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PLATELET-RICH FIBRIN IN TEMPOROMANDIBULAR DISORDERS: BIOLOGICAL BASIS, CLINICAL APPLICATIONS, AND FUTURE DIRECTIONS

FIBRINA RICA EM PLAQUETAS EM DESORDENS TEMPOROMANDIBULARES: BASES BIOLÓGICAS, APLICAÇÕES CLÍNICAS E DIREÇÕES FUTURAS

FIBRINA RICA EN PLAQUETAS EN TRASTORNOS TEMPOROMANDIBULARES: BASES BIOLÓGICAS, APLICACIONES CLÍNICAS Y DIRECCIONES FUTURAS

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ABSTRACT

Objective: To provide a comprehensive overview of the biological rationale, clinical applications, and emerging perspectives regarding the use of platelet-rich fibrin (PRF) in the management of temporomandibular disorders (TMDs). Methodology: This narrative review analyzed contemporary literature concerning PRF use in temporomandibular joint (TMJ) disorders and associated musculoskeletal conditions. Experimental studies, clinical investigations, systematic reviews, and reports exploring intra-articular PRF applications, regenerative mechanisms, pain control, and functional outcomes were evaluated. Results: PRF is an autologous biomaterial characterized by a three-dimensional fibrin matrix containing platelets, leukocytes, and multiple growth factors involved in tissue repair and regeneration. Its biological properties support angiogenesis, modulation of inflammation, cellular migration, and extracellular matrix remodeling. In the context of TMDs, PRF has been investigated as an adjunctive therapy for internal derangements, degenerative joint conditions, and TMJ dysfunction. Clinical findings suggest that PRF may contribute to pain reduction, improvement in maximum mouth opening, enhanced joint function, and tissue healing. Comparisons with conventional therapies indicate favorable outcomes, particularly when PRF is combined with minimally invasive procedures such as arthrocentesis. Nevertheless, substantial variability exists among studies regarding preparation protocols, application methods, patient selection, and outcome assessment. Consequently, current evidence remains limited by methodological heterogeneity and relatively small sample sizes.

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Conclusion: PRF represents a promising regenerative approach for TMD management due to its biological compatibility, ease of preparation, and potential therapeutic effects on pain and joint function. Although preliminary clinical outcomes are encouraging, robust randomized controlled trials and standardized protocols are required to establish its role within evidence-based treatment strategies for temporomandibular disorders.

Keywords: Platelet-rich Fibrin. Temporomandibular Disorders. Temporomandibular Joint. Arthrocentesis. Regenerative Therapy.

RESUMO

Objetivo: Fornecer uma visão abrangente da fundamentação biológica, aplicações clínicas e perspectivas emergentes do uso de fibrina rica em plaquetas (PRF) no gerenciamento de desordens temporomandibulares (DTM). Metodologia: Esta revisão narrativa analisou literatura contemporânea sobre o uso de PRF em desordens da articulação temporomandibular (ATM) e condições musculoesqueléticas associadas. Estudos experimentais, investigações clínicas, revisões sistemáticas e relatórios explorando aplicações intra-articulares de PRF, mecanismos regenerativos, controle da dor e resultados funcionais foram avaliados. Resultados: PRF é um biomaterial autólogo caracterizado por uma matriz de fibrina tridimensional contendo plaquetas, leucócitos e múltiplos fatores de crescimento envolvidos na reparação e regeneração tecidual. Suas propriedades biológicas suportam angiogênese, modulação da inflamação, migração celular e remodelamento da matriz extracelular. No contexto das DTM, PRF foi investigada como terapia adjuvante para derangements internos, condições articulares degenerativas e disfunção da ATM. Os achados clínicos sugerem que PRF pode contribuir para redução da dor, melhora na abertura bucal máxima, função articular melhorada e cicatrização tecidual. Comparações com terapias convencionais indicam resultados favoráveis, particularmente quando PRF é combinada com procedimentos minimamente invasivos como artrocentese. Entretanto, existe variabilidade substancial entre os estudos quanto aos protocolos de preparação, métodos de aplicação, seleção de pacientes e avaliação de desfechos. Consequentemente, a evidência atual permanece limitada pela heterogeneidade metodológica e tamanhos amostrais relativamente pequenos. Conclusão: PRF representa uma abordagem regenerativa promissora para o gerenciamento de DTM devido à sua compatibilidade biológica, facilidade de preparação e potenciais efeitos terapêuticos na dor e função articular. Embora os resultados clínicos preliminares sejam encorajadores, ensaios clínicos randomizados robustos e protocolos padronizados são necessários para estabelecer seu papel dentro de estratégias de tratamento baseadas em evidências para desordens temporomandibulares.

