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Ultrasound Guided Dextrose Prolotherapy: A Promising Hope for Temporomandibular Joint Dysfunction

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Authors' contributions

This work was carried out in collaboration among all authors. Author AM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors BCS and AA managed the analyses of the study. Author AA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Title of Topic: "Ultrasound guided dextrose prolotherapy: a promising hope for temporomandibular joint dysfunction".

Background & Objectives: Temporomandibular joint disorder (TMD) is a term used to describe a group of medical disorders causing temporomandibular joint (TMJ) pain and dysfunction. Prolotherapy also known as regenerative injection therapy is effective in stabilizing injured TMJ and relieving joint pain by injecting a non-pharmacological irritant solution into the region of the tendons or ligaments. Traditionally prolotherapy will do blindly. Image guided prolotherapy improves the accuracy of injections through direct visualisation of the needle into the target. Thus the present study aimed to evaluate the advantages of ultrasound guided prolotherapy with 25% dextrose for the cases with TMDS.

Methods: The present study included 15 patients with temporomandibular joint dysfunction reported to the department of oral and maxillofacial surgery. All patients were treated with two sessions of injections with 3 ml of proliferant solution (2 ml of 25% dextrose and 2% lignocaine with 1:2,00,000 adrenaline) one month apart. Follow up was done for 1 month, 3 months and 6 months. The patients were evaluated for pain, frequency of dislocation or subluxation, clicking sound,

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deviation of mouth and for maximum mouth opening both pre and post-operatively and scores were recorded and analysed with wilcoxon matched pairs test and dependent t test.
Results: Our study showed significant improvement in TMJ pain, clicking sound, deviation of mouth, number of locking episodes and mouth opening after the two sessions of injections.
Interpretation and Conclusion: Ultrasound guided prolotherapy with 25% dextrose appears promising for the treatment of symptomatic TMJ dysfunction, as evidenced by therapeutic benefits, simplicity, safety, patients; acceptance of the injection technique and lack of significant side effects.

Keywords: Temporomandibular joint; temporomandibular joint disorders; prolotherapy; dextrose; ultrasonography.

1. INTRODUCTION

Temporomandibular Joint Disorder (TMD) is the collective term used to describe a group of medical disorders causing Temporomandibular Joint (TMJ) pain and dysfunction, and it is the most common cause for orofacial pain [1]. As myriad factors can cause TMD, there are number of methods for their treatment also [2]. As surgical management is considered as a last resort for TMD, it is common for sufferers to seek out alternatives such as “Prolotherapy” [3].

Prolotherapy (PrT) is first described in 1937 by Schultz for the treatment of TMJ subluxation; the solution injected was derived from the psyllium seed. Hackett et al formalized the therapy in the 1950s as a viable therapeutic strategy to treat ligamentous laxity and related musculoskeletal conditions [4]. In 1950’s George. S. Hackett coined the term Prolotherapy from the Latin word “Proli” meaning “offspring” and from which we get the word “Proliferate” that is to grow. In 2007 Reeves defined Prolotherapy as an injection of growth factors; this growth factor production stimulates the growth of normal cells or tissue [1].

The basic principle of prolotherapy is the injection of a substance that will cause a low grade inflammatory process within the joint, attracts the fibroblast that strengthens the attachments of tendons and ligaments. This inflammatory process stabilizes the joint, improves the range of motion in hypomobile joint, helps to prevent dislocation in a hypermobile joint and relieve pain [5].

There are many solutions that can be used in Prolotherapy, including pumice, P2G (dextrose, phenol, glycerin), sodium morrhuate and more recently, platelet rich plasma, stem cell and lipoaspirate. The most common solution used is dextrose. Typical concentrations of dextrose used in Prolotherapy are from 5 to 25%. When dextrose is injected in greater than 10% solution it is presumed to be causing an osmotic (concentrated) gradient outside of the cells where it is injected. This causes some cells to lose water and lyse with the net effect being an influx of growth factors and inflammatory cells that initiates the wound-healing cascade to that specific area [6].

