

Effect of dextrose prolotherapy on internal derangement of the temporomandibular joint

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Abstract. – OBJECTIVE: This study aimed to evaluate the effect of dextrose prolotherapy in treating internal derangement of the temporomandibular joint.

PATIENTS AND METHODS: A total of 20 patients with temporomandibular joint internal derangement were enrolled in the study. The diagnosis of internal derangement was confirmed by magnetic resonance imaging (MRI). The posterior and anterior disc attachment, as well as the most tender part of the masseter muscle, were injected with 12.5% dextrose. Pain, maximum mouth opening, clicking, and deviation were assessed immediately before treatment, as well as at 2-, 4-, and 12- weeks post-treatment.

RESULTS: There was a significant improvement in the four clinical variables at the three-time intervals. Pain at two weeks was reduced by 60% (6 vs. 3.75) and by 200% (6 vs. 1.9) at 4 weeks. The maximum mouth opening was increased by 6.4 mm at 2 weeks and 7.85 mm at 4 weeks.

The percentage of patients with clicking decreased from 70%, preoperatively- to 50% at 2 weeks, 15% at 4 weeks, and 5% at 12 weeks. The ratio of patients with deviation was decreased from 80% preoperatively to 35% at 2 weeks, 15% at 4 weeks, and 5% at 12 weeks.

CONCLUSIONS: Prolotherapy is a safe and effective treatment for alleviating the symptoms of internal derangement of the temporomandibular joint.

Key Words:

Dextrose, Internal derangement, Pain, Prolotherapy, Temporomandibular joint.

Introduction

The temporomandibular joint (TMJ) is a compound synovial joint comprising the glenoid fossa of temporal bone and mandibular condyle with an intervening articular disc. The main function of the articular disc, a structure made of dense fibrous

connective tissue, is to promote joint mobility and enable more complicated movements. In a normal TMJ, the disc is situated over the head of the condyle (at the 12 o'clock position) with the posterior band positioned superior to the condyle and the intermediate zone seated superior-anterior to the condyle (at the 1 o'clock position). On mouth opening, the disc-condyle assembly translates anteriorly, although the condyle also rotates forwards, the disc relatively rotates in a backward direction over the condyle¹.

The term internal derangement of the temporomandibular joint (TMJ) indicates an abnormal relationship between the disc, the condyle, and the articular eminence that constrains proper joint function. Firstly, the term "internal derangement" was used in 1814 to refer to a specific localized mechanical disturbance in a joint. Later, it was more explicitly used to refer to the displacement of the TMJ disc, most commonly in the anteromedial direction².

The disc displacement could be with or without reduction. In disc displacement with reduction, the disc is displaced anterior to the condylar head and remains in this position as long as the mouth is closed. Upon mouth opening, the disc regains its position on the condylar head. The movement of the disc onto and off the condylar head may lead to a clicking sound. In disc displacement without reduction, the articular disc does not reduce, hindering condylar movement, and resulting in limited opening³.

The precise source of internal derangements is not clear; however, it is a complex disorder likely caused by a combination of micro- or macro-trauma, parafunctional behavior, laxity of the joint's soft tissues, and alterations in the synovial fluid's composition⁴. The aims of the internal derangement treatment include alleviating pain, reducing or eliminating joint noises, increasing the degree of mouth opening, and consequently restoring normal TMJ function. Soft diet, behavior

adjustment, analgesics, occlusal splints, intra-articular injections, physiotherapy, arthrocentesis, arthroscopy, and open joint surgery are the most common therapeutic techniques⁵.

Injecting a nonpharmacological irritant solution, such as dextrose, into the area of the tendons or ligaments is known as prolotherapy, which is also known as regenerative injection therapy. It is hypothesized that this procedure elicits a non-inflammatory or inflammatory process that ultimately leads to the deposition of new collagen fibers that strengthen lax tendons or ligaments and possibly encourage the release of local growth factors⁶.

