CASE REPORT

대한치과의사협회지 2025; 63(4): 137-152
https://doi.org/10.22974/jkda.2025.63.4.003

Degenerative temporomandibular joint disorder treated with prolotherapy: Case series

퇴행성 측두하악관절 장애에서 증식치료의 치료 효과: 증례보고

Jeong-Kui Ku[1], Jin-Won Choi[1], Young-Kyun Kim[1,2,*]

[1]Department of Oral and Maxillofacial Surgery, Section of Dentistry, Seoul National University Bundang Hospital, Seongnam, Korea
[2]K Oral and Maxillofacial Surgery Dental Clinic, Seongnam, Korea

ABSTRACT

Degenerative joint disease (DJD) of the temporomandibular joint (TMJ) is a progressive disorder marked by cartilage degradation and bone deterioration, leading to chronic pain and dysfunction. While conventional therapies such as occlusal splints, medication, physical therapy, and intra-articular injections aim to alleviate symptoms, they lack regenerative capability. This report showed the potential of prolotherapy, a regenerative injection treatment that stimulates tissue repair, in TMJ DJD patients. Four individuals received 2 or 3 prolotherapy sessions using polydeoxyribonucleotide and 20% dextrose at 3-week intervals, alongside conservative care. Outcomes were evaluated via pain intensity (VAS), maximum mouth opening (MMO), joint noise, and radiographic imaging. All patients reported notable pain relief, sustained MMO over 35 mm, and correction of mandibular deviation. Radiographs revealed cortical bone formation and improved joint surface contour. These findings suggested prolotherapy might promote structural regeneration in TMJ DJD. Further studies are warranted to confirm its long-term efficacy and safety. ***(J Korean Dent Assoc 2025; 63(4): 137-152)***

Key words : Osteoarthritis; Temporomandibular Joint Disorders; Prolotherapy; Cone-Beam Computed Tomography

Introduction

Temporomandibular disorders (TMD) are a heterogeneous group of musculoskeletal conditions encompassing pain syndromes, such as myalgia and arthralgia, as well as structural abnormalities like disc displacement and degenerative joint disease (DJD). DJD is characterized by progressive cartilage degeneration, leading to remodeling of the subchondral bone[1]. TMJ pain during mandibular movements correlates with degenerative changes in joint surfaces, including erosion, flattening, osteophyte formation, sclerosis, and subchondral cyst formation, as observed on radiographic imaging. DJD patients who report functional pain tend to exhibit more severe joint destruction[2]. Structural alterations, such as condylar flattening and erosions, are strongly associated with pain frequency and intensity in DJD patients[3,4]. Clinical and radiographic evaluations indicate that approximately 25-55% of TMD patients exhibit degenerative changes[5,6]. DJD is considered a multifactorial disorder, with some cases occurring idiopathically. Current conservative treatments focus on symptom relief and functional recovery, commonly involving nonsteroidal

Received Mar 3, 2025; Revised Mar 31, 2025; Accepted Apr 1, 2025

*Corresponding author: : Dr. Young-Kyun Kim
Department of Oral and Maxillofacial Surgery, Section of Dentistry, Seoul National University Bundang Hospital, 82 Gumi-ro 173beon-gil, Bundang-gu, Seongnam, Gyeonggi-do 13620, Korea
Tel.: +82-31-787-2780, E-mail: kyk0505@daum.net

ISSN: 0376-4672
eISSN: 2713-7961

anti-inflammatory drugs (NSAIDs), occlusal splints, and physical therapy[2]. Minimally invasive approaches, including arthrocentesis, arthroscopy, and intra-articular injections (e.g., hyaluronic acid or corticosteroids), may be employed, while surgical interventions, such as arthroplasty, condylectomy, or total joint replacement, are reserved for severe dysfunction and persistent pain[7]. However, due to limited understanding of DJD pathophysiology and the poor healing potential of avascular cartilage tissue, effective regenerative treatments remain unclear[8].

Recently, prolotherapy has emerged as a promising alternative for TMD treatment. Prolotherapy is a non-surgical regenerative therapy designed to promote cellular proliferation and restore the structural integrity of weakened ligaments and tendons[9]. Also known as "regenerative injection therapy," prolotherapy aims to stimulate the growth and proliferation of new connective tissue, strengthening periarticular ligaments, tendons, and supportive structures when applied to the TMJ[10]. Hypertonic dextrose is the most widely used proliferant, though agents such as polidocanol, manganese, zinc, growth hormone, and platelet-rich plasma (PRP) are also being explored[11]. In orthopedics, polydeoxyribonucleotide (PDRN) has been identified as an effective proliferant, but its application in TMD management remains limited.

Prolotherapy may offer a viable option for regenerating TMJ structures in DJD patients, potentially reversing degenerative changes. This study presents a case series of four patients treated with PDRN and dextrose injections at three-week intervals, demonstrating favorable clinical outcomes.

Case Report

This study was conducted in compliance with the ethical guidelines set by the institutional and national committees responsible for human experimentation, in accordance with the Helsinki Declaration of 1975, revised in 2008, with approval from the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (IRB: B-2503-960-105). Four patients who underwent TMJ prolotherapy between 2024 and 2025 at the Department of Oral and Maxillofacial Surgery were included. Patients presented with TMJ pain and restricted mouth opening, and Cone Beam Computed Tomography (CBCT) findings confirmed DJD-related changes.

The prolotherapy procedure followed an established protocol[10]. Initial pain control was achieved using 1.8 mL of mepivacaine hydrochloride (Scandonest 3%, Septodont) or 2% lidocaine (1:100,000 epinephrine, Huons, Seongnam, Korea) for auriculotemporal nerve block and superior joint space anesthesia[14]. Hypertonic dextrose or PDRN (Placentex® injection; Pharma Research, Gangneung, Korea; PolyNeo®; DongKwang Pharm, Seoul, Korea) was administered based on prior studies[15]. The dextrose injection consisted of 20% dextrose (Daehan

Table 1. Radiographic findings of degenerative joint disease[12,13]

Radiographic finding	Definition
Erosion	Bone loss and cortical bone destruction, resulting in irregular condylar/glenoid fossa morphology
Flattening of condyle	Loss of the normal convex shape, leading to a flattened condylar surface
Osteophyte formation	Bone spurs developing at the joint surface margins
Subchondral sclerosis	Increased cortical bone density in the condyle and glenoid fossa
Subchondral cyst formation	Small cystic lesions within the bone due to cartilage degeneration
Joint space narrowing	Reduction in inter-articular space due to degenerative changes

Pharm, Korea), 2% lidocaine (Huons, Seoul, Korea), and saline (Daehan Pharm, Seoul, Korea) in a 2:1:1 ratio, producing a 10% dextrose solution[16]. The anatomical injection sites for TMJ prolotherapy and the respective volumes of either dextrose or PDRN administered were as follows: Posterior disc attachment (2 cc), Anterior disc attachment (1 cc), Upper lateral capsular ligament (0.5 cc), Lower lateral capsular ligament (0.5 cc).

For injection into the superior joint space, the procedure was performed with the patient's mouth in an open position. The needle was inserted at a point located 10 mm anterior and 2 mm inferior to the canthotragal line, and advanced approximately 20 mm in an anterosuperior direction. For targeting the retrodiscal tissue (posterior attachment of the disc), the injection was also performed with the mouth open. The insertion point was set at 6 mm anterior and 2 mm inferior to the canthotragal line, with the needle directed anteriorly to a depth of approximately 20 mm. To target the anterior attachment of the disc, the procedure was performed with the patient's mouth in a closed position. The needle was inserted 15 mm anterior and 2 mm inferior to the canthotragal line, and advanced approximately 20 mm in an anteroinferior direction toward the presumed insertion of the lateral pterygoid muscle.