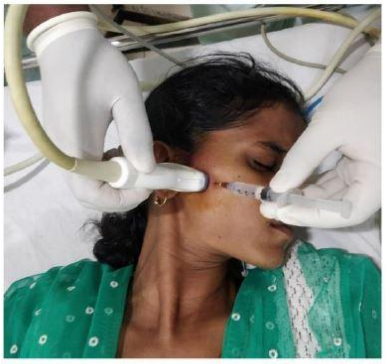
Prolotherapy has been used to successfully treat a large variety of musculoskeletal syndromes, including cervical, thoracic, and lumbar pain syndromes. In the maxillofacial region, prolotherapy has been frequently applied for the management of TMJ dysfunction [1].

Image guided prolotherapy improves the accuracy of injections through direct visualization of the needle into the target. The use of ultrasound to facilitate the identification of musculoskeletal structures and thereby improves interventional accuracy, and is rapidly becoming adapted in multiple disciplines to improve diagnostic and therapeutic safety [7]. Identification of the upper joint space of TMJ was easier with Ultrasound compared with a “blind” technique. The risk of damage to the collateral ligaments of the disk and the adjacent soft tissue associated with “blind” technique could be avoided with Ultrasound guidance [8].

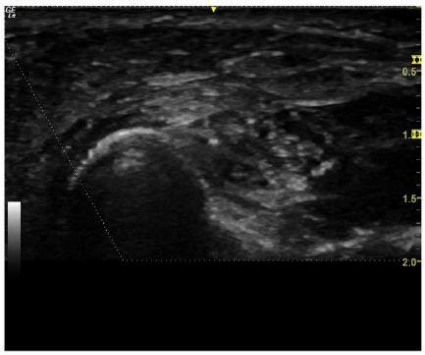
2. MATERIALS AND METHODS

The diagnosis of temporomandibular dysfunction was based on clinical examination and previous history. The criteria for inclusion in this study were patients diagnosed with temporomandibular dysfunctions from history and clinical examinations, recurrent chronic temporomandibular dislocation cases and who are willing to receive relatively painful injections. The criteria for exclusion were patients with degenerative changes in temporomandibular joint, allergy to dextrose, neurological and geriatric conditions.

The injection sites were determined by using ultrasound system [LOGIQ e 608939WX0 GE



INTRA OP INJECTION



INTRA OP USG

Fig. 1. Intra op procedure

Medical Systems (China) co ltd, Jiangsu, P R China]. Sterile ultrasound probe were placed over the temporomandibular joint and the temporomandibular joint movement were evaluated. Patient is asked to open and close the mouth to find the exact position of condylar head and glenoid fossa. Then 30-gauge one inch needle with 3 ml syringe is placed in the determined point to access into the superior joint space by ultrasound guidance. 1.5 ml of dextrose solution (2 mL of 25% dextrose and 1mL of 2% lignocaine with 1:2,00,000 adrenaline) is injected into the space and an additional 0.5 ml injected into the retrodiscal tissue, anterior discal ligament and temporomandibular joint capsule, respectively. After the dextrose injection, the passive jaw exercises will be performed to increase the distribution of the injected material. After the injection the patients were prescribed paracetamol (acetaminophen) 500 mg, one tablet every four hours as needed. After the injection, the patients are cautioned against taking aspirin or other anti-inflammatory agents to relieve the discomfort. After the injection, patients should be encouraged to be active and move the injected area.

TMJ pain as expressed by a verbal analogue from 0 to 5 scale, maximal mouth opening (MMO) measured in millimeters; clicking sound; and frequency of luxations (number of locking episodes per month) were assessed at each visit. Clinical follow ups were performed on the day of second injection (2^{nd} injection is one month after first injection), 1 month, 3 months and 6 months after the second injection.

Statistical analysis was done at the end of the follow up period and compared using tests from the SPSS program version 17.0 (Chicago, IL). When p-value is 0.05, it is considered statistically significant.

