



Comparison of Autologous Blood Injection and Dextrose Prolotherapy in the Treatment of Chronic Recurrent Temporomandibular Dislocation: A Randomized Clinical Trial

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Abstract

Introduction Prolotherapy is a minimally invasive technique that aims to functionally restore or repair the soft and hard tissues of the TMJ by injecting a stimulant. The present study was conducted to compare the effectiveness of dextrose and autologous blood injection (ABI) as prolotherapy agents in the treatment of patients with chronic recurrent TMJ dislocation (CRTD).

Materials and Method Thirty-two patients were divided into two groups—ABI and dextrose ($n = 16$ each). The superior joint space was located by means of cantho-tragal line and lavage. Delivery of prolotherapy agent was performed by single-needle technique. An elastic bandage was applied for a week and rehabilitation was initiated three weeks after the treatment. Pain level, joint hypermobility, maximal mouth opening, and frequency of dislocations were recorded at various follow-up intervals up to one year post-treatment.

Results No significant difference ($p > 0.05$) was seen for the values between both groups at all time intervals in the pain level. At the 6-month and annual follow-ups, the mouth opening of the patients treated with ABI was significantly lower ($p < 0.01$) as compared to those treated with dextrose. The patients treated with ABI therapy exhibited fewer dislocations ($p < 0.05$) within the following year.

Conclusion Prolotherapy is a relatively noninvasive, safer, and effective treatment modality with a high success rate for patients with CRTD. Both, ABI and dextrose, proved effective in reducing the pain and joint hypermobility associated with CRTDs within a week. ABI proved to be more efficient in reducing the mouth opening and limiting the dislocation of TMJ as compared to dextrose therapy.

Keywords Temporomandibular joint · TMJ disorders · Joint dislocations · Prolotherapies

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Introduction

Dislocation of the temporomandibular joint (TMJ) indicates anterior dislodgement of the condylar head from its normal anatomic position. The condyle assumes a position anterior to the articular eminence and is prevented from sliding back to the condylar fossa. Spasm of muscles of mastication, laxity of ligaments of the joint, increased size or abnormal position of the articular eminences, or neurological discrepancies are some of the causative factors leading to recurrent dislocations of the TMJ [1].

Over time, several modalities have been reported with clinically satisfactory success for the treatment of TMJ dislocations. Surgical correction of the aberrance in the TMJ by condylectomy or augmentation of articular eminence is undoubtedly a direct approach to the problem. However,

these procedures carry a certain risk of complications such as infection of the joint, injury to the facial nerve, paresthesia, and those associated with general anesthesia [2]. Consequently, less invasive, conservative techniques are preferred by the patients as well as the surgeons.

Proliferative injective therapy, or ‘prolotherapy’ in short, is a minimally invasive technique that aims to functionally restore or repair the soft and hard tissues of the TMJ by injecting a stimulant. Various solutions such as dextrose, sodium morrhuate, phenols, and platelet-rich plasma have been tried for this purpose [3]. Dextrose is a commonly used agent in prolotherapy owing to its biocompatibility, ease of availability, and feasibility.

Another prolotherapy technique, first described by Brachmann in 1964, is autologous blood injection (ABI). The technique was seldom used over the years and has now resurfaced owing to recent studies. The principle of ABI closely resembles the pathophysiology of bleeding into any joint of the body such as the knees or elbows [2]. The injected blood evokes an inflammatory response, followed by cytokine-mediated repair.

The purpose of our present study was to compare the effectiveness of dextrose and ABI prolotherapy in the treatment of patients with chronic recurrent TMJ dislocation

(CRTD). To the best of our knowledge, a clinical trial to compare the effectiveness of the two prolotherapy agents has not yet been conducted. The prospective clinical trial was carried out to determine which of the two prolotherapy agents is more effective in improving the functionality and in reducing the number of recurrences in these patients. In this study, we considered a null hypothesis that ‘there is no difference in the effectiveness of both, ABI and dextrose prolotherapy, in reducing the mouth opening and limiting the dislocation of TMJ.’