Different substances have been utilized for prolotherapy, but hypertonic dextrose is the most commonly utilized solution since it is affordable, accessible, and safe to inject⁷. Dextrose solution has been used at various concentrations ranging from 10% to 50%^{8,9}. The superior joint space and pericapsular soft tissues are usually injected during traditional prolotherapy of the TMJ¹⁰.

Patients and Methods

This is a prospective clinical study conducted on 20 patients with clinical symptoms of internal derangement of the temporomandibular joints. The study was conducted at the Department of Maxillofacial Surgery of a university teaching hospital over a period of 2 years (August 2020-August 2022). The study was accepted by the institutional ethical committee and conducted in accordance with the ethical standards of the Helsinki Declaration (1964 and its 7th revision in 2013) regarding human experimental study. The purpose of the study was explained to the patients and written informed consent for participation in the study was obtained.

The diagnostic clinical criteria of internal derangement of the temporomandibular joints are the presence of one or more of the following observations in one or both temporomandibular joints: pain, audible clicking, restricted mouth opening (less than 35 mm) and mandibular deviation on opening. The disc displacement was confirmed by sagittal magnetic resonance imaging (MRI) (Figure 1).

The following observations were registered before prolotherapy, and at 4-, 8-, and 12- weeks after therapy.

1. Pain in the TMJ: the pain was recorded by the patient on a numerical scale value from 0 to 10, where 0 indicates no pain and 10 is the most severe pain.

2. Maximum mouth opening was recorded using a millimeter ruler placed between the incisal edges of the upper and lower incisors, during unassisted maximum mouth opening.
3. Clicking of the TMJ.
4. Deviation of the mandible upon opening.

The prolotherapy solution was prepared by mixing 0.75 ml of 50% dextrose, 0.75 ml of sterile distilled water, and 1.5 ml of 2% lidocaine in a 3 ml syringe loaded with a 30-gauge needle. The resulting prolotherapy solution was 12.5% dextrose. The patient was placed in a semisupine position and the side of the face and preauricular area were prepared with iodine solution. Then a drape was placed.

The first injection site, which targeted the posterior disc attachment, was made at a point approximately 5 mm anterior to the tragus. The patient was instructed to open the mouth widely, which was kept open by inserting a bite block between the posterior teeth. The needle was directed medially and slightly anteriorly to avoid perforation of the ear. The needle was advanced to approximately 2 cm and 1 ml of the solution was delivered slowly after confirming negative aspiration.

The second injection site targeted the disc attached to the tendon of the upper lateral pterygoid muscle. This was located by palpating the depression anterior to the condyle while the mouth was closed. The needle was directed medially and slightly anteriorly to its full or nearly full length, and 1 ml of the solution was slightly injected.

The third injection site was at the insertion of the masseter muscle into the zygomatic arch.

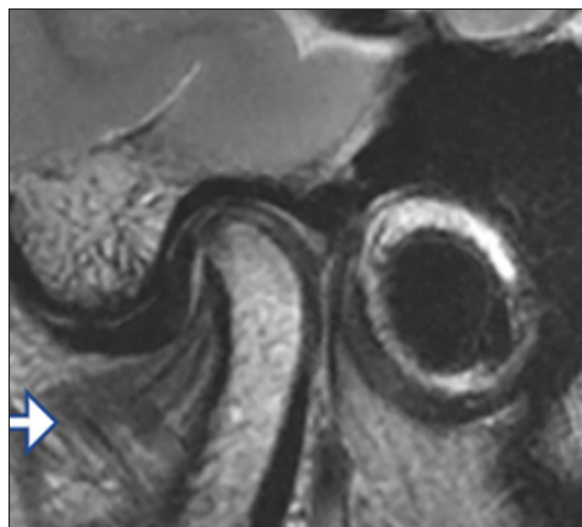


Figure 1. MRI showing anterior disc displacement in closed mouth position.

The patient was apprized to clench the teeth, and 1 ml of solution was deposited on the most rigid portion of the muscle, which was also the most tender (Figure 2).

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences version 25 (IBM Corp., Armonk, NY, USA). Comparison of the means of pain score and maximum mouth opening was made using ANOVA, and the frequency of clicking and deviation was evaluated by the Chi-square test. Statistical significance was considered at $p \leq 0.05$.