3. RESULTS

There were 8 men and 7 women with mean age 30.6 years (range18 – 52). All patients tolerated the TMJ injection well without serious complications. Among the 30 injections in the 15 patients, 18 injections patient complained of mild pain. That we managed with acetaminophen 500 mg BD for 3 days. For one case the pain was severe, for that case we managed with Tramadol BD for 2 days. Two patients had transient facial palsy due to the anaesthetic inclusion in the injected solution. As the effect of anaesthesia diminishes the facial palsy was also resolved. Another most common side effect is a temporary change in the dental occlusion. One of our 15 patients developed occlusal discrepancy after prolotherapy injection.

3.1 Verbal Analogue Scale Score for Pain

Pain score levels were reduced significantly by the following injections of our dextrose solution, which was demonstrated on Fig. 2. The mean (SD) pain score on the Verbal analogue scale for pain on function was 2.13 (0.83) before the injection, which decreased to 0.53 (0.83) consistently from the first session to the end of the study. The data acquired from the patients and the statistical evaluations are shown in Table 1.

3.2 Frequency of Dislocation or Subluxation

The frequency of locking episodes significantly decreased through the follow up in this study. The preoperativefrequencies of dislocation or subluxation were 13.53 and it reduced to 0.67 after 6 months post-operative.

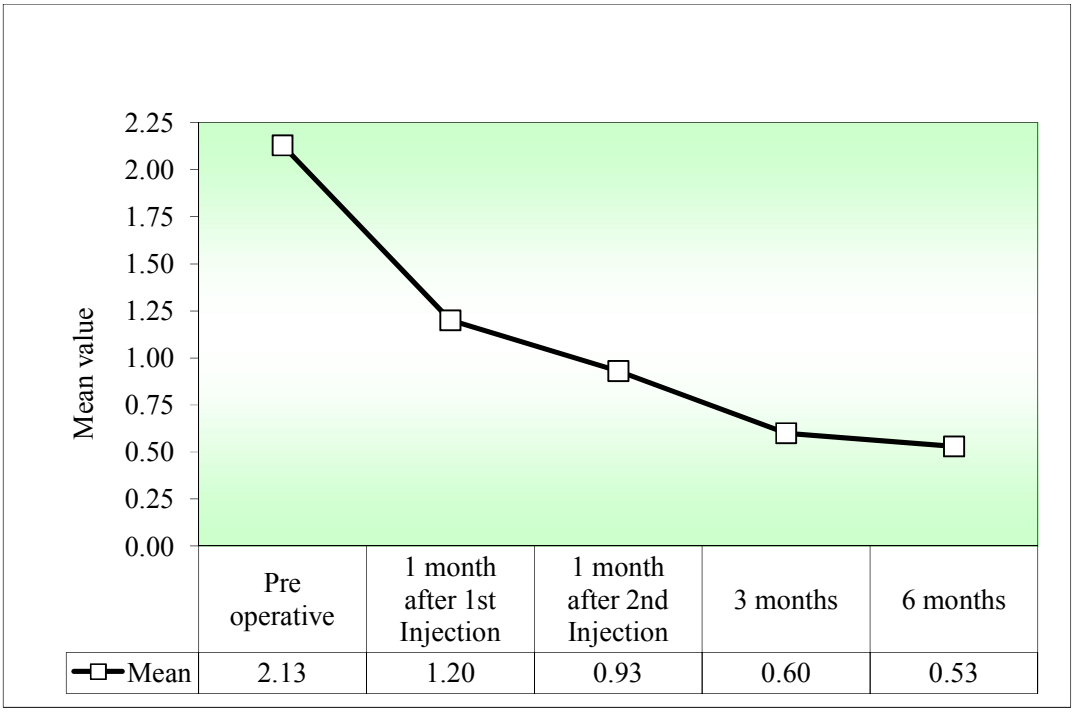


Fig. 2. Comparison of different treatment time points with respect to pain scores

Table 1. Comparison of different treatment time points with respect to pain scores by wilcoxon matched pairs test

Times	Mean	Standard Deviation
Pre-operative	2.13	0.83
1 month after first injection	1.2	0.86
1 month after second injection	0.93	0.80
3 months after second injection	0.60	0.74
6 months after second injection	0.53	0.83

3.3 Clicking Sound

Clicking sound was present in all patients at the beginning of the study. The sound was lost in 9 patients at the end of the study. There is 60% sound reduction after 6 months.