Palavras-chave: Fibrina Rica em Plaquetas. Desordens Temporomandibulares. Articulação Temporomandibular. Artrocentese. Terapia Regenerativa.

RESUMEN

Objetivo: Proporcionar una descripción general exhaustiva de la fundamentación biológica, aplicaciones clínicas y perspectivas emergentes del uso de fibrina rica en plaquetas (PRF) en el tratamiento de trastornos temporomandibulares (TTM). Metodología: Esta revisión narrativa analizó la literatura contemporánea sobre el uso de PRF en los trastornos de la articulación temporomandibular (ATM) y las condiciones musculoesqueléticas asociadas. Se evaluaron estudios experimentales, investigaciones clínicas, revisiones sistemáticas e informes que exploraban aplicaciones intra-articulares de PRF, mecanismos regenerativos, control del dolor y resultados funcionales. Resultados: PRF es un biomaterial autólogo caracterizado por una matriz de fibrina tridimensional que contiene plaquetas, leucocitos y

múltiples factores de crecimiento implicados en la reparación y regeneración tisular. Sus propiedades biológicas apoyan la angiogénesis, la modulación de la inflamación, la migración celular y la remodelación de la matriz extracelular. En el contexto de los TTM, PRF ha sido investigada como terapia adyuvante para derangements internos, condiciones articulares degenerativas y disfunción de la ATM. Los hallazgos clínicos sugieren que PRF puede contribuir a la reducción del dolor, mejora en la apertura bucal máxima, función articular mejorada y cicatrización tisular. Las comparaciones con terapias convencionales indican resultados favorables, particularmente cuando PRF se combina con procedimientos mínimamente invasivos como la artrocentesis. Sin embargo, existe una variabilidad sustancial entre los estudios con respecto a los protocolos de preparación, métodos de aplicación, selección de pacientes y evaluación de resultados. En consecuencia, la evidencia actual sigue siendo limitada por la heterogeneidad metodológica y los tamaños de muestra relativamente pequeños. Conclusión: PRF representa un enfoque regenerativo prometedor para el tratamiento de TTM debido a su compatibilidad biológica, facilidad de preparación y posibles efectos terapéuticos en el dolor y la función articular. Aunque los resultados clínicos preliminares son alentadores, se requieren ensayos clínicos aleatorizados robustos y protocolos estandarizados para establecer su papel dentro de estrategias de tratamiento basadas en evidencia para los trastornos temporomandibulares.

Palabras clave: Fibrina Rica en Plaquetas. Trastornos Temporomandibulares. Articulación Temporomandibular. Artrocentesis. Terapia Regenerativa.

1 INTRODUCTION

Temporomandibular disorders (TMDs) encompass a group of musculoskeletal and joint conditions affecting the temporomandibular joint (TMJ), masticatory muscles, and associated structures. They represent one of the most common causes of chronic orofacial pain and may significantly impair mandibular function and quality of life (Schiffman *et al.*, 2014). Although conservative approaches remain the cornerstone of TMD management, growing interest has emerged in regenerative therapies aimed at addressing underlying tissue degeneration and inflammation.

Among these regenerative approaches, platelet-rich fibrin (PRF) has attracted increasing attention due to its biological properties. PRF consists of a fibrin scaffold enriched with platelets, leukocytes, and growth factors capable of modulating inflammation and promoting tissue repair (Choukroun *et al.*, 2006; Miron *et al.*, 2017). Through the release of PDGF, TGF-β, VEGF, and insulin-like growth factor (IGF), PRF may stimulate angiogenesis, extracellular matrix synthesis, and regenerative processes within the TMJ environment.

Recent investigations have explored PRF as an adjunct to arthrocentesis and other minimally invasive TMJ procedures. Clinical studies have reported reductions in pain intensity, improvements in maximum mouth opening, and enhanced joint function following PRF application (Xu *et al.*, 2023). Nevertheless, considerable variability exists regarding PRF preparation methods, treatment protocols, and outcome assessment, making it difficult to establish definitive clinical recommendations. Consequently, a critical review of the available evidence is needed to clarify the role of PRF in contemporary TMD management.