For post-procedural pain management, patients receiving PDRN injections were prescribed Clanza 100 mg (Aceclofenac, United Pharm, Seoul, Korea) once daily (qd) for 7 days or Brufen 200 mg (Ibuprofen, Samil Pharm, Korea) for 2 days. Patients receiving dextrose injections were prescribed Tyrenol (Acetaminophen, 500 mg, Johnson & Johnson, Seoul, Korea). No additional interventions were performed during the prolotherapy treatment or follow-up period. Patients using stabilization splint were advised to continue applying it throughout the treatment period. If patients were not using splints before treatment, they were recommended to have one fabricated after their symptoms improved.

Case 1

A 30-year-old male patient presented with right TMJ pain that developed approximately two years after the extraction of a third molar. He reported stiffness and a grinding sensation (crepitus) in the right TMJ, particularly after prolonged mastication. The patient had a history of bruxism and unilateral mastication. On palpation, tenderness was noted in the right TMJ (VAS 7-8), with concurrent right temporal pain. Radiographic examination revealed cortical irregularities and erosive changes in the right condyle (Fig. 1). The patient was diagnosed with myofascial pain and degenerative TMJ arthritis.

Treatment aimed to control pain and inflammation while stabilizing the TMJ. An occlusal stabilization splint was fabricated, and prolotherapy was initiated. The first injection of PDRN was administered on the initial visit, with acetaminophen prescribed for post-procedure pain relief. Two weeks later, an occlusal splint was delivered. After three weeks, the crepitus evolved into intermittent clicking. Mandibular deviation during mouth opening was absent, and the MMO was over 40 mm. However, residual pain (VAS 6) warranted a second prolotherapy session using dextrose solution.

Three weeks post-treatment, joint noise decreased further, and pain was reduced (VAS 4-5). A third prolotherapy session using PDRN was performed. Following the final injection, Celebrex (Celecoxib, Viatris, Korea) and Imotun (Avocado-Soybean Unsaponifiable Extract, Chong Kun Dang Pharm, Korea) were prescribed for two weeks. At the six-month follow-up, the patient reported significant pain relief (VAS 1-2), with clicking persisting but without functional discomfort. Radiographic images demonstrated cortical bone reformation and recovery of previously eroded condylar surfaces (Fig. 2).

Case 2

A 29-year-old female patient had experienced inter-

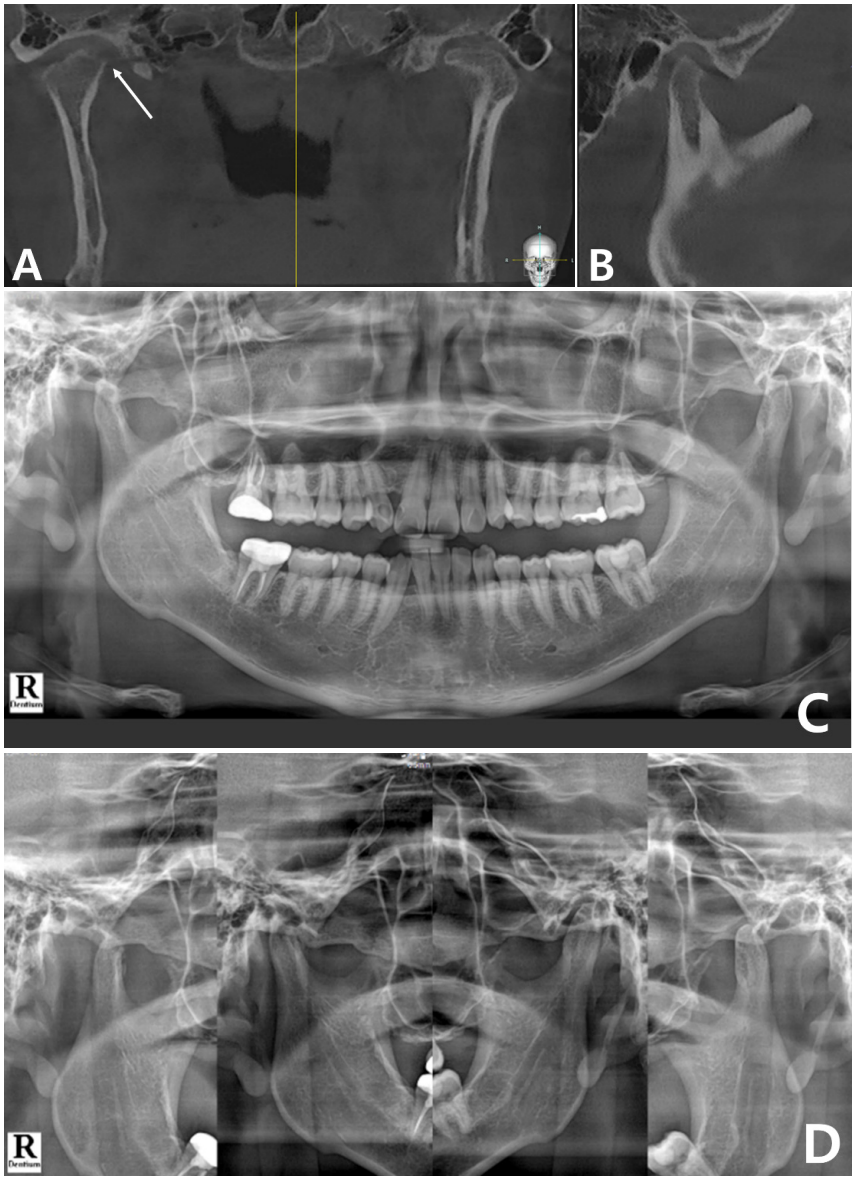

Figure 1. Initial radiographs show sclerosis and irregular morphology of the cortical bone in the right condyle (arrow), along with evidence of erosive changes. A. Coronal cone-beam computed tomography (CBCT) image. B. Sagittal CBCT image. C. Panoramic radiograph. D. TMJ-specific panoramic radiograph.