3.4 Deviation of Mouth

86.67% patients have deviation of mouth pre operatively, after 6 months post injection it reduced to 33.33%.

3.5 Maximum Mouth Opening

Maximum mouth opening was measured as the gap between the upper right first central incisor and the lower right first central incisor and decreased up to1 month after second injection then it started increasing, which may be attributed to strengthening the ligaments. The data acquired from the patients and the statistical evaluations are shown in Table 2. Comparison between the sessions had shown a tendency to decrease in the maximum mouth opening, which was statistically significant Fig. 3.

4. DISCUSSION

Prolotherapy as a treatment modality has been used to enhance tendon, ligament, and joint healing for over last sixty years [2]. In the maxillofacial region, prolotherapy has been frequently used for the management of temporomandibularjoint dysfunction(TMD).

Table 2. Comparison of different treatment time points with respect to mouth opening scores by dependent t test

Times	Mean	Standard deviation	P value
Pre-operative	45.27	9.38	-
1 month after 1st injection	40.07	8.97	0.0001*
1 month after 2nd injection	39.73	9.05	0.0001*
3 month after 2nd injection	40.60	9.26	0.0001*
6 months after 2nd injection	41.67	9.66	0.0027*

*$p<0.05$

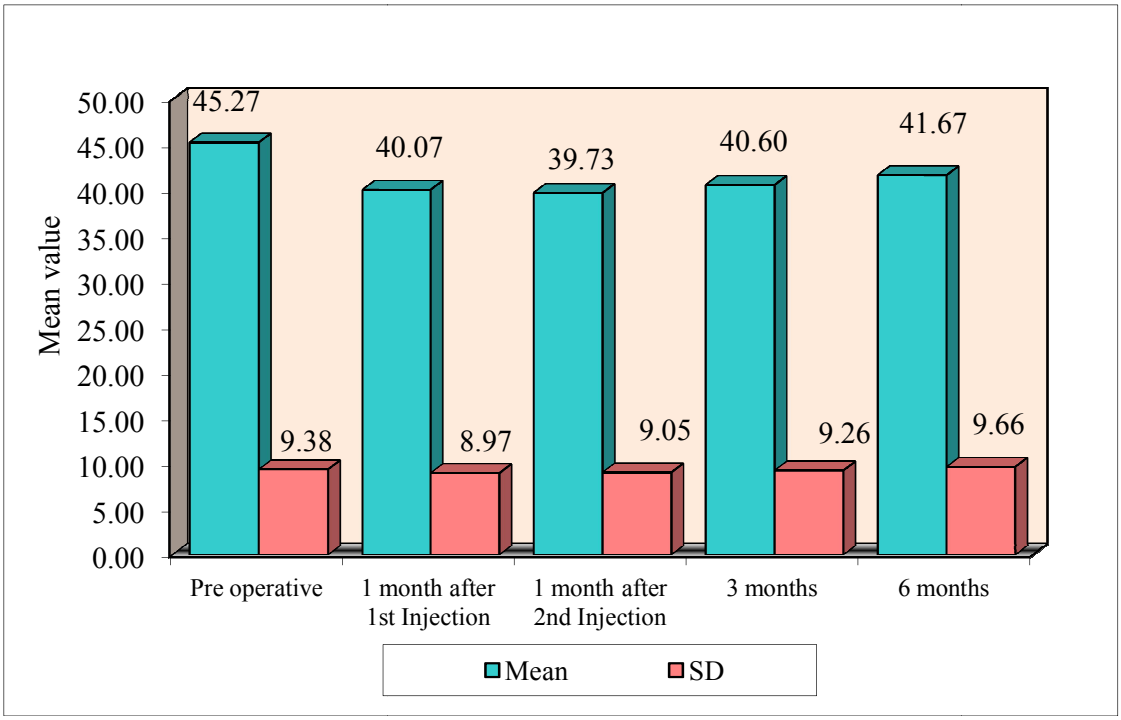


Fig. 3. Comparison of different treatment time points with respect to mouth opening scores

