

Ultrasound-guided Platelet-rich Plasma Prolotherapy for Temporomandibular Disorders

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Purpose: Temporomandibular disorder (TMD) is one of the most common diseases causing chronic orofacial pain. Prolotherapy is called 'regenerative injection therapy' or 'growth factor stimulation injection', and it induces the functional reactivation of tissues such as ligaments and tendons. The aim of this study is to evaluate the efficacy of ultrasound-guided prolotherapy with platelet-rich plasma (PRP) for the patients who had the TMD symptoms, especially in temporomandibular joint (TMJ) pain, restricted mouth opening, and TMJ sound.

Methods: Twenty-seven patients visited Chosun University Dental Hospital with the symptoms of pain, restricted mouth opening, and TMJ sound were included in this study. When the patients visited the hospital, we measured; the degree of pain, range of mouth opening (ROM), and TMJ sound, and grouped them according to their chief complaints. TMJ pain and ROM were measured both at the first visit and the fourth week after the PRP injection, and also evaluated the impact of the treatment on their daily activities.

Results: After the treatment, the patients in the TMJ pain group showed some improvement (visual analogue scale [VAS] 5.6 to 3.6), and the patients in the restricted mouth opening group exhibited increased ROM (26 mm to 32 mm; $p < 0.05$). On the other hand, the patients in the TMJ sound group had no improvement.

Conclusions: PRP prolotherapy could be effective for the treatment of TMJ pain and restricted mouth opening. However, further studies are still necessary in terms of TMJ sound and long-term effect of PRP prolotherapy.

Key Words: Arthrocentesis; Platelet-rich plasma; Prolotherapy; Temporomandibular joint disorders; Ultrasonography

INTRODUCTION

Temporomandibular joint disorder (TMD) is one of the most common diseases causing chronic pain in orofacial area. As many factors cause TMD, there are a number of methods for treatments for TMD, and surgery is the last method to be considered.¹⁻⁵⁾ Arthrocentesis is a method to clean the inside of the temporomandibular joint (TMJ) by injecting syringes into the upper articular cavity under the local anesthesia. The major purpose of arthrocentesis is the

reduction of pain and relaxation of the disc by washing out the inflammatory mediators from TMJ to enhance its activity.⁶⁾ Identification of the superior joint space is important for the successful arthrocentesis, and a recent study has reported that ultrasonography can be helpful to find the superior joint space during intra-articular and extra-articular injections.⁷⁾

Prolotherapy is called 'regenerative injection therapy' or 'growth factor stimulation injection', and it induces the reactivation of function of tissues such as ligaments and

tendons. It could be applied to musculoskeletal diseases resulting from the weakness of the ligaments and tendons. Several clinical studies showed that prolotherapy stimulated the growth of newly formed tissues of ligaments and tendons using injection and resulted in increased diameter of collagen fibers and ligaments up to 60%.⁹⁾ The materials of injection were dextrose, platelet-rich plasma (PRP), glycerine, phenol, glucose and etc.⁹⁻¹³⁾

Prolotherapy has been used for 80 years. In 1937, Schultz¹⁴⁾ reported the treatment of TMJ hypermobility using prolotherapy for the first time. Prolotherapy has been used for the treatment of hyperactivity of the TMJ, which induces an inappropriate hinge movement of TMJ. It might result in sustainable stability of TMJ by healing unstable area, and enhance the effects of growth factors by raising the level of growth factors or inducing the regeneration and tissue growth.¹⁵⁾ Autogenous PRP concentrates were developed in the 1970s, and Whitman et al.¹⁶⁾ were the first to present a method for preparation and use of PRP to accelerate healing processes. PRP stimulate tissue regenerations by releasing numerous growth factors that stimulate proliferation, differentiation and migration of cells.¹⁷⁾ In addition, PRP injections could promote optimization of healing environment and facilitate earlier functional rehabilitation of joints.¹⁸⁾

Therefore, the aim of this study is to evaluate the efficacy of ultrasound-guided prolotherapy with PRP for the patients who had the TMD symptoms, especially in TMJ pain, restricted mouth opening, and TMJ sound.

