

Systematic Review TMJ Disorders

Platelet-rich plasma for the therapeutic management of temporomandibular joint disorders: a systematic review

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Abstract. This systematic review aimed to investigate whether intra-articular injections of platelet-rich plasma (PRP) are beneficial for the treatment of degenerative temporomandibular disorders, such as temporomandibular joint osteoarthritis (TMJ-OA) and disc displacement with osteoarthritic lesions, when compared to other treatments, such as injections of hyaluronic acid (HA) or saline. An electronic search of the MEDLINE and Scopus databases was performed using combinations of the terms “temporomandibular” and “platelet rich plasma”, to identify studies reported in English and published up until May 2017. A hand-search of relevant journals and the reference lists of selected articles was also performed. The initial screening identified 153 records, of which only six fulfilled the inclusion criteria and were included in this review. Of these studies, three compared PRP with HA, while three compared PRP with Ringer’s lactate or saline. Four of the studies found PRP injections to be superior in terms of improvements in mandibular range of motion and pain intensity up to 12 months after treatment, while the remaining two studies found similar results for the different treatments. There is slight evidence for the potential benefits of intra-articular injections of PRP in patients with TMJ-OA. However, a standardized protocol for PRP preparation and application needs to be established.

Key words: temporomandibular disorders; platelet-rich plasma; intra-articular injections; temporomandibular joint osteoarthritis.

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Temporomandibular disorders (TMD) are a group of disorders that affect the temporomandibular joint (TMJ), the associated musculoskeletal tissues, or both¹. TMD include degenerative conditions of the articulating surfaces of the TMJ, with osteoarthritis (OA) being the most prevalent, as well as TMJ disc displacement,

which refers to disruption of the physiological relationship between the articulating surfaces and the TMJ disc². Epidemiological studies have shown that up to 8.9% of the general population suffer from TMJ-OA, and the reported prevalence of TMJ-OA in TMD patients is up to 55.6%^{3,4}. Moreover, up to 44.2% of

TMD patients present with TMJ disc displacement, although this is not always accompanied by degenerative articular changes⁵.

TMJ-OA is a degenerative disorder that includes erosive changes to the cartilage layers, subchondral bone loss, and synovitis⁶. Unlike OA of the knee, which is

mainly attributed to obesity, aging, and trauma, the causes of TMJ-OA remain unclear; excessive mechanical loading accompanied by a diminished host adaptive ability is the leading hypothesis^{6,7}. In cases of TMJ disc displacement, a pathological contact is established between the articulating surfaces. In some patients, this leads to the disruption of cartilage homeostasis and osteoarthritic changes, due to overload, excessive wear, and inferior adaptability⁸. Despite the fact that a clear correlation between the two disorders has not yet been established, it appears that there is a relationship, and some patients present with disc displacement that precedes TMJ-OA.

Currently, the therapeutic management of degenerative disorders of the TMJ is focused on alleviating the functional pain and establishing normal range of mandibular motion in these patients. Non-invasive modalities are the first course of treatment, which include physiotherapy, the use of a stabilization splint, and medications to relieve symptoms^{9,10}. For patients in whom the symptoms persist and the severity of the degeneration is greater, minimally invasive treatments may be applied, such as lavage, hyaluronic acid and corticosteroid injections, arthrocentesis, and arthroscopy^{11,12}.

Hyaluronic acid (HA) is a natural glycosaminoglycan produced by synovial cells that is naturally present in the synovial fluid¹³. HA is considered an essential component of synovial fluid, participating in joint lubrication, and the degradation of HA is usually observed in cases of TMJ degeneration^{13,14}. Intra-articular HA injections into the TMJ have been used for the treatment of TMJ-OA and internal derangement for many years, showing positive results regarding mouth opening and a decrease in pain intensity^{15,16}. Despite the extensive literature on the subject, the exact mechanism of action of HA remains unclear, although it is thought that the positive effects are the result of the increase in viscosity of the synovial fluid, restoration of nutrition, and reduction of inflammatory mediators^{15,17}.