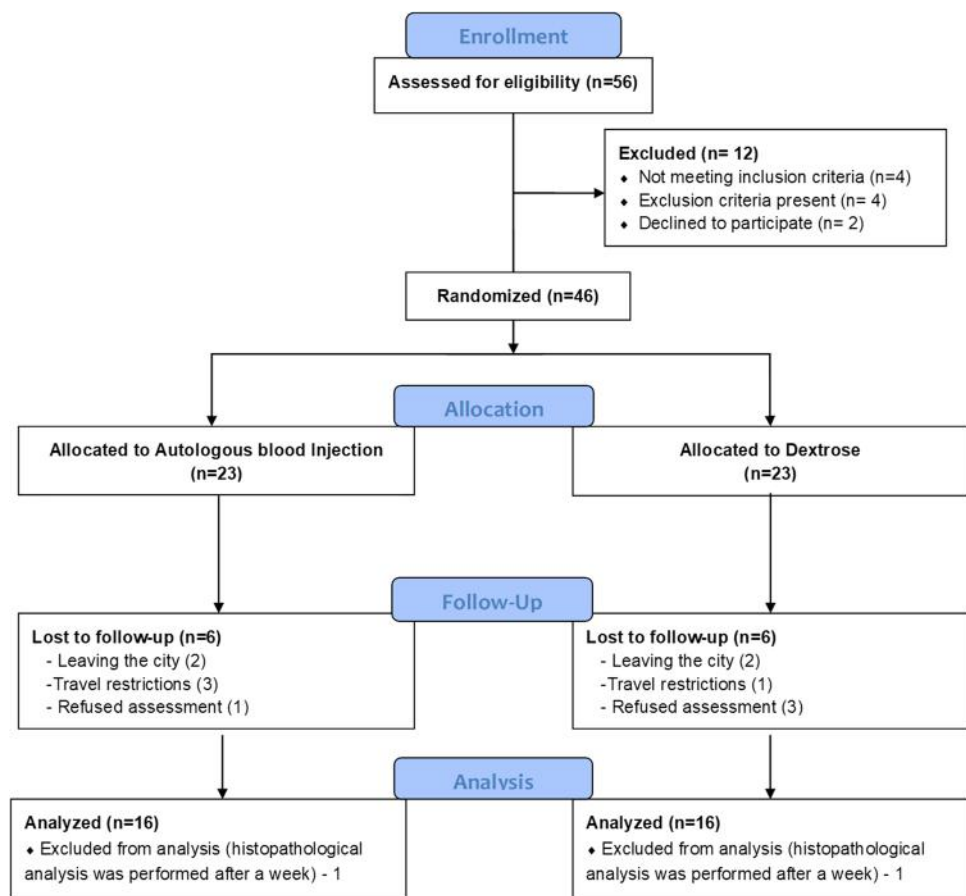
Material and Methods

Selection of Patients

The present prospective randomized clinical trial was conducted on a total of 32 patients of age 18 years and above, who reported to our institution with CRTD (Fig. 1). The inclusion and exclusion of patients in the study were based on two criteria, similar to those described by Nitzan, Daif, and Gagnani et al. [4–6]:

(i) Clinical—Multiple episodes of TMJ dislocation (uni- or bilateral). Signs and symptoms associated with

Fig. 1 CONSORT flow diagram



TMJ dislocations such as the presence of clicking sounds, crepitus, hypermobility, increased mouth opening, and level of pre-auricular pain were also recorded, but were not strict criteria for inclusion.

(ii) Radiographic—Position of the condyle with relation to the articular eminence on wide mouth opening was assessed by Orthopantomogram and a trans-pharyngeal TMJ view (in open and closed mouth positions).

Patients with connective tissue syndromes, psychological abnormalities, bleeding disorders, pregnancy, and allergy to anesthetics were excluded from the study [6].