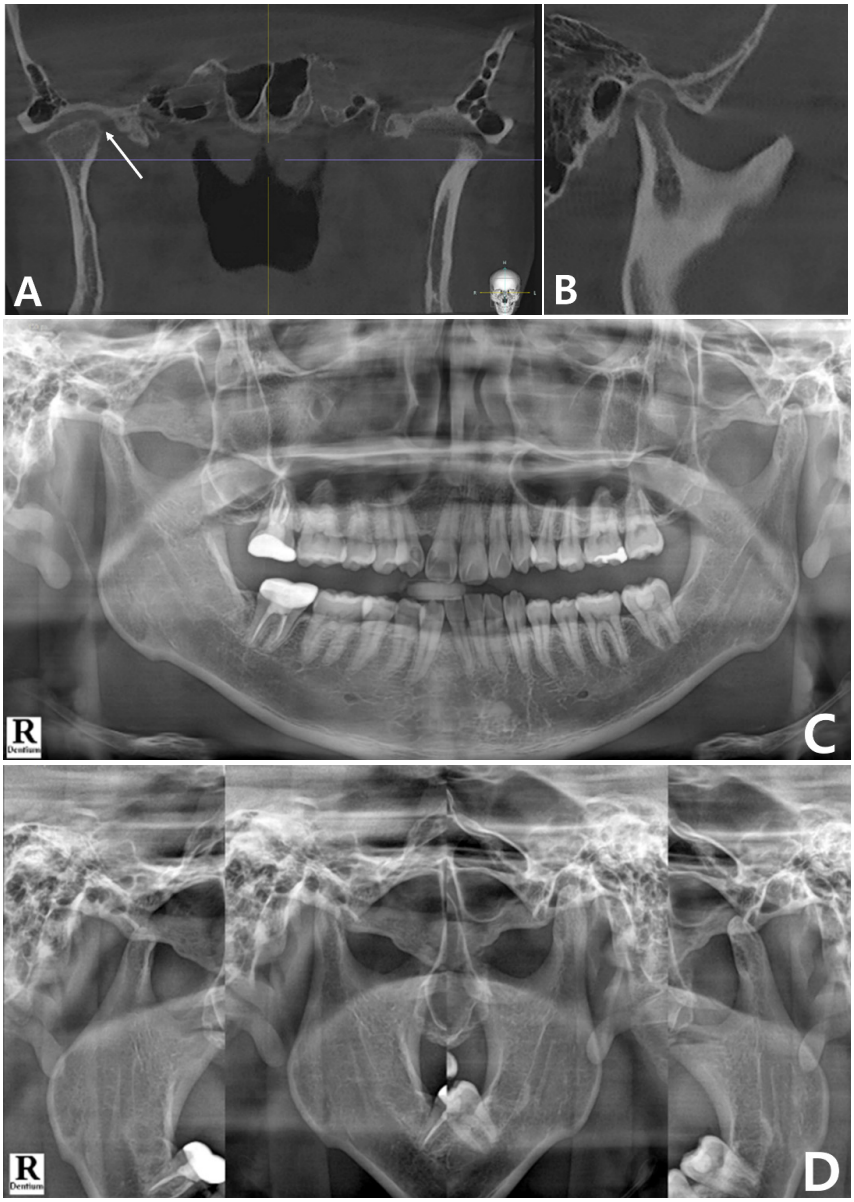

Figure 2. Six months post-treatment radiographs show cortical bone regeneration and increased bone density in the previously eroded condylar surface(arrow). A. Coronal cone-beam computed tomography (CBCT) image. B. Sagittal CBCT image. C. Panoramic radiograph. D. TMJ-specific panoramic radiograph.

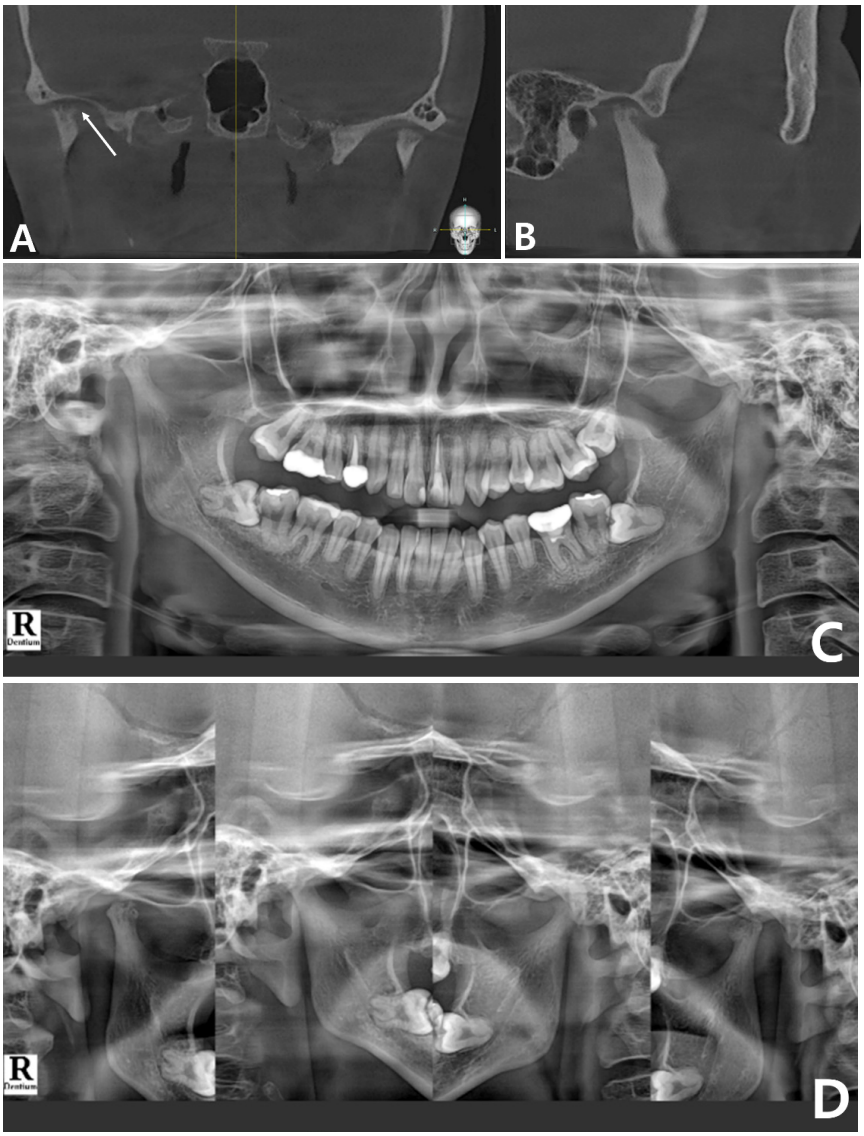

Figure 3. Initial radiographs show hypoplasia and asymmetry of both condyles, along with bone resorption and cortical bone loss in the right condyle(arrow). A. Coronal cone-beam computed tomography (CBCT) image. B. Sagittal CBCT image. C. Panoramic radiograph. D. TMJ-specific panoramic radiograph.

mittent right TMJ pain for two years, which worsened after consuming tough food. She reported discomfort during prolonged mouth opening and a crepitus-like noise in the TMJ. She experienced persistent TMJ pain during mastication (VAS 4-5). Radiographic findings revealed condylar irregularities and erosive changes bilaterally, with more severe degenerative changes in the right condyle (Fig. 3). The patient was diagnosed with bilateral degenerative TMJ arthritis.

The first prolotherapy session involved a PDRN injection in the right TMJ, with acetaminophen prescribed for pain relief. Three weeks later, her MMO was measured at 35 mm, and pain had resolved. Crepitus had transitioned into clicking, prompting a second prolotherapy session using dextrose solution. After the second session, pain and joint noise were completely resolved. An occlusal stabilization splint was fabricated.