MATERIALS AND METHODS

This study population consisted of 31 patients who had visited for TMD symptoms at the Department of Oral and Maxillofacial Surgery of the Chosun University Dental Hospital (CUDH) from March 2012 to July 2014. All patients were carried out functional assessment of TMD symptoms in the Department of Oral Medicine of CUDH.

The inclusion criteria were confined to TMJ dysfunctions, from medical history, radiography, range of mouth opening, and palpation of the masticatory muscles and TMJ in orofacial area. The exclusion criteria included involuntary movement of mandible, TMJ dislocation, degenerative changes in TMJs and chronic myofascial pain. In addition, 4 patients

were excluded because they didn't visit at follow-up evaluation. Finally, 27 patients (7 men and 20 women) were included. The duration of TMD symptoms ranged from 5 days to 15 years and the average was 26.2 ± 35.1 months.

To evaluate the efficacy of prolotherapy, the patients were grouped into three subgroups: TMJ pain, restricted mouth opening, and TMJ sound, on the basis of TMJ dysfunctional assessment of the patients. If a patient had more than two TMJ dysfunctions, they were distributed separately. Therefore, among the 27 subjects, there were 19 patients in the TMJ pain group, 10 patients in the restricted mouth opening group, and 4 patients in the TMJ sound group. There were 5 patients who had TMJ pain and restricted mouth opening together, and one patient with TMJ pain and TMJ sound. No patient had all of three symptoms simultaneously (Fig. 1).

Before the injection procedure, informed consents were obtained from all patients. PRP was collected out of peripheral blood from the ulnar vein of the patient with injection syringe including 2 mL anticoagulant agent (CPDA-1). After mixing the collected blood, they were placed in a centrifuge rotor (HC-1000; Huons, Seongnam, Korea) with PRP preparation kit (sPRP Kit, Huons; Fig. 2). Centrifugation parameters were set to 3,200 rpm, and the centrifugation time was 9 minutes, and then buffy-coat layer was collected. After harvesting the buffy-coat layer, 3 mL PRP solution was

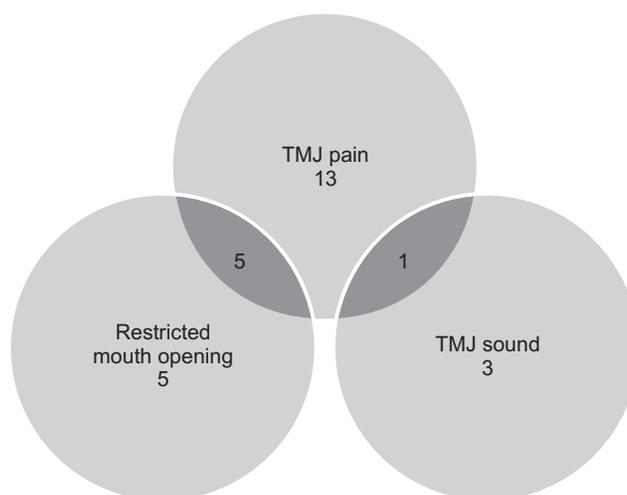


Fig. 1. Subgroups in the studied population. There were 5 patients who had temporomandibular joint (TMJ) pain and restricted mouth opening together, and one patient with TMJ pain and TMJ sound. No patient had all of three symptoms simultaneously.