The study protocol was approved by the institutional ethical review board, and a pilot study was performed on five patients in the year 2019, the data of which were not included in the final results. The methodology and feasibility of the study were confirmed, with few refinements in the protocol. The final study protocol was registered in the Clinical Trials Registry of India (CTRI No.: CTRI/2020/10/028382). The sample size was determined using the expected proportion of successful cases in each group, values of which are estimated from literature and using appropriate statistical formulas (attached as supplementary material). Randomization was performed by means of an online randomization tool [7]. The participants were assigned to either of the two groups ($n = 16$

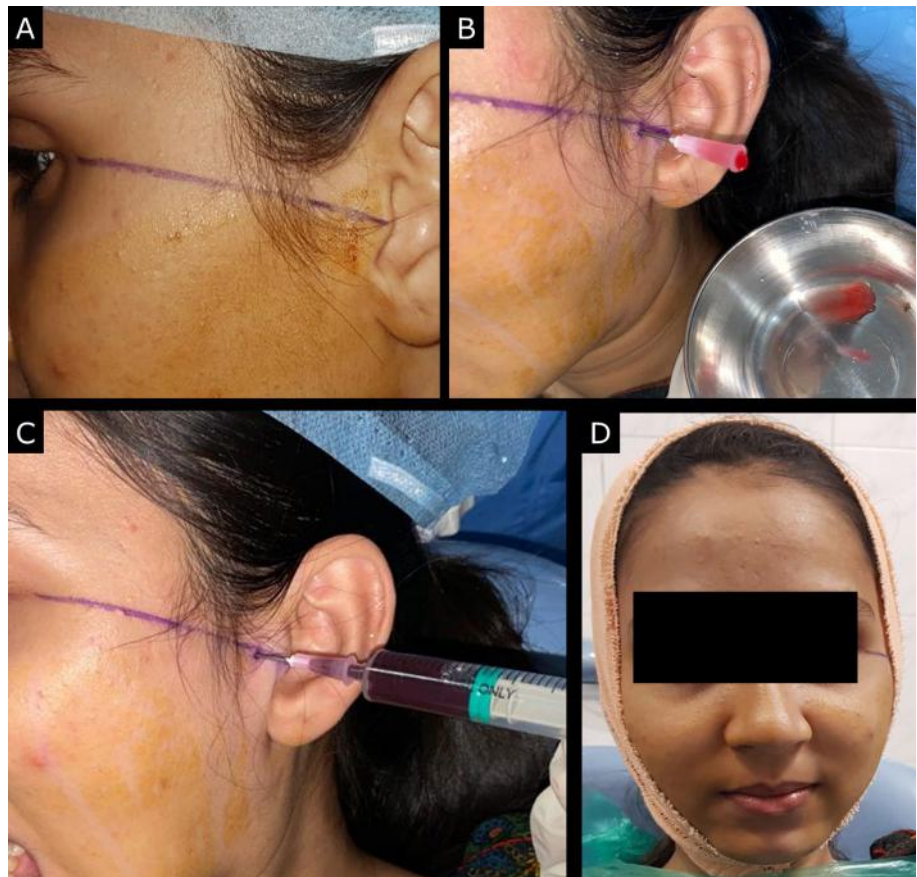
each): one treated with ABI and the other treated with 50% dextrose prolotherapy.

Procedure

The patients were explained about CRTDs and the available treatment modalities. They were also explained the benefits and possible complications of prolotherapy. Informed consent was obtained followed by elicitation of frequency of dislocation, maximal mouth opening, hypermobility, and clicking/crepitus. Baseline evaluation of pain was performed by the visual analog scale (VAS) followed by routine blood investigations and radiographic assessment.

The procedure was performed as described by Daif in their study [5]. The skin overlying the TMJ would scrub via an antiseptic solution, and the external auditory meatus was blocked with cotton soaked in normal saline. The auriculotemporal nerve was anesthetized by means of local infiltration of lignocaine with 1:200000 adrenaline. The articular fossa was located at a point 10 mm anterior to the tragus of the ear and 2 mm inferior to the cantho-tragal line (Fig. 2A). At this coordinate, an 18-gauge needle was inserted into the superior joint space. Lavage of TMJ was carried out with Ringer’s lactate, and then, the syringe was disjoined with the needle still in the same position place (Fig. 2B). A

Fig. 2 A Preliminary preparations and marking of cantho-tragal line, B lavage of temporomandibular joint with Ringer’s lactate, C autologous blood injection, D application of elastic bandage



syringe filled with the respective prolotherapy agent was then connected to the needle, and the agent was injected into the joint space (Fig. 2C).

