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Prolotherapy versus Arthrocentesis in the Management of a Hypermobile Temporomandibular Joint-A Systematic Review

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ABSTRACT

Background: Prolotherapy and arthrocentesis are non-surgical treatment modalities employed for the conservative management of temporomandibular joint (TMJ) hypermobility which may be diagnosed as luxation or subluxation of the joint. Symptomatic TMJ hypermobility is a crippling condition and demands immediate treatment and subsequent follow up.

Aim: The aim of this study is to assess the efficacy of prolotherapy when compared to arthrocentesis as non-surgical management of TMJ hypermobility.

Objectives: To evaluate the effectiveness of prolotherapy and arthrocentesis in the management of TMJ hypermobility.

Methods: Electronic databases of PubMed, Google Scholar and Cochrane central register of controlled trials were searched for related studies along with search of relevant journals. Title and abstract scanning was done to evaluate for inclusion. Bibliography of identified studies was scanned to include studies published outside the electronic database.

Results: Two authors assessed the 49 articles identified from electronic search based on inclusion criteria and research question. 2 were excluded after removing duplicates and 42 were excluded after reading titles. 5 studies were evaluated in detail after reading the abstract and full text. 2 studies were included based on the inclusion criteria and research question.

Conclusion: On the basis of current literature there is evidence that the concomitant use of prolotherapy with arthrocentesis may be superior in the management of TMJ hypermobility as compared to their individual use. The authors suggest formulation of well-designed randomised controlled trials to formulate a step ladder like treatment protocol for the management of TMJ hypermobility. This will help to achieve optimum amelioration of the quality of life of the individual.

Key words: Temporomandibular joint, TMD, TMJ pain, Prolotherapy, Arthrocentesis

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INTRODUCTION

Temporomandibular joint (TMJ) is an articulation formed bilaterally by the head of the condyle of mandible and glenoid or mandibular fossa of the temporal bone [1,2]. Biomechanics and neuromuscular control of TMJ comprises of the muscles of mastication, lateral and accessory ligaments as well as neural impulses transmitted by the mandibular division of trigeminal nerve [3–5].

Temporomandibular joint capsule is the most vital structure which stabilizes the joint and it is reinforced by the lateral ligament [2,6,7].

TMJ dislocation or hypermobility is defined as an excessive abnormal displacement of the mandibular condyle where condylar head lies anterior to the articular eminence during wide mandibular opening, such as yawning and laughing, while the reduction can be achieved without professional assistance [5,8].

Morphological factors like shape of the condyle, glenoid fossa, articular eminence, zygomatic arch and squamotympanic fissure influence the direction and type of dislocation of the head of the condyle from the glenoid fossa.

Other factors such as age, type of dentition, etiology, duration of hypermobility and function of the masticatory muscles contribute significantly in the pathogenesis and management of temporomandibular joint dislocation [9]. TMJ dislocation is rare, but it impacts the individual gravely and requires immediate medical attention.

Dislocation or hypermobility is generally categorized as habitual dislocation, complete (luxation) or partial (subluxation), unilateral or bilateral, acute, and chronic protracted or chronic recurrent [10,11]. Anterior dislocation of the condyle is the most commonly encountered type [12].

Other types include superiorly into the middle cranial fossa, medial, lateral and posterior, which are rare and commonly associated with trauma [13–16]. Acute dislocation is the displacement of condylar head anterior to the articular eminence and its inability to revert to its original position [17].

Acute TMJ dislocation severely affects overall and oral health of the individual due to pain and discomfort while speaking and mastication. Since the social and psychological implications are high, TMJ dislocation should be considered as a debilitating condition.

Management of TMJ dislocation involves moving the condyle backwards into the glenoid fossa by manual manipulation with/out local anaesthesia or sedation [18]. In chronic TMJ subluxation, the patient is able to manually maneuver the mandible into normal position [19].

However in acute TMJ luxation the pain due to muscular spasm and intra-articular effusion due to this open-locking situation, the patient is unable to self maneuver the mandible and needs the help of an experienced practitioner. Thus, in subluxation cases the condyle can be relocated through self manipulation by the patient, but in TMJ luxation this is not possible [20].

Conservative treatment modalities to manage acute dislocation include manual reduction with/out anaesthesia or sedation, gag reflex assisted reduction and manual reduction under general anaesthesia [18,21].