Results

The 20 patients enrolled in the study completed the follow-up period. The mean age of the patients was 34 (± 18) years with an age range of 18-58 years. There were 12 females and 8 males, with a female-to-male ratio of 1.5:1 (Table I).

The pain scores were significantly reduced during the three follow-up periods, compared to the pretreatment scores. Pain was reduced by 60% (6 vs. 3.75) at two weeks and by 200% (6 vs. 1.9) at 4 weeks (Table II). There was also a statistically significant improvement in maximum mouth opening. The mouth opening was increased by 6.4 mm at 2 weeks and 7.85 mm at 4 weeks (Table III). The effect on the clicking sound of the temporomandibular joint was statistically significant. Preoperatively, the percentage of clicking patients was 70%. This ratio was decreased after injection



Figure 2. The three injection sites in prolotherapy.

to 50% at 2 weeks, 15% at 4 weeks, and 5% at 12 weeks (Table IV). The effect on mandibular deviation was also significant. The percentage of patients with deviation decreased from 80% preoperatively to 35% at 2 weeks, 15% at 4 weeks, and 5% at 12 weeks (Table V).

Discussion

The TMJ capsule and ligaments may be weakened due to various pathologies affecting the TMJ, such as joint subluxations, disc displacements, muscle spasms, and myofascial pain dysfunction syndrome. Patients with disc displacement usually complain of TMJ clicking,

Table I. Age and sex distribution of the sample.

Age range (years)	Male	Female	Total
18-28	4	5	9
29-38	2	3	5
39-48	2	2	4
49-58	0	2	2
Total	8	12	20

Table II. Pain scores.

Pain score	Pretreatment	2 weeks	4 weeks	12 weeks
No.	20	20	20	20
Mean	5.95	3.75	1.9	0.68
Median	6.0	4.0	2.0	1.0
SD	1.63	1.58	0.85	0.74
f-ratio value	65.00571			
p-value	<0.0001			

restricted mouth opening, pain during chewing and at rest, restricted lateral movement away from the affected side, and mandibular deviation to the affected side during mouth opening.

Splints are the most commonly used conservative treatment. They permit free mandibular motion, reduce muscle spasms, inhibit full flexion of elevator muscles, and allow cognitive awareness. Recently, 3D splints have been shown to be superior to conventional splints. Patients who use this type of 3D splint report feeling more satisfied because they are more aesthetically pleasing and lighter than conventional splints and may have occlusal contact points that are more precisely built¹¹.

A stable TMJ is defined as having both condyles in the most superior position within the glenoid fossa with the articular disc in place and closely related to the eminence and the condyle while the upper and lower teeth are in maximum interdigitation with even multiple contacts between the teeth¹². Orthopedic TMJ instability is often associated with pain in the cervicofacial region and cervical instability. Adina et al¹³ found that kinesiotherapy followed by rapid maxillary expansion

improved the function of cervical vertebrae and reduced cervicofacial pain within the first two weeks.

The patients selected for the present study complained of the clinical signs and symptoms of TMJ internal derangement. Although the clinical examination is useful in diagnosing patients with temporomandibular disorders (TMD), the diagnostic accuracy is questionable. Therefore, the clinical diagnosis was confirmed by MRI findings. This procedure agreed with that of Kumar et al¹⁴ who recommended MRI for diagnosing disc displacement.

The most popular proliferant utilized in prolotherapy is dextrose. It is inexpensive, readily available, and safe. A wide variety of dextrose concentrations have been utilized, including 10%, 12.5%, 15%, and 25%. Dextrose concentrations >10% have been shown to be effective, thus 12.5% dextrose was prepared for the present study due to its inflammatory capacity. A dextrose concentration of more than 10% works partly by causing inflammation. Histopathological observations after an injection included hemorrhage, inflammation, necrosis, and vascular alterations in the ligaments and adjacent soft tissues¹⁵. The

Table III. Maximum mouth opening (mm).