At the six-month follow-up, the patient remained pain-free (VAS 0) and maintained a normal MMO of 36 mm. Radiographic imaging showed smooth reformation

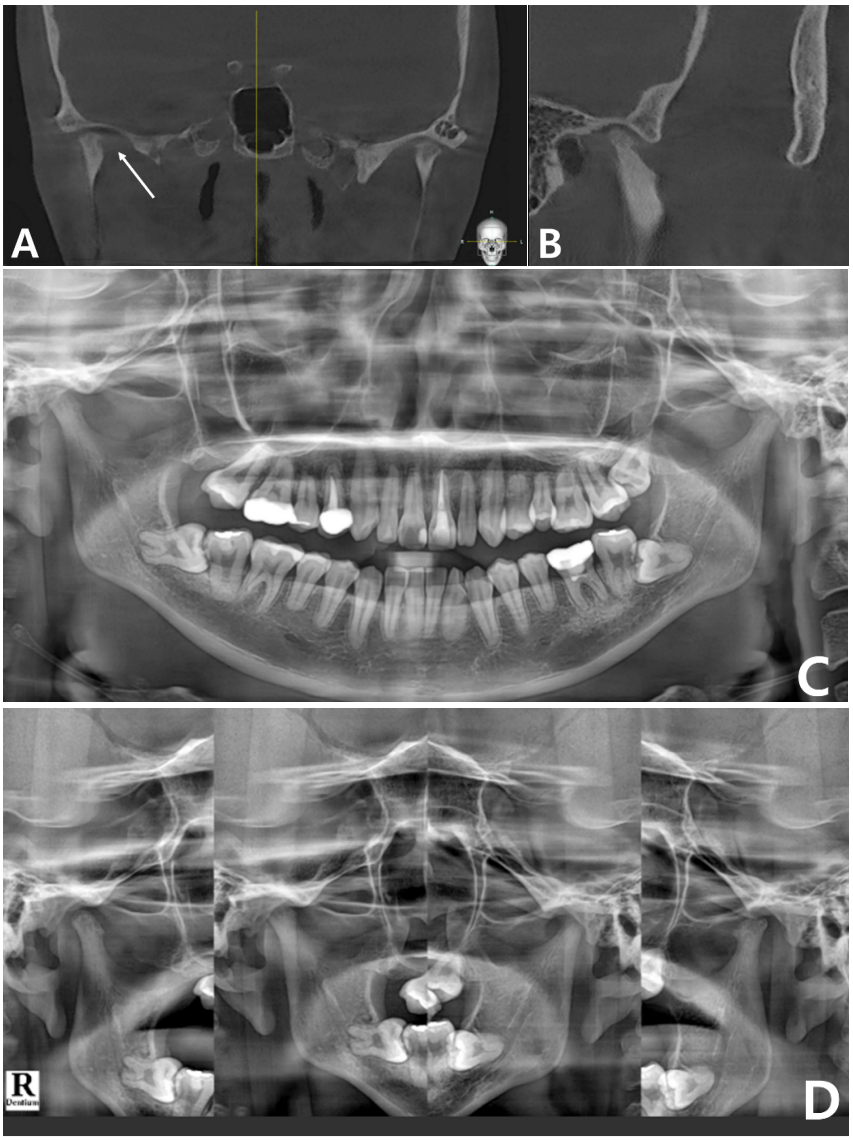

Figure 4. Six months post-treatment radiographs show cortical bone reformation in the right condyle, with the previously smoothing of the previously irregular condylar surface(arrow). A. Coronal cone-beam computed tomography (CBCT) image. B. Sagittal CBCT image. C. Panoramic radiograph. D. TMJ-specific panoramic radiograph.

of previously irregular condylar surfaces (Fig. 4).

Case 3

A 43-year-old male patient had experienced clicking sounds and pain in the right temporomandibular joint (TMJ) for approximately one year, with worsening symptoms over the past month. At the initial visit, joint noise had disappeared, but the patient reported persistent right TMJ pain (VAS 3) and a history of bruxism. The maximum mouth opening (MMO) was within the normal range (40 mm). Radiographic imaging revealed erosive changes in the cortical bone of the right condyle, while the left condyle showed morphological changes but maintained an intact cortical margin (Fig. 5). The patient was diagnosed with degenerative TMJ arthritis and was initially prescribed Celebrex and Imotun for pain management. One week later, the patient returned for follow-up, reporting

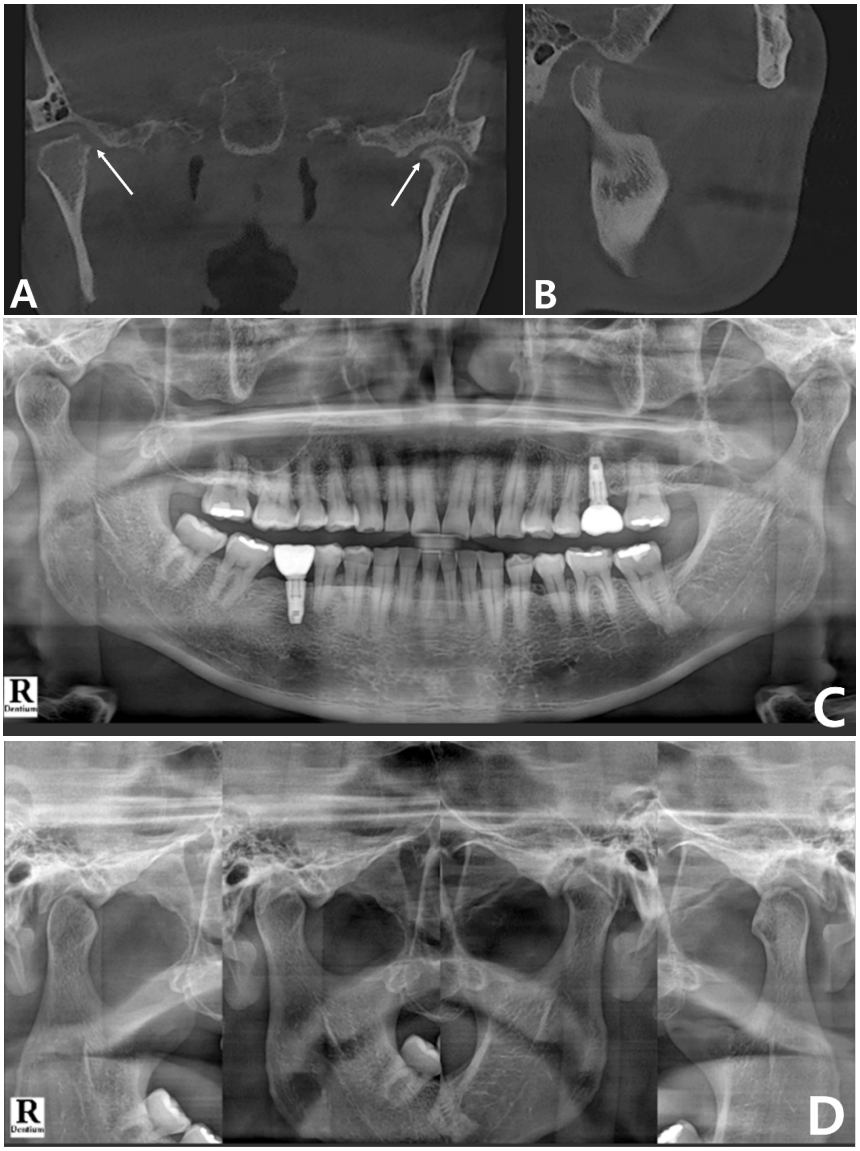

Figure 5. Initial radiographs show erosive changes in the cortical bone of the right condyle, while the left condyle shows deformation but retains a relatively thick cortical margin(arrow). A. Coronal cone-beam computed tomography (CBCT) image. B. Sagittal CBCT image. C. Panoramic radiograph. D. TMJ-specific panoramic radiograph.

reduced pain, but MMO had decreased to 30 mm. Active mouth opening elicited right TMJ pain, and palpation of the lateral aspect of the right TMJ confirmed tenderness.