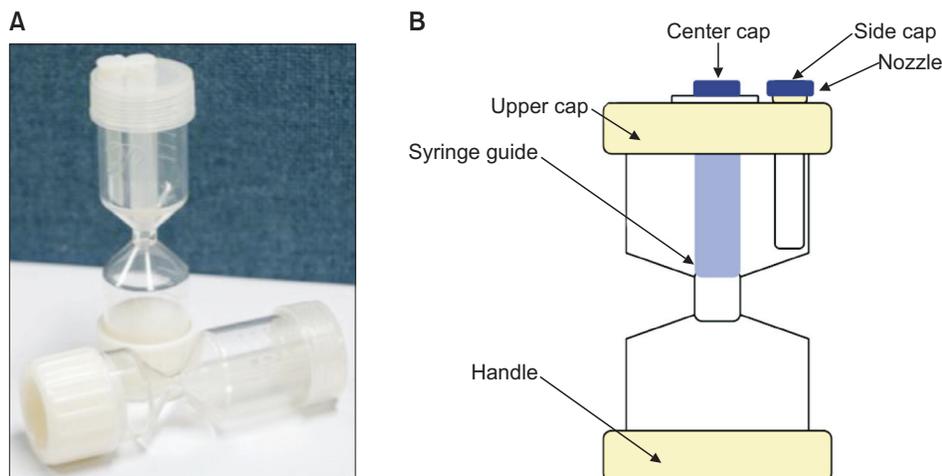


Fig. 2. Platelet plasma protein preparation kit (A) and its schematic view (B).

made with adding the plasma for optimal injection of unilateral TMJ.

The injection sites were determined using ultrasound system (SA6000II; Medison Co. Ltd, Seoul, Korea). Sterile ultrasound probe was placed over the TMJ, perpendicular to the zygomatic arch and handled for the best view. And then TMJ movement was evaluated. Condylar and glenoid fossa surfaces appeared as hyperechoic lines on the sonograms, while the articular disc was identified as a thin area of hyperechogenicity surrounded by a hypoechoic halo between the two lines. After a disinfection procedure was carried out with povidone-iodine solution, a 25 gauge needle with 3 mL syringe was placed in the determined point to access into the superior joint space by ultrasound guidance. Following pumping manipulation to confirm the location of the needle, 1.5 mL of PRP was injected into the superior joint space and then seeing the sonogram, additional 0.5 mL was injected into the retrodiscal tissue, anterior discal ligament, and finally TMJ capsule, respectively (Fig. 3). After the PRP injection, the passive jaw exercise was performed to increase the distribution of the injected material. Clinical follow-up was performed 4 weeks after the procedure. The following parameters were analyzed in detail for the purpose of this study: changes in the range of mouth opening and the intensity of pain, and the discomfort with their symptoms. The range of mouth opening was measured by millimeters at the first visit and the fourth week after the treatment. The visual analogue scale (VAS) with the scale from 0 to 10 was used to measure the degree of pain and daily discomforts with their symptoms.

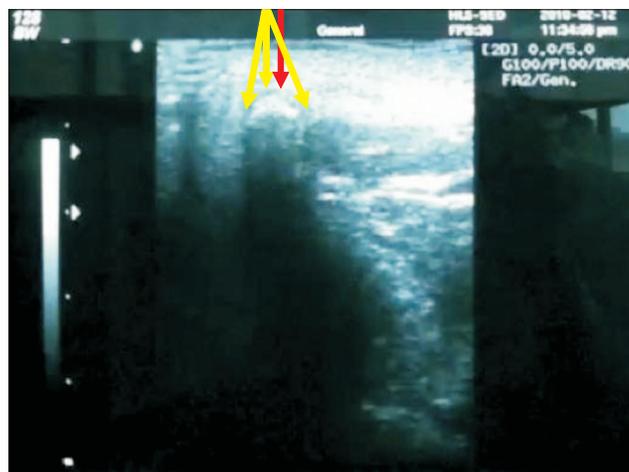


Fig. 3. Temporomandibular joint (TMJ) ultrasound image and injection point. Black arrow indicates superior joint space, and left gray arrow indicates retrodiscal tissue, right gray arrow indicates anterior discal ligament, and middle gray arrow indicates TMJ capsule.

All statistical analyses were performed using IBM SPSS Statistics software for Windows (version 20.0; IBM Co., Armonk, NY, USA). To find out the difference in VAS scores, statistical analysis was performed using the Wilcoxon signed ranks test. Statistical significance was defined as $p < 0.05$, with a 95% confidence interval.

This study was approved by the Chosun University Dental Hospital Ethics Committee (CDMDIRB-1218-96).