Maximum mouth opening	Pretreatment	2 weeks	4 weeks	12 weeks
No.	20	20	20	20
Mean	32.3	38.7	40.15	41.05
Median	32	38.5	40	41.0
SD	4.89	2.07	1.19	0.86
<i>f</i> -ratio value	71.588			
<i>p</i> -value	<0.0001			

Table IV. Clicking sounds of the temporomandibular joint.

Clicking	Present No. (%)	Absent No. (%)	Total No. (%)
Preoperative	14 (70)	6 (30)	20 (100)
2 weeks	10 (50)	10 (50)	20 (100)
4 weeks	3 (15)	17 (85)	20 (100)
12 weeks	1 (5)	19 (95)	20 (100)

Chi-square test: $df=3$, $\chi^2=28.18$, $p=0.000023$.

Table V. Mandibular deviation on mouth opening.

Deviation on opening	Present No. (%)	Absent No. (%)	Total No. (%)
Preoperative	16 (80)	4 (20)	20 (100)
2 weeks	7 (35)	13 (65)	20 (100)
4 weeks	3 (15)	17 (85)	20 (100)
12 weeks	1 (5)	19 (95)	20 (100)

Chi-square test: $df=3$, $\chi^2=29.69$, $p=0.000002$.

inflammatory mediators also lead to the release of growth factors and activation of fibroblasts, which result in the formation of new collagen fibers that strengthen the flaccid ligaments¹⁶.

The present study showed a significant improvement in pain, clicking, mouth opening, and deviation at 2 weeks after prolotherapy, as well as after 4 and 12 weeks. Our findings are in accordance with those of Priyadarshini et al⁹ who also used a mixed solution of dextrose 50% (0.75 ml), lignocaine 2% with adrenaline (1.5 ml), and bacteriostatic water (0.75 ml) for internal derangement. They noted a significant improvement in pain, clicking, and mouth opening; however, no significant improvement in mandibular deviation was noted. Zhou et al¹⁰ attempted auriculotemporal nerve block and dextrose prolotherapy in exercise therapy for TMJ closed lock and pain at rest and on mastication substantially decreased in all patients and mandibular function and mouth opening significantly improved at 2 weeks follow-up. Hauser et al¹⁷ treated patients with chronic TMJ dysfunction using 15% dextrose, considering parameters such as pain, range of motion, pharmacological therapy, depression, and patient satisfaction; the results showed a reduction in pain and an improvement in quality of life.

Louw et al¹⁸ evaluated three monthly intra-articular injections (20% dextrose/0.2% lidocaine or 0.2% lidocaine) in 42 participants (with 54 joints) TMJ dysfunction and found a notable improvement in pain, range of jaw motion, and mouth opening compared with masked control injection at 3 months; clinical improvements prevailed at 12 months. Refai¹⁹ reported that 91% of consecutive patients had improvement after dextrose injection for TMJ and Cömert Kiliç and Güngörmüş²⁰ reported 79% pain improvement with the use of dextrose (79%). Ungor et al²¹ injected 10% dextrose in four injections at 6-week intervals for patients with TMJ dislocation and tracked them for 6 months. They found that pain scores decreased significantly and TMJ locking diminished in all patients; however, maximum mouth opening and clicking sounds showed no significant changes.

Prolotherapy has been shown by Dasukil et al²² to improve quality-of-life functional limitations, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap; and its beneficial effects persisted two years after the termination of treatment. Dasukil et al²³ studied 25 patients suffering from various TMJ disorders and found that prolotherapy reduced tenderness in the TMJ and masticatory

muscles with significant improvement in mouth opening. The effect of the treatment in improving clicking and deviation of TMJ was also found to be statistically significant. The beneficial effect of prolotherapy in TMJ hypermobility has also been shown by Memeş²⁴ and Taşkesen and Cezairli²⁵.

An *in vitro* study by MacIver and Tanelian²⁶ showed the analgesic mechanism of dextrose. Nociceptive C fibre firing rates rapidly increase in hypoglycaemic environments before quickly returning to normal after hypoglycemia is corrected. The efficacy of dextrose injection for chronic pain may be explained by ameliorating the relative perineuronal hypoglycemia¹⁸. Growth factors are released in response to hypertonic dextrose solutions, which then provoke fibroblast proliferation and the development of stronger connective tissue²⁷. Anterior disc displacement could be avoided by strengthening the posterior disc attachment.