The first PDRN prolotherapy injection was administered in the right TMJ. Immediately after the procedure, manual mobilization techniques were performed, restoring MMO to 40 mm. For short-term pain control, Tyrenol was prescribed for three days. At the three-week follow-up, symptoms had improved, but mild pain (VAS 2) persisted during mastication. A second prolotherapy session using dextrose was administered. Three weeks later, significant symptom improvement was noted, with residual pain reduced to a minimal level (VAS 1). To achieve complete symptom resolution, a third PDRN injection was performed. The patient was prescribed Clanza for two weeks. Due to the patient's distant residence, fabrication of an occlusal stabilization splint was recommended at a nearby dental clinic.

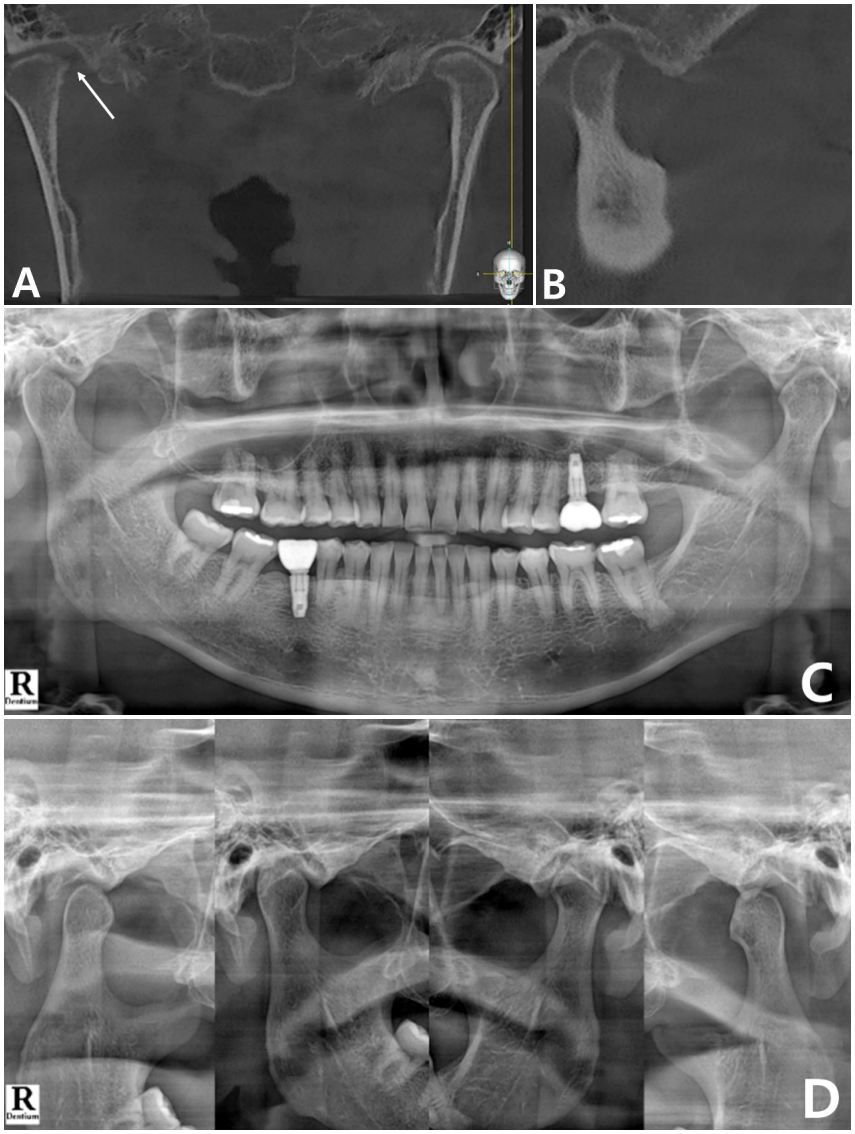

Figure 6. Six months post-treatment radiographs show distinct cortical bone formation in the right condyle, with smoothing of the previously irregular joint surface(arrow). A. Coronal cone-beam computed tomography (CBCT) image. B. Sagittal CBCT image. C. Panoramic radiograph. D. TMJ-specific panoramic radiograph.

At the six-month follow-up, the patient reported near-complete pain relief, with an MMO of 45 mm. Final radiographic imaging revealed distinct cortical bone formation around the right condyle, with the previously irregular joint surface appearing smoother compared to the initial X-ray (Fig. 6).

Case 4

A 30-year-old female patient presented with a four-month history of severe tenderness in the left TMJ upon palpation (VAS 5) and pain during mouth opening. Mandibular deviation to the left was observed upon opening, but MMO was within the normal range (46 mm). No joint noise was detected. The patient had been using an occlusal stabilization splint for two months, fabricated at

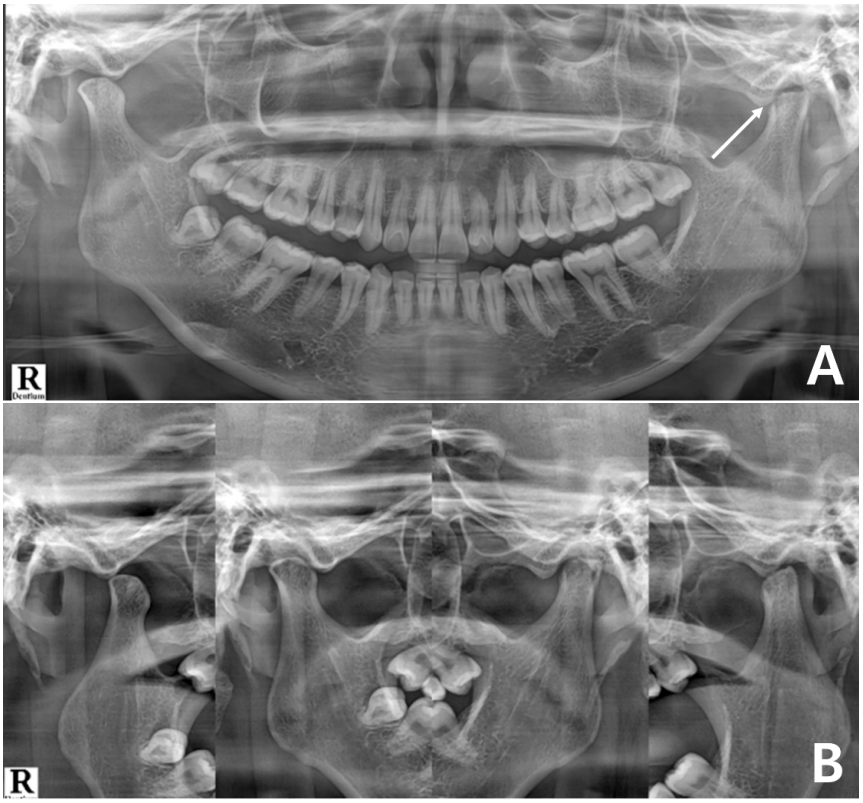

Figure 7. Initial radiographs show severe degenerative changes and bone resorption in the left condyle(arrow). A. Panoramic radiograph. B. TMJ-specific panoramic radiograph.

another dental clinic. However, a recent CBCT revealed severe degenerative changes in the left condyle, prompting referral for further treatment (Fig. 7). The patient was diagnosed with degenerative TMJ arthritis.

While continuing splint therapy, the first PDRN prolotherapy injection was administered to the left TMJ. Three weeks later, the patient reported significant symptom improvement. However, due to the severity of degenerative changes in the left condyle, a second prolotherapy session using dextrose was performed. At the next follow-up, three weeks after the second injection, the patient described near-complete resolution of pain (VAS 2). A third PDRN injection was administered to promote joint recovery, and Clanza was prescribed for two weeks.