RESULTS

Twenty-seven patients (7 men and 20 women) were included in this study. The mean age was 43.0 ± 17.3 years.

In the TMJ pain group, the comparison of pain intensity by

Table 1. Comparison of parameters at baseline and 4 weeks follow up in the TMJ pain and restricted mouth opening groups

Subgroup	Baseline	4 Weeks	p-value
TMJ pain (VAS)	5.8±1.6	3.7±2.6	0.026*
Restricted mouth opening (mm)	25.0±8.2	36.2±4.9	0.012*

Values are presented as mean±standard deviation.

TMJ, temporomandibular joint; VAS, visual analogue scale.

*p<0.05 (by Wilcoxon signed ranks test).

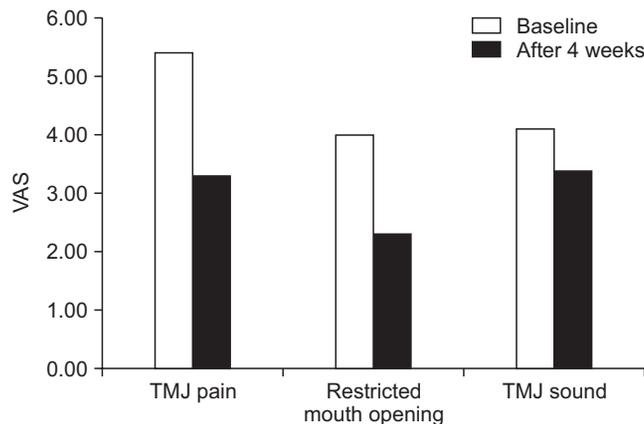
VAS score at the baseline and 4 weeks follow up, suggested a beneficial effects of the performed procedure (5.6 to 3.6). In the restricted mouth opening group, the comparison of the range of mouth opening (by millimeters) also suggested similar results, increased from 25 mm to 36 mm. On the other hand, no improvement had been reported in the subgroup of TMJ sound. There was statistical significant improvement in the TMJ pain and restricted mouth opening group (p<0.05) (Table 1).

In the comparison of daily discomforts with TMD symptoms by VAS scores, all the subgroups responded improvement (TMJ pain: 5.4 to 3.3; restricted mouth opening: 4.0 to 2.3; TMJ sound: 4.1 to 3.4, respectively) (Fig. 4).

In the questionnaire survey about the efficacy of performed procedure, 17 patients in the TMJ pain group, 7 patients in the restricted mouth opening group, and one patient in the TMJ sound group answered that it was effective. However, 3 patients in the TMJ sound group responded negatively over the performed procedure. Another questionnaire about willingness to subsequent procedure, all patients in the restricted mouth opening group answered that they were willing to receive subsequent therapy. However, all patients in the TMJ sound group responded that they did not want another procedures. In the TMJ pain group, 4 patients answered that they did not want subsequent therapy because of the ineffectiveness (2 patients) and the pain during injection (2 patients).

DISCUSSION

Prolotherapy has been used to enhance tendon, ligament, and joint healing for over sixty years.¹⁹⁾ Prolotherapy induces rapid inflammation reaction so that new tendons and ligaments can be formed. Temporary stresses of the cells increase cytokine release and growth factor activity with macrophage

**Fig. 4.** Comparison of daily discomfort reported by patients at baseline and 4 weeks follow up in the subgroups. TMJ, temporomandibular joint; VAS, visual analogue scale.