For group I, 3 ml of autologous blood was withdrawn from the patient's cubital fossa, 2 ml was injected into the upper joint space and 1 ml was injected into the pericapsular tissues, whereas for group II, 3 ml of 50% dextrose was taken in a 5 ml syringe, 2 ml was injected into the upper joint space and 1 ml was injected around the pericapsular tissues.

The procedure was repeated on the opposite side in the same manner in case of bilateral involvement. Restriction of mouth opening is crucial for the success of prolotherapy for which an elastic head bandage was applied (Fig. 2D). Patients were advised to wear it for the entire day through the first week and only nocturnally in the second week. Antibiotics and analgesics were prescribed for five days post-therapy. The patients were advised to follow a soft food diet for the first two weeks.

Rehabilitation by exercises gradually controlling the range of motion of mouth opening was initiated from the third week onwards. Patients were advised to perform these exercises in front of the mirror for a more fine-tuned control and to ensure the correctness of the technique. A follow-up clinical and radiographic assessment was carried out after three days, one week, two weeks, one month, three months, six months, and one year post-therapy. The collected data were statistically analyzed to assess the comparative effectiveness of ABI and dextrose prolotherapy in the management of CRTD.

Results

The study population comprised 14 (43.8%) males and 18 (56.3%) females. The age of the patients ranged from 25 to 55 years with a mean of 36.63 years ($SD = \pm 8.769$). A statistically nonsignificant difference between the demographic parameters of both groups prevented any influence on the outcomes by these characteristics.

There was a statistically significant reduction in the number of patients exhibiting TMJ hypermobility (gauged by maximal mouth opening) and clicking sounds in both the groups, on the postoperative 7th-day follow-up. There was a statistically nonsignificant difference ($p > 0.05$) seen for the values between both groups at all time intervals in the pain level (Fig 3). A statistically significant reduction ($p < 0.05$) was noted in the number of patients exhibiting clicking sounds associated with TMJ, at the 1-week follow-up interval in both groups.

At the 6-month and annual follow-ups, the mouth opening of the patients treated with ABI was significantly lower ($p < 0.01$) as compared to those treated with dextrose (Table 1). Consequently, the patients treated with ABI

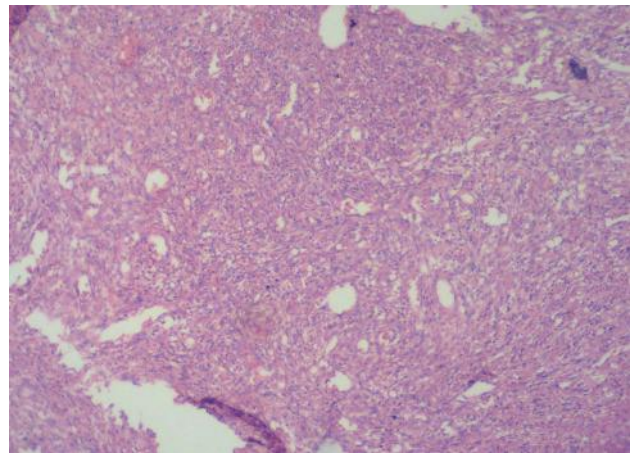


Fig. 3 Microscopic visualization of the formed granulation tissue one week post-treatment (H and E, original magnification $\times 100$)

therapy exhibited fewer dislocations ($p < 0.05$) within the following year.

Discussion

The mechanism of action of prolotherapy is to invoke a mild inflammatory response by injecting a foreign agent into the joint and pericapsular tissues [8]. Temporary cellular stress causes a release of cytokines and increased growth factor activity. These factors cause the migration of macrophages to the site and the multiplication of reparative cells specific to the tissue. A combination of an organized blood clots and loses fibrous tissue forms, which maintains joint stiffness. In addition, this exposure of cartilage to blood results in a disturbance of cartilage matrix turnover and in a decrease in the chondrocyte metabolism causing localized contraction [9, 10].

