Differences between those studies and the present findings may be related to variability in preparation protocols, concentration of biologically active components, follow-up duration, and disease severity.

Maximum inter-incisal opening

Maximum inter-incisal opening serves as an important functional parameter reflecting mandibular mobility and restoration of joint mechanics. In the present study, both treatment groups demonstrated progressive increases in mouth opening throughout follow-up; however, intergroup differences were not statistically significant.

Improvement in mouth opening after treatment likely occurred secondary to pain reduction, decreased intra-articular inflammation, improved lubrication, and restoration of joint biomechanics. Reduced pain may permit greater functional use of the joint and improved muscle coordination.

These findings agree with study by Moraissi E et al. [13] and Akbar et al. [14] that reported improved mandibular mobility after minimally invasive intra-articular interventions. Similar results have also been reported with platelet concentrates and arthrocentesis procedures.

The absence of significant intergroup differences may indicate that both interventions effectively reduce functional limitations irrespective of differences in their biological mechanisms.

Lateral mandibular excursion

Lateral mandibular movement reflects coordinated function of the temporomandibular joint and masticatory muscles [20]. In the current study, both groups demonstrated significant intragroup improvements without statistically significant differences between groups.

Improvement in lateral excursion can likely be explained by reduction of muscular guarding and restoration of physiologic disc-condyle movement following decreased intra-articular inflammation [21]. Similar observations have been reported in studies evaluating arthrocentesis, platelet concentrates, and conservative management protocols.

Although ozone produced slightly greater numerical improvement, the difference did not achieve statistical significance, suggesting comparable effectiveness between treatment modalities for this parameter [21].

MRI evaluation and regenerative changes

An important strength of the present study was inclusion of MRI evaluation to assess biological and structural alterations after treatment rather than relying exclusively on clinical findings.

MRI findings at 12 months revealed significantly greater regenerative changes in the ozone group compared with the i-PRF group. A substantially larger proportion of patients receiving ozone demonstrated marked regenerative changes.

The regenerative effects associated with ozone therapy may be explained by enhanced oxygen utilization, stimulation of cellular metabolism, activation of antioxidant enzymes, and improved local microcirculation [21]. These mechanisms facilitate tissue repair and remodeling processes [22].

Although i-PRF contains growth factors capable of stimulating tissue regeneration, the comparatively lower regenerative response observed may be related to the single-dose administration protocol used in the study [22]. Multiple injections or adjunctive procedures may potentially enhance regenerative potential [23].

These findings partially differ from studies by Jingjing Xu [15[and Ghoneim N et al. [16], which suggested superior long-term regenerative outcomes with platelet concentrates. Such discrepancies may arise because previous investigations frequently combined platelet products with arthrocentesis, whereas the current study assessed isolated intra-articular injections.

Overall interpretation of findings

The present study suggests that both i-PRF and ozone therapy can be considered effective minimally invasive interventions for management of unilateral ADDwR. However, ozone demonstrated superior pain reduction and more favorable MRI evidence of regeneration.

The superiority of ozone observed in the present investigation may be attributed to its simultaneous anti-inflammatory, analgesic, and metabolic actions. In contrast, i-PRF mainly exerts regenerative effects and may require repeated administration for maximal clinical benefit.

The findings further support increasing evidence suggesting that minimally invasive biologically active therapies may provide greater benefit than conservative treatment alone.

Limitations: despite encouraging findings, several limitations should be considered:

1. The study was conducted at a single center, which may reduce external validity and generalizability.
2. The follow-up period for clinical assessment was limited to six months, while MRI assessment was performed at twelve months; longer follow-up periods could provide stronger evidence regarding treatment stability.
3. The sample size, although statistically calculated, remained relatively limited for broader population extrapolation.
4. Blinding of operators and participants was difficult because treatment protocols differed substantially.
5. The ozone group received repeated injections, whereas the i-PRF group received a single injection, potentially influencing comparative outcomes.
6. Patient-reported quality-of-life measures and psychosocial factors were not evaluated.
7. Biomarkers of inflammation and regeneration were not investigated and therefore biological mechanisms could not be objectively confirmed.

Future recommendations: future studies should consider:

1. Multicenter randomized controlled trials with larger sample sizes.
2. Longer follow-up periods exceeding 24–36 months.
3. Evaluation of repeated i-PRF administration protocols.
4. Assessment of combined modalities such as arthrocentesis with i-PRF or ozone.
5. Inclusion of inflammatory biomarkers including interleukin-6, TNF-α, and matrix metalloproteinases.
6. Incorporation of patient-centered outcomes such as quality of life and functional disability indices.
7. Three-dimensional imaging and quantitative MRI analyses to assess structural regeneration.

Overall, the present findings indicate that ozone therapy may represent a promising minimally invasive therapeutic alternative for managing unilateral anterior disc displacement with reduction while also demonstrating substantial regenerative potential within the temporomandibular joint.

CONCLUSION

Within the limitations of the present study, both intra-articular injectable platelet-rich fibrin (i-PRF) and ozone therapy demonstrated significant clinical effectiveness in the management of unilateral anterior disc displacement with reduction of the temporomandibular joint by reducing pain and improving mandibular function. However, ozone therapy exhibited comparatively superior outcomes with greater pain reduction and more pronounced regenerative changes on MRI evaluation. Therefore, ozone therapy may be considered a promising minimally invasive treatment modality for managing temporomandibular joint internal derangement, although further long-term multicenter studies with larger sample sizes are required to validate these findings and establish standardized treatment protocols.

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