migration. Then, the level of specific repair cells increase, which make ligaments and tendons more endurable.⁹⁾ Indications of prolotherapy contain damaged ligaments or tendons, joint pain during functioning, and patient's desire for treatments.¹⁹⁾ In the previous studies, prolotherapy was used for different parts of the body rather than TMJ. It was used for the anterior cruciate ligament laxity, finger arthritis, chronic headache, lumbar pain, and coccygodynia, and revealed satisfactory results.²⁰⁻²³⁾ Recently, many studies reported that prolotherapy showed satisfactory effects in the TMD patients with pain, limited mouth opening, and clicking. Hakala and Ledermann²⁴⁾ reported that in 71% of TMD patients showed alleviated pain, 42% showed no pain at all, and 78% had reduced clicking as a result of prolotherapy. Ungor et al.²⁵⁾ also reported that the TMJ pain was improved by VAS score (from 62.00 to 22.80) and TMJ sounds were reduced in 8 patients after the prolotherapy, even though the change in the mouth opening range was not statistically significant. Therefore, TMJ prolotherapy can be advantageous to patients with TMD that is refractory to or has shown only limited success with physical medicine, dietary restrictions, and home care, and also can be advantageous to patients who have not had adequate improvement with oral appliances, or are unable or unwilling to wear such appliances, and who are unsuitable or unwilling candidates for TMJ surgery.¹⁹⁾ On the other hand, prolotherapy can be contraindicated to patients with an allergy on materials, infections, excessive bleeding, impaired healing, hemophilia and parafunctions such as bruxism and clenching.⁹⁾

Recently, prolotherapy using PRP has been actively investigated. The advantages of this method would be the safety of the material and a zero possibility of hypersensitivity to injected plasma.¹⁷⁾ PRP contains several types of growth factors and cytokines, therefore it also promotes the healing of the bone and soft tissues. To promote healing by using cytokines is based on the interactions with the rapid inflammatory reactions from prolotherapy which increases the level of growth factors and induces tissue regeneration.²⁶⁾ Clinically, it is used for neural damage, osteoarthritis, myocardial injury, bone regeneration, and also in plastic surgery. However, there has been a few of studies for the treatment of TMD using PRP. Machon et al.²⁷⁾ reported that when autologous blood was injected in the 25 patients with chronic recurrent TMJ dislocation, the success rate was about 80% and there was no recurrence until the next follow up after one year. Kütük et al.²⁸⁾ reported that after the injection of PRP to the rabbits with TMJ osteoarthritis, there was the bone regeneration on the side of PRP injection. A recent clinical preliminary reported that application of the intra-articular injections of PRP into the TMJ had a positive impact on the reduction of the intensity of pain experienced by patients treated for TMJ dysfunction.¹⁷⁾ However, there have been no clinical studies assessing the overall symptoms related to TMD including the intensity of pain, range of motion, and TMJ sound, as we know.

In this study, the study population was confined to patients with TMJ symptoms because the PRP was administrated in intra-articular region. In the TMJ pain group, the comparison of pain intensity by VAS score suggested a beneficial effect of the performed procedure (5.6 to 3.6). In the restricted mouth opening group, the comparison of the range of mouth opening also suggested similar results, increased from 25 mm to 36 mm. On the other hand, no improvement had been reported in the subgroup of TMJ sound. This was possibly due to small sample size (n=4).

In the questionnaire survey about the efficacy of the PRP injection, 80.6% of the evaluated patients answered that it was effective. Another questionnaire about willingness to subsequent procedure revealed that 80.6% of the evaluated patients were willing to receive subsequent therapies. Notably, all patients in the restricted mouth opening group answered that they were willing to receive subsequent

therapy. These results were similar in the arthrocentesis study.²⁹⁾ However, there is a difference between these two methods. The purpose of arthrocentesis is to reduce the negative pressure in disc through the lavage and wash out the inflammatory mediators. On the other hand, PRP injection focuses on the induction of functional recovery by means of regenerating weakened tissues.

Ultrasound was used for prolotherapy in this study. In general, a skillful technique is required during TMJ prolotherapy since the cannula should be injected in the superior joint space through the blind technique. However, ultrasound enabled us to identify the joints and other adjacent structures so that the accuracy allows for higher rate of success. Also, ultrasound has an economical advantage compared to arthroscopy. Ultrasound-guide prolotherapy is excellent tool for clinicians to raise the postoperative success rate.

In conclusion, ultrasound guided-prolotherapy using PRP would be readily accessible to TMD patients, economical and also highly satisfactory treatment. It is expected as a new alternative treatment for TMJ pain and restricted mouth opening. However, further studies are still necessary in terms of TMJ sound and long-term effect of PRP prolotherapy.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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