No complications were noted in the present study. The reported complications of prolotherapy are extremely rare, yet the possibility of complications cannot be ruled out. The most common complication reported in the literature is allergy to solution. Dextrose being an extract of corn, can cause allergic reactions in susceptible individuals. Although rare, allergy to lidocaine may occur. Few authors^{28,29} have reported complications involving prolotherapy. Shehata et al²⁸ noted temporary facial nerve paralysis in 9% of patients and Jeelani et al²⁹ found an ipsilateral posterior open bite following injection.

The weakness of this study is the absence of a positive or negative control group, a relatively small sample size, and a short follow-up period. In addition, no post-injection MRI of the joint was performed to correlate the clinical improvement of symptoms with imaging changes in the joint and disc position.

Conclusions

Prolotherapy is a safe, effective conservative treatment for patients with internal derangement of the TMJ. Prolotherapy has significantly alleviated joint pain, and improved joint motion and clicking.

Ethics Approval

All methods were carried out in accordance with relevant guidelines and regulations and all experimental protocols were reviewed and approved by the Ethical Committee of Kurdistan Board of medical specialties (No. 5120).

Informed Consent

Written informed consent was obtained from all the subjects and/or their legal guardians for study participation.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interests

The authors declare no conflict of interest.

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None.

Authors' Contributions

The authors contribute to all sections of the study.

References

- 1) de Leeuw R. Internal derangements of the temporomandibular joint. *Oral Maxillofac Surg Clin North Am* 2008; 20: 159-168.
- 2) Young AL. Internal derangements of the temporomandibular joint: a review of the anatomy, diagnosis, and management. *J Indian Prosthodont Soc* 2015; 15: 2-7.
- 3) Santos KC, Dutra ME, Warmling LV, Oliveira JX. Correlation among the changes observed in temporomandibular joint internal derangements assessed by magnetic resonance in symptomatic patients. *J Oral Maxillofac Surg* 2013; 71: 1504-1512.
- 4) Dijkgraaf LC, de Bont LG, Otten E, Boering G. Three-dimensional visualization of the temporomandibular joint: a computerized multisectional autopsy study of disc position and configuration. *J Oral Maxillofac Surg* 1992; 50: 2-10.
- 5) Abouelhuda AM, Kim YK, Hegazy SA. Non-invasive different modalities of treatment for temporomandibular disorders: review of literature. *J Korean Assoc Oral Maxillofac Surg* 2018; 44: 43-51.
- 6) Hakala RV. Prolotherapy (proliferation therapy) in the treatment of TMD. *Cranio* 2005; 23: 283-288.
- 7) Nagori SA, Jose A, Gopalakrishnan V, Roy ID, Chattopadhyay PK, Roychoudhury A. The efficacy of dextrose prolotherapy over placebo for temporomandibular joint hypermobility: A systematic review and meta-analysis. *J Oral Rehabil* 2018; 45: 998-1006.
- 8) Zarate MA, Frusso RD, Reeves KD, Cheng AL, Rabago D. Dextrose Prolotherapy Versus Lidocaine Injection for Temporomandibular Dysfunction: A Pragmatic Randomized Controlled Trial. *J Altern Complement Med* 2020; 26: 1064-1073.
- 9) Priyadarshini S, Gnanam A, Sasikala B, Elave-nil P, Raja Sethupathy Cheeman S, Mrunalini R, Krishna Kumar Raja VB. Evaluation of prolotherapy in comparison with occlusal splints in treating internal derangement of the temporomandibular joint - A randomized controlled trial. *J Cranio-maxillofac Surg* 2021; 49: 24-28.
- 10) Zhou H, Xue Y, Liu P. Application of auriculo-temporal nerve block and dextrose prolotherapy in exercise therapy of TMJ closed lock in adolescents and young adults. *Head Face Med* 2021; 17: 11.
- 11) Sirbu AA, Bordea R, Lucaciu O, Braitoru C, Szuhaneck C, Campian RS. 3D Printed Splints an Innovative Method to Treat Temporomandibular Joint Pathology. *Revi Chim (Bucharest)* 2018; 69: 3087-3089.
- 12) Martin D, Cocconi R. Orthodontic dental casts: the case for routine articulator mounting. *Am J Orthod Dentofacial Orthop* 2012; 141: 8-14.
- 13) Adina S, Dipalma G, Bordea IR, Lucaciu O, Feurdean C, Inchingolo AD, Septimiu R, Malcangi G, Cantore S, Martin D, Inchingolo F. Orthopedic joint stability influences growth and maxillary development: clinical aspects. *J Biol Regul Homeost Agents* 2020; 34: 747-756.
- 14) Kumar R, Pallagatti S, Sheikh S, Mittal A, Gupta D, Gupta S. Correlation Between Clinical Findings of Temporomandibular Disorders and MRI Characteristics of Disc Displacement. *Open Dent J* 2015; 9: 273-281.
- 15) Dagenais S, Wooley J, Hite M, Green R, Mayer J. Acute toxicity evaluation of proliferol: a dose-escalating, placebo-controlled study in swine. *Int J Toxicol* 2009; 28: 219-229.
- 16) Vankdoth S, Reddy AS, Talla H, Vijayalaxmi N, Madhulatha G. Prolotherapy: a venturing treatment for temporomandibular joint disorder. *IJSS Case Reports and Reviews* 2014; 7: 27-30.
- 17) Hauser RA, Hauser MA, Blakemore KA. Dextrose prolotherapy and pain of chronic TMJ dysfunction. *Prac Pain Manag* 2007; 7: 49-57.
- 18) Louw WF, Reeves KD, Lam SKH, 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: 820-832.
- 19) Refai H. Long-term therapeutic effects of dextrose prolotherapy in patients with hypermobility of the temporomandibular joint: a single-arm study with 1-4 years' follow up. *Br J Oral Maxillofac Surg* 2017; 55: 465-470.
- 20) Cömert Kiliç S, Güngörmüş M. Is dextrose prolotherapy superior to placebo for the treatment of temporomandibular joint hypermobility? A ran-