Fullerton and Reeves defined Prolotherapy as the injection of growth factors or growth factor production stimulants, to promote growth and repair of normal cells and tissue [9]. Prolotherapy induces rapid inflammation reaction so that new tendons and ligaments can be formed. In prolotherapy, proliferating agents are injected directly into stretched or torn ligaments, resulting over a few weeks' time in the loss of pain in the affected area and return to normal function of the associated painful skeletal articulation [10].

Dextrose was selected as the main ingredient in our injecting solution because it is the most common proliferant used in prolotherapy, is readily available, is inexpensive when compared with other proliferants, and has a high safety profile [11]. A wide variety of dextrose concentrations have been used with varying degrees of success. Clinical improvement of patients with TMJ pain and dysfunction was achieved after TMJ prolotherapy with 12.5%, 15%, and 25% dextrose injections. The results of our study indicate that tightening of loose ligaments by injection of dextrose (15 % - 20%,) is feasible. Hakala and Ledermann believed that a precise concentration of dextrose is not critical so long as it is strongly hypertonic and causes adequate cell wall lysis to attract fibroblasts and begin the regenerative process [5]. In our study we used 2 ml 25% dextrose and 1 ml 2% Lignocaine with 1:2,00,000 adrenaline, so the effective concentration of the dextrose is almost 15% - 20%. A AFoudaexplained in his article as concentrations of over 10% have been reported to operate in part through inflammatory

mechanisms to form new collagen fibers, and in part by regeneration, while a concentration of less than 10% dextrose acts as an anti-inflammatory agent [6].

Ahn et alstudied on injured rat Achilles tendon (transected and sutured) injected with 20% dextrose, showed significantly more fibroblasts on blinded histologic review at 4 weeks compared with injured but non-injected control tendons [12,13]. Kim et al reported that single injection of either 5% dextrose (D5W) or 20% dextrose made hypertonic with saline (1100 mOsm) into non-injured rat Achilles tendon resulted in a significant increase in tendon diameter and fibroblast counts per high-power field (hpf) compared with equimolar (1100-mOsm) saline [12,14].

A study by Oh and colleagues demonstrated non-inflammatory collagen bundle thickening at 8 weeks in the transverse carpal ligament rabbit equivalent after a single injection of 0.05 mL of 10%dextrose into the carpal tunnel equivalent (sub-synovial space) through a small incision with a 30-gauge needle. This study was followed by 3 randomized, masked, 2-armstudies that compared 10%dextrose versus normal saline. Energy absorption and load to failure of the sub-synovial connective tissue (SSCT) were measured using a standardized approach. The 3 studies demonstrated consistent and significant increases in tensile load to rupture, total energy absorption to rupture, and thickening of the SSCT [12,15].

In our study age group of the patients varied from 18 to 52 years, with mean age of 30.6. Hence age group of our study confirmed with the study of Refai, who found mean age as 29.7 years [16], A AFouda's mean age was 30 years [6].

Zhou et al stated a hypothesis that higher concentrations of dextrose have a longer hypertonic effect and induce a stronger tissue repair reaction [8]. The standard 50% concentration of dextrose is usually considered to be too irritating to use directly so, we used 2 mL of 25% dextrose and 1 mL of 2% lignocaine with 1:2,00,000 adrenaline into a 3-mL syringe for each TMJ. S K Majumdar et al used same concentration of dextrose (25% dextrose) like as but in a different manner. They gave auriculotemporal nerve block using 2 ml of 2% lidocaine followed by an interval of 10 min after which the proliferant was injected [17]. A AFouda also used 25% dextrose [6]. Ross A Hauser et al. used 15% dextrose, 0.2% lidocaine solution with a total of two to four cc's of solution used per temporomandibular joint [3].