2 METHODOLOGY

A narrative literature review was performed to evaluate the biological rationale and clinical applications of platelet-rich fibrin (PRF) in temporomandibular disorders (TMDs). Relevant publications were identified through searches in PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar up to June 2026. The search terms included “platelet-rich fibrin,” “PRF,” “temporomandibular disorder,” “temporomandibular joint,” “TMJ,” “arthrocentesis,” “orofacial pain,” and “joint regeneration.” Clinical studies, randomized controlled trials, observational studies, systematic reviews, meta-analyses, and experimental investigations examining PRF use in TMD management were included. Particular emphasis was placed on studies evaluating pain reduction, mandibular function, maximum mouth opening, inflammatory modulation, and tissue regeneration. Additional references were

identified through manual screening of bibliographies from relevant articles. The evidence was qualitatively synthesized to discuss biological mechanisms, current clinical indications, treatment outcomes, limitations of the existing literature, and future research directions.

3 RESULTS

3.1 BIOLOGICAL RATIONALE SUPPORTING INTRA-ARTICULAR PRF USE

The classification proposed by Dohan Ehrenfest *et al.* (2009) established that platelet concentrates differ fundamentally according to their leukocyte and fibrin content, distinguishing pure platelet-rich plasma (P-PRP) from leukocyte- and platelet-rich fibrin (L-PRF). This distinction is directly relevant to TMJ applications because the polymerization and final architecture of the fibrin matrix considerably influence the strength and growth-factor trapping/release potential of the membrane, with leukocyte populations exerting a strong influence on the release of certain growth factors, particularly TGF-β1 (Dohan Ehrenfest *et al.*, 2012). This slow, sustained release profile is frequently cited as the biological basis for using PRF-derived liquid formulations (i-PRF) as intra-articular injectables rather than single-bolus growth-factor solutions.

3.2 PRF AS AN ADJUNCT TO ARTHROCENTESIS IN TMJ OSTEOARTHRITIS AND INTERNAL DERANGEMENT

Several randomized controlled trials have evaluated intra-articular i-PRF following arthrocentesis. In a double-blind RCT involving 36 patients with TMJ osteoarthritis, the i-PRF group and the control group (arthrocentesis alone) showed significant differences in pain levels and in maximum mouth opening (MMO), lateral movement, and protrusive movement over 12 months of follow-up ($p < 0.001$) (Işık *et al.*, 2022). Similarly, in a preliminary controlled prospective study of i-PRF injections for internal derangement with joint clicking, clicking disappeared entirely in 14 of 20 patients one week after the first injection and in all patients after the second injection, although it recurred in two patients by six months (Manafikhi *et al.*, 2022).

Comparative trials between platelet concentrates have also been reported. A randomized trial comparing i-PRF and PRP injections after arthrocentesis in 14 patients (28 joints) with internal derangement assessed pain, maximal mouth opening, lateral and protrusive movement, joint sounds, and radiographic disc position and joint effusion at monthly intervals over six months (Sharma *et al.*, 2023).

3.3 CONCENTRATED GROWTH FACTOR (CGF) AS A RELATED PRF-DERIVED FORMULATION

CGF, a higher-density second-generation platelet concentrate, has shown outcomes consistent with those reported for i-PRF. In an RCT of 60 patients with TMJ osteoarthritis diagnosed by CBCT, comparing CGF combined with sodium hyaluronate (CGF+SH) against sodium hyaluronate alone, the CGF+SH group showed significant improvement in VAS pain scores, the Helkimo Clinical Dysfunction Index, and condylar remodeling on CBCT at 2 weeks, 3 months, and 6 months after treatment (Jia *et al.*, 2024). In an earlier retrospective series, a single intra-articular injection of 1 mL CGF in patients with joint degeneration and disc displacement with/without reduction reduced VAS pain scores and joint clicking while increasing mouth opening (İnce *et al.*, 2017).

3.4 SYSTEMATIC REVIEWS AND META-ANALYSES

Pooled evidence supports a modest but consistent analgesic effect. A meta-analysis of 12 RCTs comparing intra-articular PRP/PRF with control after TMJ arthrocentesis found that pain scores were significantly reduced with PRP/PRF compared with control at one month (MD: −0.96), three months (MD: −1.22), and six months or more (MD: −1.61) (Nagori *et al.*, 2024). Restricting the analysis to i-PRF specifically, a scoping review of eight studies (five RCTs, 213 patients) reported that articular pain at three months decreased to 0–25% of baseline values in the i-PRF group versus 38–50% in the control groups, while mandible mobility increased to 121–153% in the i-PRF groups compared with 115–120% in controls (Sielski *et al.*, 2023). A more recent meta-analysis restricted to i-PRF (13 studies from 332 screened) similarly found significant within-group pain reduction at 3–6 and 8–12 months for i-PRF alone or combined with arthrocentesis or arthroscopy (Araújo *et al.*, 2026).