- domized clinical trial. *Int J Oral Maxillofacial Surg* 2016; 45: 813-819.
- 21) Ungor C, Atasoy KT, Taskesen F, Cezairli B, Dayisoylu EH, Tosun E, Senel FC. Short-term results of prolotherapy in the management of temporomandibular joint dislocation. *J Craniofac Surg* 2013; 24: 411-415.
- 22) Dasukil S, Arora G, Shetty S, Degala S. Impact of prolotherapy in temporomandibular joint disorder: a quality of life assessment. *Br J Oral Maxillofac Surg* 202; 59: 599-604.
- 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: 115-120.
- 24) Memiş S. Evaluation of the effects of prolotherapy on condyles in temporomandibular joint hypermobility using fractal dimension analysis. *J Korean Assoc Oral Maxillofac Surg* 2022; 48: 33-40.
- 25) Taşkesen F, Cezairli B. Efficacy of prolotherapy and arthrocentesis in management of temporomandibular joint hypermobility. *Cranio* 2020; 16: 1-9.
- 26) MacIver MB, Tanelian DL. Activation of C fibers by metabolic perturbations associated with tourniquet ischemia. *Anesthesiology* 1992; 76: 617-623.
- 27) Dagenais S, Mayer J, Wooley JR, Haldeman S, Hite M. Acute toxicity evaluation of proliferol: a dose-escalating, placebo-controlled study in rats. *Int J Toxicol* 2007; 26: 451-463.
- 28) Shehata E. Prolotherapy with 12.5% dextrose to treat temporomandibular joint dysfunction (TMD). *Int J Oral Craniofac Sci* 2019; 5: 15-19.
- 29) Jeelani S, Krishna S, Reddy J, Reddy V. Prolotherapy in Temporomandibular Disorders: an Overview. *Open J Dent Oral Med* 2013; 1: 15-18.