The histopathological picture of the injected area after one week has been described as comprising of hemorrhage, inflammation, necrosis, and vascular changes in adjacent soft tissues [9, 10]. These findings were confirmed by a microscopic examination of the formed tissue performed for one of our cases (Fig. 4).

A similar condition is created in ABI as noted in trauma and bleeding into other joints of the body. However, unlike repair following an injury, disruption of tissue architecture does not occur in prolotherapy. Even so, immobilization is needed for one week to permit clot formation in a controlled manner. Researchers have found that patients with intermaxillary fixation following ABI had more successful outcomes as compared to those without [11]. A simple elastic bandage has been demonstrated to be sufficient for the same purpose by Gagnani and Hasson et al. [6, 12]. It is simpler and more

Table 1 Intergroup comparison of maximum mouth opening in millimeters

Group		Mean	Std. deviation	Std. error mean	T value	p value
Preoperative	ABI	22.75	3.768	.942	-.604	.551#
	Dex	23.56	3.847	.962		
Postoperative 3rd day	ABI	23.88	3.931	.983	-.240	.812#
	Dex	24.19	3.430	.857		
7th day	ABI	25.38	4.113	1.028	-.095	.925#
	Dex	25.50	3.266	.816		
15th day	ABI	27.56	4.427	1.107	.476	.638#
	Dex	26.93	2.658	.686		
1 month	ABI	29.00	4.147	1.037	1.109	.276#
	Dex	27.60	2.667	.689		
3rd month	ABI	30.75	3.416	.854	1.832	.077#
	Dex	28.73	2.631	.679		
6th month	ABI	32.81	3.468	.867	3.069	.005**
	Dex	29.60	2.165	.559		
1 year	ABI	36.88	2.217	.554	7.312	.000**
	Dex	30.60	2.558	.660		

ABI Autologous blood injection, Dex Dextrose

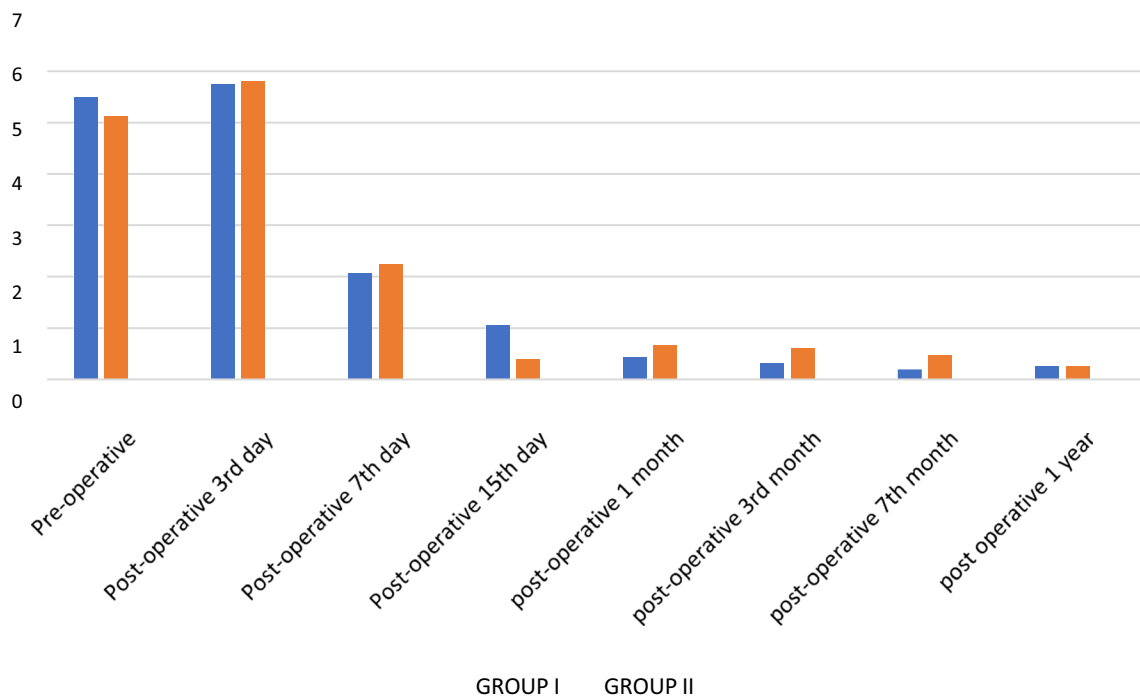


Fig. 4 Intergroup comparison of mean pain levels as measured by visual analog scale

comfortable for the patients as compared to IMF and was, therefore, preferred in our study.