3.5 HETEROGENEITY ACROSS PREPARATION PROTOCOLS AND OUTCOME MEASURES

Across the identified trials, considerable variability was observed in centrifugation protocols, injection volume and frequency, follow-up duration, and outcome instruments (VAS, MMO, Helkimo index, joint sounds, imaging), which several reviews explicitly note as a limitation to pooling data and generating standardized clinical recommendations (Nagori *et al.*, 2024; Araújo *et al.*, 2026).

4 DISCUSSION

The evidence gathered in this review suggests that PRF-derived products, whether prepared as a solid membrane, a liquid injectable (i-PRF), or a concentrated growth factor formulation (CGF), share a common biological premise: a fibrin scaffold capable of trapping and gradually releasing platelet- and leukocyte-derived growth factors within the joint space. This sustained-release mechanism differentiates PRF conceptually from PRP, which delivers a more immediate but shorter-lived growth-factor bolus, and may partly explain why several trials report PRF outcomes that are equal to or slightly better than PRP, particularly for pain control over intermediate follow-up periods.

Clinically, the most consistent finding across studies is a reduction in pain intensity when PRF is used as an adjunct to arthrocentesis, rather than as a stand-alone intervention. Improvements in maximum mouth opening are also frequently reported, although the magnitude and statistical significance of this outcome vary more across trials than pain outcomes do. This pattern likely reflects the multifactorial nature of restricted mouth opening in TMDs, which depends not only on intra-articular inflammation but also on myofascial, occlusal, and psychosocial components that a purely intra-articular injection cannot address.

The heterogeneity identified in preparation protocols represents a substantial barrier to clinical translation. Differences in centrifugation speed and time, injected volume, number of sessions, and interval between injections make it difficult to define an optimal PRF protocol for TMJ application, in contrast to more standardized protocols already established for L-PRF in periodontal and oral surgery. Similarly, the coexistence of several distinct PRF subtypes (L-PRF, i-PRF, CGF) with different fibrin density, leukocyte content, and growth-factor release kinetics is rarely acknowledged in comparative analyses, and many systematic reviews pool these subtypes together despite their biologically distinct behavior. This may partially explain the considerable statistical heterogeneity (I^2 values exceeding 80% in several meta-analyses) observed in pooled pain outcomes.

Sample sizes across the available RCTs remain small, generally ranging from 14 to 60 patients per trial, and follow-up periods rarely extend beyond 12 months. This limits conclusions about the durability of clinical benefit and precludes any inference about long-term structural or regenerative effects on the condyle or disc, despite some radiographic signals of condylar remodeling in CGF studies. Blinding is also inconsistently reported, and patient-reported outcomes such as pain are inherently susceptible to placebo response,

particularly in a minimally invasive procedure such as arthrocentesis that already produces symptomatic improvement on its own.

From a translational standpoint, the available data support a role for PRF as a low-cost, autologous, easily prepared adjunct to arthrocentesis in patients with TMJ osteoarthritis or internal derangement who have not responded adequately to conservative therapy. However, the current evidence does not yet justify PRF as a first-line or stand-alone intervention, nor does it allow firm conclusions about superiority over hyaluronic acid or corticosteroid injections, given the mixed comparative results reported in the literature. Future research should prioritize head-to-head trials comparing standardized PRF subtypes against each other and against established comparators, using core outcome sets, longer follow-up, and imaging-based structural endpoints to determine whether the clinical improvements observed translate into genuine tissue regeneration rather than symptomatic relief alone.

5 CONCLUSION

Platelet-rich fibrin, in its various clinical formulations, represents a biologically plausible and technically accessible adjunct for the management of temporomandibular disorders, particularly when combined with arthrocentesis in patients with TMJ osteoarthritis or internal derangement. Current evidence points to consistent short- to medium-term improvements in pain and, to a lesser and more variable extent, in maximum mouth opening. Nevertheless, the heterogeneity in PRF preparation protocols, the small sample sizes of available trials, and the limited follow-up duration constrain the strength of these conclusions. Standardization of PRF preparation and application protocols, together with larger and longer-term randomized controlled trials directly comparing PRF subtypes with one another and with conventional therapies, is required before PRF can be firmly incorporated into evidence-based treatment algorithms for temporomandibular disorders.

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