Platelet-rich plasma (PRP) is a biological therapy that comprises a concentrate of platelets from the patient's blood¹⁸. PRP is obtained through the withdrawal of blood and centrifugation to acquire a high concentration of platelets, which in some cases can exceed 2,000,000/ μ l¹⁹. This concentrate has shown great potential as a therapeutic modality due to the abundance of growth factors that it contains²⁰. Despite the fact that the exact mechanism of action of PRP remains unknown, it has

become popular in sports medicine and orthopaedics, and has emerged as a promising treatment for degenerative cartilage defects and OA²¹. This is mainly attributed to its anti-inflammatory and analgesic properties, as well as the positive outcomes obtained in clinical studies when it has been administered intra-articularly into joints with a cartilage pathology, such as knee OA^{22,23}. More specifically, proof of concept has been established and there is substantial scientific evidence to support the potential effects of PRP on cartilage defects²⁴. Furthermore, PRP has several advantages as a course of treatment, as it is easily obtained and prepared, and is associated with few postoperative complications²⁵.

Recently, PRP injections have been applied intra-articularly into the TMJ in patients with TMJ-OA and disc displacement. Despite the extensive literature on the application of PRP in other joints, especially the knee, its application as a treatment in the TMJ is relatively new. Furthermore, it is not yet clear whether the positive results obtained in the treatment of pathological cartilage features and OA in other joints can be extrapolated to the management of TMJ-OA and disc displacement accompanied by cartilage degeneration. Therefore, this systematic review of the literature was performed to determine the effectiveness of intra-articular PRP injections in patients with TMD compared to other treatments, such as injections of HA or saline.

Materials and methods

The aim of this review was to test the null hypothesis that the treatment of degenerative TMD with intra-articular injections of PRP is not superior to intra-articular injection of another substance.

A systematic literature review was performed following the guidelines of the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)²⁶. The first step in the systematic review was to use the PICO format to define a clinical question: the population (P) was patients with TMD in comparative studies, the intervention (I) was patients treated with PRP injections, the comparison (C) was patients treated with other types of intra-articular drug therapy or placebo, and the outcome (O) was the improvement in TMD symptoms.

Search strategy

An electronic search of the MEDLINE and Scopus databases was performed for

papers in English published up to May 2017. In addition, relevant journals covering TMD were examined, and a hand-search was performed of the reference lists of the primary studies to identify additional results. The following terms were used in the search strategy: [temporomandibular AND (platelet OR plasma OR (plasma rich in growth factor) OR (platelet AND rich AND plasma))].

Inclusion criteria

Randomized clinical trials (RCTs) were included in this review. The study population comprised patients who had been diagnosed with TMJ-OA or anterior disc displacement with or without reduction (ADDwR/ADDwoR), together with degenerative changes in the articulating structures of the TMJ. Patients in the study group received intra-articular injections of PRP or plasma rich in growth factors (PRGF) after arthrocentesis or arthroscopy, while patients in the control group received intra-articular injections of HA or saline or Ringer's lactate solution after arthrocentesis or arthroscopy.

The primary outcome variables used to assess the efficacy of treatment were maximum mouth opening (MMO, in millimetres) and pain intensity. A 10-point visual analogue scale (VAS) was used for the assessment of pain intensity, with 0 as the absence of pain and 10 as the worst pain imaginable. The secondary outcome variables were joint sounds and findings on magnetic resonance imaging (MRI) and cone beam computed tomography (CBCT).

Data collection and analysis

All relevant studies were analyzed separately by two reviewers based on the inclusion criteria listed above for final selection. The analysis was done first at the title and abstract level and then at the full-text level. Any disagreement was resolved by discussion.

A form was used to collect standard information from each article, including the following: mention of the study being an RCT, randomization procedure, experimental design, use of blinding, follow-up, patient characteristics (such as age, sex, sample size, diagnosis, and previous treatments), therapeutic study protocol and control, methods used to assess the treatment (such as pain intensity on a VAS and MMO, before and after treatment), and drop-outs.

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