Concerns have been raised by some authors with respect to degeneration of articular cartilage or the development of fibrous or bony ankylosis following prolotherapy in the past, which led to a reluctance among clinicians to use the technique [8]. Blood in the TMJ area after surgery in patients

with their jaw immobilized can lead to complications such as asymmetrical mandible or ankylosis. It is, therefore, crucial to mobilize the TMJ by physiotherapy once a stable scaffold of fibrous tissue is formed. For this purpose, we initiated rehabilitation from the third week onwards. None of the patients in our study exhibited any of these complications in either of the groups.

New mesenchymal cells and stromal matrix get deposited in an organized fashion within six to eight weeks. The granulation tissue ultimately gets replaced by mature fibrous tissue at the TMJ capsule and ligament [9, 10]. The newly created fibrous hurdle hinders the condyle from attaining an abnormal position in front of the articular eminence. In accordance with these processes, there was a significant reduction in maximal mouth opening in both the groups three months post-treatment which accounted for the absence of recurrent dislocations indicating the success of the therapy.

Only one patient in the ABI group and three patients in the dextrose group needed a second injection after an additional episode of dislocation. Repeated injections proved to be effective without any side effects and were well tolerated by the patients. However, there are currently no standard criteria defined for the number of injections needed and the intervals between them. The condition was resolved for the patient in the ABI group after the second injection. On the other hand, the patients in the dextrose group required a third injection at the third-month follow-up.

Overall, while the success rate was 87.5% at the end of three months, a 100% success rate was achieved by the end of the study. This was radiographically confirmed by the position of the condyle posterior to the articular eminence for all the cases in both the groups at the six-month and annual follow-up.

The relatively noninvasive procedure of prolotherapy involves the delivery of the agent without surgical exposure to the joint space. Therefore, the technique is essentially a blind one, and the position of the TMJ is confirmed by means of trained visualization of the articular fossa point and a successful lavage [5]. The use of a single needle for lavage and injection of the agent eliminated the risk of blood flowing out through the second point of injection associated with the conventional two-needle technique. This technique was essentially suitable for ABI, wherein the injected blood was retained within the superior joint space. Additional advantages of the single-needle technique include more stability, increased efficiency, and a lesser risk of causing direct damage to the facial nerve or other postoperative complications [2, 5, 13]. Furthermore, the procedure can be carried out under local anesthesia, thereby eliminating the potential physical and psychological effects of general anesthesia on the patients [14]. The procedure would be particularly beneficial in patients who cannot be surgically operated because of systemic diseases or other reasons.

The present study presents itself with certain limitations. The sample size was relatively smaller; a larger sample size would yield more reliable clinical data. Furthermore, the inclusion of attrition bias due to incomplete outcome data in some cases further reduced the sample size and subsequently the reliability of our results for the clinicians for utilizing them in clinical decision-making. A longer follow-up period

would provide a higher quality of clinical evidence in terms of the long-term effectiveness of the two agents. These limitations could be considered in future studies for confirmation of our findings and to obtain more clinically reliable data. The effectiveness and efficiency of other prolotherapy agents could also be compared to those used in our study, with an objective to determine the safest and most effective one.

Conclusion

Prolotherapy is a viable treatment modality with a high success rate for patients with CRTD. Multiple injections may be needed to achieve clinical success; however, they are well tolerated by the patients. The technique has fewer postoperative complications as compared to other surgical techniques, making it a safer choice of treatment for patients, particularly those with systemic disorders. Overall, both ABI and dextrose proved effective in reducing the pain and joint hypermobility associated with CRTDs within a week. ABI proved to be more efficient in reducing the mouth opening and limiting the dislocation of TMJ as compared to dextrose therapy.

Declarations

Conflict of interest The authors have no conflicts of interest to declare.

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