In this study a series of 2 injections, 1 month apart was performed and patients followed up for 1 month after 2nd injection, 3 month and 6 month. S K Majumdar et al and Zhou et al performed single injection technique also called modified technique [17,18]. Refai et al and Ungor et al performed 4 injections at 6 weeks apart [4,11]. Mustafa et al also performed 4 injections at monthly interval like us [19].

This study showed a statistically significant decrease in pain intensity through all the study periods from 2.13 to 0.53 after 6 months. In the study conducted by Refai the preoperative pain score was 6.72 and it reduced to 0.61 in last follow up (1 – 4 year) [16]. In Ross A Hauser et al study the starting pain level was 5.9 and it reduced to 2.5 at the end of the study [3]. But in the study of Wynand Francois Louw et al. there is reduction of pain score from 7.8 to 4.3 [20].

In this study there is 60% sound reduction after 6 months of follow-up. It is contradict to Refai et al. study where there is no improvement in clicking sound [11]. But in the study by Ungor et al there is 87.5% reduction of clicking sounds after prolotherapy [4].

In our study preoperative frequency of dislocation or subluxation were 13.53 and it reduced to 0.67 after 6 months postoperative. In a study conducted by Ungor et al. it was only 2.1 preoperative and there is complete reduction of episodes of dislocation or subluxation [4]. But in the study of Cezairli et al. the preoperative mean frequency of subluxation was 1.7 and reduced to 0.6 after 3 month follow up [21].

In this study the mean Mouth opening values showed a statistically significant decrease and slowly increasing after 2 months. These findings could be explained based on the histologic findings of Oh et al examining dextrose prolotherapy in the rabbit carpal tunnel, where 1 forepaw was randomly injected with 10% dextrose solution and the contralateral paw was injected with a similar amount of 0.9% saline solution as a control. These findings showed that the saline solution side has minimal changes whereas the dextrose side showed progressive non-inflammatory sub synovial connective tissue fibrosis, with vascular proliferation and thickening of collagen bundles [15]. In our study mean

Mouth opening was 45.27 preoperatively and it reduced to 41.67 after 6 month postoperative period. It is almost similar to the study of Ungor et al there preoperative mouth opening was 44.4 and after 4 sessions of prolotherapy was 35.1 [4]. Our observation about mouth opening was somewhat similar to the study conducted by Majumdar et al where preoperative mouth opening was 43.65 and 6 month postoperative was 39.83 [17].

Ultrasound enabled us to identify the joints and other adjacent structures so that the accuracy allows higher rate of success. Also, ultrasound has an economical advantage compared to arthroscopy and other imaging modalities. Ultrasound-guide prolotherapy is excellent tool for clinicians to raise the postoperative success rate [2].

The limitations of this study were the small sample size, short term evaluation, lack of a control group due to ethical concerns about placebo injections and not being able to compare the Prolotherapy with other treatment modalities in the management of TMD.

5. CONCLUSION

With limited period of follow up, 25% Dextrose prolotherapy yields promising results in the management of temporomandibular joint dysfunction (TMD) in terms of post injection improvement of TMJ pain, clicking, deviation of mouth, episodes of locking and maximal mouth opening. This technique appears promising for the treatment of symptomatic TMJ Dysfunction, as evidenced by the therapeutic benefits, simplicity, safety, patients' acceptance of the injection technique, and lack of significant side effects. However, continued research into prolotherapy's effectiveness in patient populations with large sample size and long-term follow-up is needed.

CONSENT AND ETHICAL APPROVAL

After obtaining ethical committee clearance and providing the patients with informed consent, the study group included 15 patients with the temporomandibular joint dysfunction reported to department of Oral and Maxillofacial Surgery.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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