At the six-month follow-up, the patient reported complete pain resolution (VAS 0), with no observed mandibular deviation during mouth opening. The MMO remained stable at 46 mm. Radiographic imaging showed evidence of cortical bone reformation in the left condyle, with a reduction in the initial bone resorption findings and an overall stabilization of the joint structure (Fig. 8).

All patients experienced significant pain reduction and improved mouth opening (MMO) within three prolotherapy sessions. Radiographic evaluations conducted six months post-treatment confirmed bone regeneration in previously degenerated TMJ regions (Table 2).

Discussion

The primary objectives in the treatment of DJD are functional restoration and pain relief. Available treatment modalities can be categorized into non-invasive, minimally invasive, and surgical approaches[7]. Intra-articular

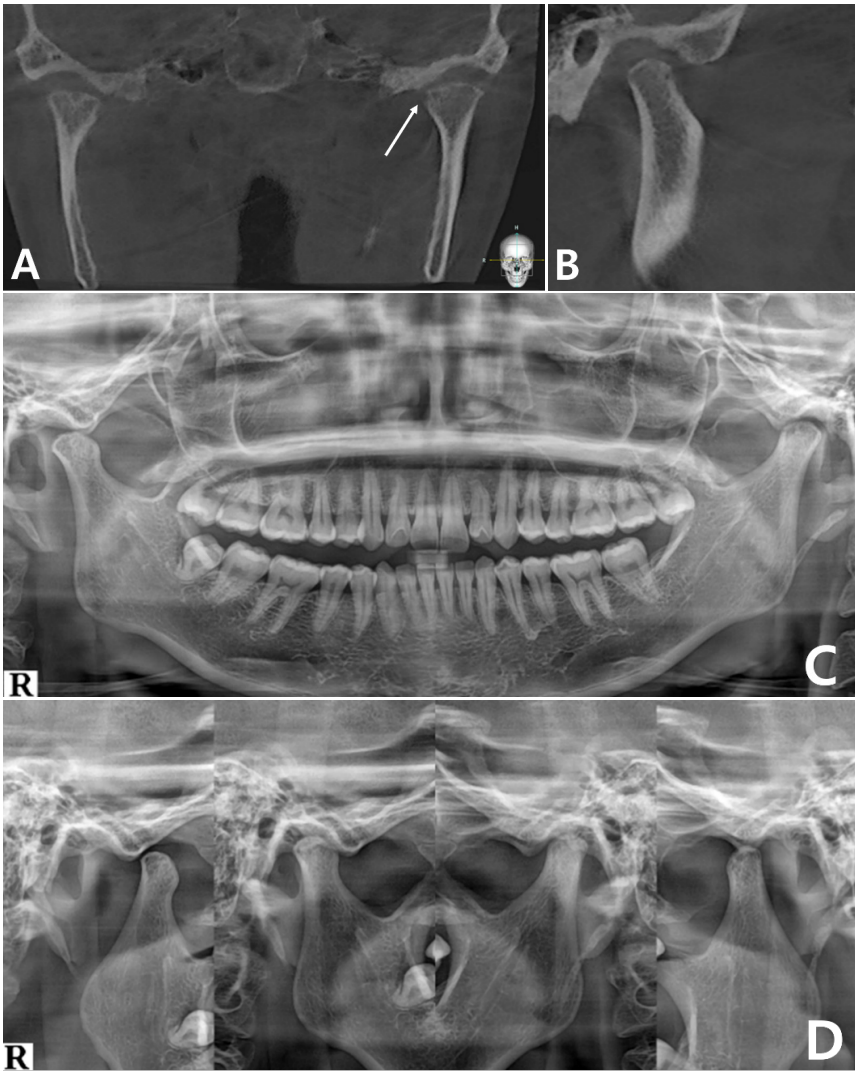

Figure 8. Six months post-treatment radiographs show cortical bone reformation in the left condyle, with a reduction in bone resorption and a more stabilized joint structure(arrow). A. Coronal cone-beam computed tomography (CBCT) image. B. Sagittal CBCT image. C. Panoramic radiograph. D. TMJ-specific panoramic radiograph.

Table 2. Patient characteristics, prolotherapy treatment process, and treatment outcomes

Case No.	Sex/ age	Chief complaint	Pre-VAS/ MMO	1st agent	2nd agent	3rd agent	Final VAS/MMO	Bone regeneration at six months post-treatment
1	M/30	Pain and crepitus	7-8/40 mm	PDRN (4 cc)	Dextrose (4 cc)	PDRN (4 cc)	1-2/40 mm	O
2	F/29	Pain and crepitus	4-5/35 mm	PDRN (4 cc)	Dextrose (4 cc)		0/36 mm	O
3	M/43	Pain and clicking	3/40 mm	PDRN (4 cc)	Dextrose (4 cc)	PDRN (4 cc)	0/45 mm	O
4	F/30	Pain	5/46 mm	PDRN (4 cc)	Dextrose (4 cc)	PDRN (4 cc)	0/46 mm	O

VAS: visual analog scale, MMO: maximum mouth opening, PDRN: polydeoxyribonucleotide.

hyaluronic acid injections have been considered beneficial for TMJ osteoarthritis; however, their superiority over arthrocentesis remains debated[17]. Steroid injections and platelet-rich plasma (PRP) therapy have demonstrated effects comparable to those of arthrocentesis[18]. Arthrocentesis, which removes inflammatory mediators and disrupts adhesions within the joint, is widely utilized, though its efficacy remains controversial. Despite its potential benefits, it primarily targets inflammation reduction rather than cartilage or bone regeneration[19]. To date, no established treatment has been shown to regenerate degenerated cartilage in TMJ DJD[12,18]. In this case series, four patients who underwent prolotherapy combined with conservative treatment exhibited radiographic evidence of joint regeneration in addition to symptomatic relief. Unlike conventional treatments that focus solely on symptom management, prolotherapy appeared to facilitate joint tissue repair. Consistent with prior studies reporting pain reduction in DJD patients exhibiting osteophyte formation and new bone growth[3,4], our findings suggest that prolotherapy-induced joint regeneration contributed to functional recovery without residual pain. Moreover, prolotherapy is theorized to stimulate tissue regeneration by modulating the inflammatory response, aligning with its fundamental regenerative mechanism. The combination of prolotherapy with conservative management and active mandibular mobilization exercises may have played a pivotal role in enhancing therapeutic outcomes.

Patients with chronic pain-related DJD exhibit distinct inflammatory and anti-inflammatory cytokine profiles compared to patients with general TMD. Notably, they show increased levels of inflammatory Monocyte Chemoattractant Protein-1 (MCP-1), decreased levels of anti-inflammatory Omentin-1, and a downregulation of the transcription of Transforming Growth Factor beta 1 (TGF-β1), an essential anti-inflammatory growth factor[13]. Mélou et al. (2023) reported that various inflammatory and catabolic mediators, along with multiple signaling pathways, influence the progression of DJD[7]. Key inflammatory cytokines, such as Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-1 beta (IL-1β), and matrix-degrading enzymes, including Matrix Metalloproteinases (MMP-3, MMP-9, MMP-13) and A Disintegrin and Metalloproteinase with Thrombospondin Motifs (ADAMTS-4, ADAMTS-5), play crucial roles in joint degeneration. Additionally, various signaling pathways, such as estrogen, Hypoxia-Inducible Factor (HIF), Extracellular Signal-Regulated Kinase (ERK), Notch, β-catenin, Indian Hedgehog, Fibroblast Growth Factor (FGF), p38 Mitogen-Activated Protein Kinase (p38 MAPK), and PI3K/Akt, have been implicated in DJD pathophysiology[20,21,22]. Prolotherapy, through intra-articular injection of proliferative agents, can stimulate fibroblast proliferation via both inflammatory and non-inflammatory pathways, thereby strengthening weakened or inflamed connective tissues and reducing pain[23]. Fibroblasts facilitate angiogenesis, cellular proliferation, and collagen deposition by activating key growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), connective tissue growth factor (CTGF), and epidermal growth factor (EGF)[24]. This dynamic tissue remodeling process distinguishes prolotherapy from conventional TMD treatment strategies by promoting structural repair and regeneration rather than merely alleviating symptoms.

Despite ongoing research on the mechanism of action of prolotherapy, its precise biological processes remain incompletely understood. The primary hypothesized mechanism is tissue regeneration, with the effects varying based on the specific proliferant injected. Hypertonic dextrose, typically used at concentrations of 10-25%, induces cell wall lysis and fibroblast activation, triggering the release of growth factors such as PDGF, TGF-β, EGF, basic-FGF (bFGF), and insulin-like growth factor (IGF)[16,25]. These growth factors promote fibroblast activation, collagen precursor formation, and tissue remodeling, mimicking the body's natural healing

processes[11]. Additionally, dextrose provides essential nutrients for damaged cells, exerts potential direct effects on peripheral nerves, facilitates fibrous tissue formation, and has been reported to contribute to ligament, tendon, and cartilage regeneration[26]. However, nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided during prolotherapy, as they interfere with the controlled inflammatory response necessary for tissue repair. While hypertonic dextrose is generally considered safe, caution is advised in patients with uncontrolled or severe diabetes. Since dextrose-based prolotherapy relies on an initial inflammatory response to initiate tissue regeneration, its efficacy may be diminished by NSAIDs or corticosteroids, which suppress this inflammatory phase.

In contrast to NSAIDs and corticosteroids, polydeoxyribonucleotide (PDRN) has been shown to exert anti-inflammatory effects without inducing metabolic side effects or triggering inflammation. Due to its ability to stimulate tissue proliferation, PDRN has been increasingly utilized as a therapeutic option for osteoarthritis in major joints[27]. Derived from salmon sperm DNA, PDRN consists of a mixture of deoxyribonucleotide polymers, with chain lengths ranging from 50 to 2000 base pairs[27]. It serves as a source of pyrimidines and purines, stimulating nucleotide synthesis through salvage pathways. PDRN has been found to downregulate pro-inflammatory mediators, including Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and High Mobility Group Box 1 (HMGB1), thereby reducing inflammation. Simultaneously, it upregulates Vascular EGF (VEGF), promoting tissue repair and wound healing[28]. Additionally, PDRN has been observed to modulate key inflammatory cytokines, including TNF-α, IL-1, IL-6, HMGB1, and IL-10, suggesting a potential regulatory role in anti-inflammatory processes. Notably, PDRN exerts its regenerative effects through the activation of adenosine A2A receptors (ADORA2A), which have been shown to play a critical role in musculoskeletal tissue regeneration[27]. Given the essential function of adenosine receptors in inflammation suppression[29], PDRN has emerged as a promising therapeutic agent for managing inflammation in DJD[30]. While in vitro studies have demonstrated its chondroprotective effects, and animal models have shown significant arthritis attenuation compared to controls, clinical studies on TMJ applications remain scarce[31,32].

In cases of degenerative changes in the TMJ, conventional treatments primarily aim to reduce excessive joint loading using occlusal stabilization splints and restrict mandibular movements that exacerbate pain[7]. Additionally, in cases of severe acute bone destruction, anterior open bite may develop, necessitating orthognathic correction to restore occlusion in DJD patients[33,34]. However, these approaches do not facilitate direct bone regeneration and fail to address the structural deterioration of the condyle. In this study, we report successful cases in which 2-3 sessions of prolotherapy not only alleviated TMD symptoms but also contributed to condylar regeneration. All patients received two to three sessions of prolotherapy depending on their clinical response. Prolotherapy generally requires multiple injections to achieve a regenerative effect, as a single session may not sufficiently stimulate fibroblast activation and collagen synthesis. Previous studies have reported favorable outcomes with repeated injections, especially in cases involving joint structures with limited vascularity[35]. The decision to discontinue further injections was based on the resolution of clinical symptoms, functional recovery and radiographic evidence of joint stabilization. Conversely, repeated injections were considered in cases where pain persisted, mouth opening remained restricted, or radiographic findings showed ongoing joint degeneration. In some cases, dextrose was used as a single intermediate injection between PDRN treatments. Hypertonic dextrose acts as a strong inflammatory stimulant, initiating tissue regeneration through controlled inflammation, while PDRN exerts anti-inflammatory and proliferative effects to support sustained healing. The alternating use of these agents was based on their complementary

mechanisms, with dextrose promoting initial stimulation and PDRN maintaining regenerative momentum. Since there are no standardized protocols or guidelines for TMJ prolotherapy, we utilized a combination of 10% hypertonic dextrose and PDRN, aiming to enhance pain relief, joint function improvement (e.g., increased mouth opening), and structural recovery. This approach was complemented by occlusal splint therapy to mitigate excessive joint loading. Future prospective studies are warranted to determine the optimal injection intervals, the most effective proliferative agents, and the best combination of adjunctive conservative therapies to achieve the most favorable outcomes in DJD patients.

One limitation of this study is the use of both hypertonic dextrose and PDRN in the same anatomical region across different time points, which may limit the ability to evaluate the independent effects of each proliferant. Future studies should consider designing comparative protocols with distinct injection sites or isolated monotherapy groups to better differentiate the therapeutic roles of each agent. Additionally, this study is the lack of direct evaluation of surrounding TMJ ligaments, which play a significant role in joint stability and movement. Future research incorporating imaging-based ligament assessment using magnetic resonance imaging and ultrasonography may provide deeper insight into the biomechanical impact of prolotherapy.

This case series demonstrates the potential of prolotherapy as a regenerative treatment for TMJ DJD. Unlike conventional symptomatic treatments, prolotherapy may promote joint tissue regeneration, particularly with the use of hypertonic dextrose and PDRN. These findings suggest prolotherapy as a promising intervention for TMJ DJD, warranting further studies to evaluate long-term efficacy and clinical stability.

Conflicts of Interest: None

References

1. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP, et al. Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications: recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. J Oral Facial Pain Headache 2014; 28: 6-27.
2. Song H, Lee JY, Huh KH, Park JW. Long-term changes of temporomandibular joint osteoarthritis on computed tomography. Sci Rep 2020; 10: 6731.
3. Cömert Kiliç S, Kiliç N, Sümbüllü MA. Temporomandibular joint osteoarthritis: cone beam computed tomography findings, clinical features, and correlations. Int J Oral Maxillofac Surg 2015; 44: 1268-74.
4. Bae S, Park MS, Han JW, Kim YJ. Correlation between pain and degenerative bony changes on cone-beam computed tomography images of temporomandibular joints. Maxillofac Plast Reconstr Surg 2017; 39: 19.
5. Jeon KJ, Lee C, Choi YJ, Han SS. Analysis of three-dimensional imaging findings and clinical symptoms in patients with temporomandibular joint disorders. Quant Imaging Med Surg 2021; 11: 1921-31.
6. Fan PD, Xiong X, Cheng QY, Xiang J, Zhou XM, Yi YT, et al. Risk estimation of degenerative joint disease in temporomandibular disorder patients with different types of sagittal and coronal disc displacements: MRI and CBCT analysis. J Oral Rehabil 2023; 50: 12-23.
7. Mélou C, Pellen-Mussi P, Jeanne S, Novella A, Tricot-Doleux S, Chauvel-Lebret D. Osteoarthritis of the temporomandibular joint: a narrative overview. Medicina (Kaunas) 2022; 59: 8.
8. Chung MK, Wang S, Alshanqiti I, Hu J, Ro JY. The degeneration-pain relationship in the temporomandibular joint: Current understandings and rodent models. Front Pain Res (Lausanne) 2023; 4: 1038808.
9. Yilmaz O, Candirli C, Balaban E, Demirkol M. Evaluation of success criteria for temporomandibular joint arthrocentesis. J Korean Assoc Oral Maxillofac Surg 2019; 45: 15-20.
10. Park JS, Ku JK, Kim YK, Yun PY. Efficacy of dextrose pro-

lotherapy on temporomandibular disorder: a retrospective study. J Korean Assoc Oral Maxillofac Surg 2024; 50: 259-64.
11. Waluyo Y, Artika SR, Wahyuni IN, Gunawan AM, Zainal AT. Efficacy of prolotherapy for osteoarthritis: a systematic review. J Rehabil Med 2023; 55: jrm00372.
12. Cardoneanu A, Macovei LA, Burlui AM, Mihai IR, Bratoiu I, Rezus II, et al. Temporomandibular joint osteoarthritis: pathogenic mechanisms involving the cartilage and subchondral bone, and potential therapeutic strategies for joint regeneration. Int J Mol Sci 2022; 24: 171.
13. Kapos FP, Exposto FG, Oyarzo JF, Durham J. Temporomandibular disorders: a review of current concepts in aetiology, diagnosis and management. Oral Surg 2020; 13: 321-34.
14. Zhou H, Xue Y, Liu P. Application of auriculotemporal nerve block and dextrose prolotherapy in exercise therapy of TMJ closed lock in adolescents and young adults. Head Face Med 2021; 17: 11.
15. Bizzoca D, Brunetti G, Moretti L, Piazzolla A, Vicenti G, Moretti FL, et al. Polydeoxyribonucleotide in the treatment of tendon disorders, from basic science to clinical practice: a systematic review. Int J Mol Sci 2023; 24: 4582
16. Mustafa R, Güngörmüş M, Mollaoğlu N. Evaluation of the efficacy of different concentrations of dextrose prolotherapy in temporomandibular joint hypermobility treatment. J Craniofac Surg 2018; 29: e461-5.
17. Tolba YM, Omar SS, Nagui DA, Nawwar MA. Effect of high molecular weight hyaluronic acid in treatment of osteoarthritic temporomandibular joints of rats. Arch Oral Biol 2020; 110: 104618.
18. Chung PY, Lin MT, Chang HP. Effectiveness of platelet-rich plasma injection in patients with temporomandibular joint osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Oral Surg Oral Med Oral Pathol Oral Radiol 2019; 127: 106-16.
19. Bergstrand S, Ingstad HK, Møystad A, Bjørnland T. Long-term effectiveness of arthrocentesis with and without hyaluronic acid injection for treatment of temporomandibular joint osteoarthritis. J Oral Sci 2019; 61: 82-8.
20. Ye T, Sun D, Mu T, Chu Y, Miao H, Zhang M, et al. Differential effects of high-physiological oestrogen on the degeneration of mandibular condylar cartilage and subchondral bone. Bone 2018; 111: 9-22.
21. de Alcântara Camejo F, Azevedo M, Ambros V, Caporal KS, Doetzer AD, Almeida LE, et al. Interleukin-6 expression in disc derangement of human temporomandibular joint and association with osteoarthrosis. J Craniomaxillofac Surg 2017; 45: 768-74.
22. Luo P, Feng C, Jiang C, Ren X, Gou L, Ji P, et al. IL-37b alleviates inflammation in the temporomandibular joint cartilage via IL-1R8 pathway. Cell Prolif 2019; 52: e12692.
23. Dasukil S, Shetty SK, Arora G, Degala S. Efficacy of prolotherapy in temporomandibular joint disorders: an exploratory study. J Maxillofac Oral Surg 2021; 20: 115-20.
24. Siadat AH, Isseroff RR. Prolotherapy: Prolotherapy: potential for the treatment of chronic wounds? Adv Wound Care (New Rochelle) 2019; 8: 160-7.
25. Louw WF, Reeves KD, Lam SK, Cheng AL, Rabago D. Treatment of temporomandibular dysfunction with hypertonic dextrose injection (prolotherapy): a randomized controlled trial with long-term partial crossover. Mayo Clin Proc 2019; 94: 820-32.
26. Waluyo Y, Budu, Bukhari A, Adnan E, Haryadi RD, Idris I, et al. Changes in levels of cartilage oligomeric proteinase and urinary C-terminal telopeptide of type II collagen in subjects with knee osteoarthritis after dextrose prolotherapy: a randomized controlled trial. J Rehabil Med 2021; 53: jrm00196.
27. Ryu K, Ko D, Lim G, Kim E, Lee SH. Ultrasound-guided prolotherapy with polydeoxyribonucleotide for painful rotator cuff tendinopathy. Pain Res Manag 2018; 2018: 8286190.
28. Jeong W, Yang CE, Roh TS, Kim JH, Lee JH, Lee WJ. Scar prevention and enhanced wound healing induced by polydeoxyribonucleotide in a rat incisional wound-healing model. Int J Mol Sci 2017; 18: 1698.
29. Veronesi F, Dallari D, Sabbioni G, Carubbi C, Martini L, Fini M. Polydeoxyribonucleotides (PDRNs) from skin to musculoskeletal tissue regeneration via adenosine A2A receptor

involvement. J Cell Physiol 2017; 232: 2299-307.
30. Seo JH, Kim WK, Kang KW, Lee S, Kang BJ. Anti-inflammatory effects of polydeoxyribonucleotide and adipose tissue-derived mesenchymal stem cells in a canine cell model of osteoarthritis. J Vet Sci 2024; 25: e68.
31. Gennero L, Denysenko T, Calisti GF, Vercelli A, Vercelli CM, Amedeo S, et al. Protective effects of polydeoxyribonucleotides on cartilage degradation in experimental cultures. Cell Biochem Funct 2013; 31: 214-27.
32. Park J, Park HJ, Rho MC, Joo J. Viscosupplementation in the therapy for osteoarthritic knee. Appl Sci 2021; 11: 11621.
33. Kang MG, Park YJ, Huh KH, Kho HS. Clinical characteristics of temporomandibular disorders presenting posterior open bite - a report of 12 cases. J Dent Sci 2021; 16: 861-7.
34. Choi YS, Kwak HJ, Kim SH, Song IJ, Nam YJ, Kim BJ, et al. Arthrocentesis and intermaxillary traction appliance in a patient with unilateral posterior open bite caused by temporomandibular osteoarthritis: a case report. J Korean Dent Assoc 2023; 61: 731-41.
35. Rabago D, Slattengren A, Zgierska A. Prolotherapy in primary care practice. Prim Care 2010; 37: 65-80.