For the management of chronic protracted dislocation the conservative treatment modalities include manual reduction with/out anaesthesia or sedation, manual reduction under general anaesthesia, elastic traction with intermaxillary fixation, traction with bone hooks and mandibular guidance therapy [22,23].

Conservative treatment for recurrent dislocation includes avoiding wide opening of the mouth during daily activities, physiotherapy, use of occlusal splints, chemical capsuloraphy using intra articular and/or extra articular sclerotic agents (like alcohol, sodium tetradecyl sulphate, sodium psyliate, sodium monoruate), autologous blood capsuloraphy, PRP capsuloraphy, botulinum toxin, prolotherapy, arthrocentesis [24–28]. Surgical techniques include eminoplasty (reduction or augmentation), interpositional eminoplasty, lateral pterygoid myotomy, condylectomy, temporalis tendon scarification, miniplates and capsular plication [29–33].

Prolotherapy is also known as proliferation therapy. It was first introduced by Louis Schultz in 1937 for treatment of painful TMJ subluxation [34]. This therapeutic injection technique has been in use in clinical practice for decades and is used to treat various chronic conditions.

Over the years it has been given different names such as proliferative injection therapy, proliferant injection, sclerotherapy, regenerative injection therapy, and growth factor stimulation injection therapy. It consists of scheduled injections of an irritant solution at or near multiple sites of connective tissue dysfunction over a period of several months, which is assumed to cause re-inflammation and subsequent symptomatic relief.

However, the clinical outcome of TMJ dislocation treated with dextrose prolotherapy has been evaluated in only a limited number of studies [35–39].

TMJ arthrocentesis is a minimally invasive treatment which is defined as the lavage of the joint space without visualising using sterile needles and sterile irrigants, which could be drugs or other therapeutic substances [40]. It functions by removing intra-articular adhesions by hydraulic pressure from irrigants in the upper joint space and reducing the pain by removing inflammatory mediators from the joint space [41].

Symptomatic relief is achieved due to the removal of these inflammatory mediators and changes in intra-articular pressure. The aim was to systematically evaluate the efficacy of prolotherapy compared with arthrocentesis in the management of TMJ hypermobility.

Structured question

In the non-surgical management of temporomandibular joint hypermobility, is dextrose prolotherapy superior to arthrocentesis or vice versa in post treatment sequelae?

Pico analysis

- Population: Temporomandibular joint hypermobility.
- Intervention: Prolotherapy.
- Comparison: Arthrocentesis.
- Outcome: Pain relief.

MATERIALS AND METHODS

This review was done in accordance with guidelines given by Cochrane Handbook of Systematic Review.

Inclusion criteria

Studies were selected using the following inclusion criteria. All studies including:

- All types of studies including patients with temporomandibular joint hypermobility.
- Studies using prolotherapy and arthrocentesis for management of temporomandibular joint hypermobility.
- Studies published in English language only.

Exclusion criteria

Studies were excluded based on the following exclusion criteria.

- Studies which used surgical techniques for temporomandibular joint hypermobility.
- Studies which included temporomandibular joint dysfunction.
- Ongoing studies in which results have not yet been published.

Search method for the identification of studies

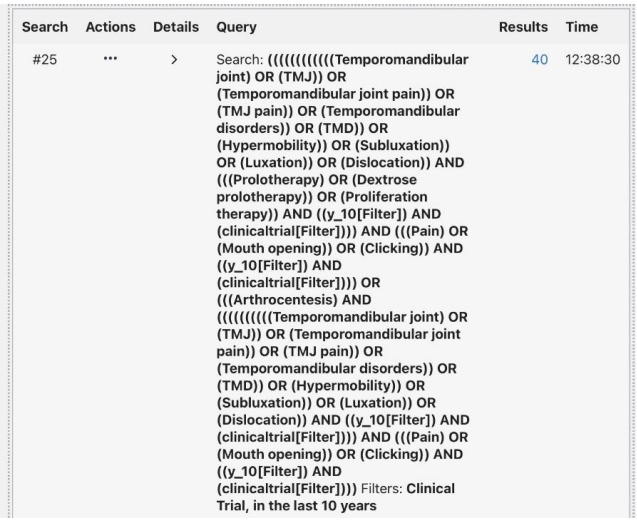
To identify the studies to be included for detailed evaluation in systematic review, following search strategy was developed for each database searched:

- PubMed (All types of study design published from 2001-2021).
- The Cochrane Central Register of clinical Trials (All types of study design published from 2001-2021).
- Google Scholar (All types of study design published from 2001-2021).

Pubmed search strategy

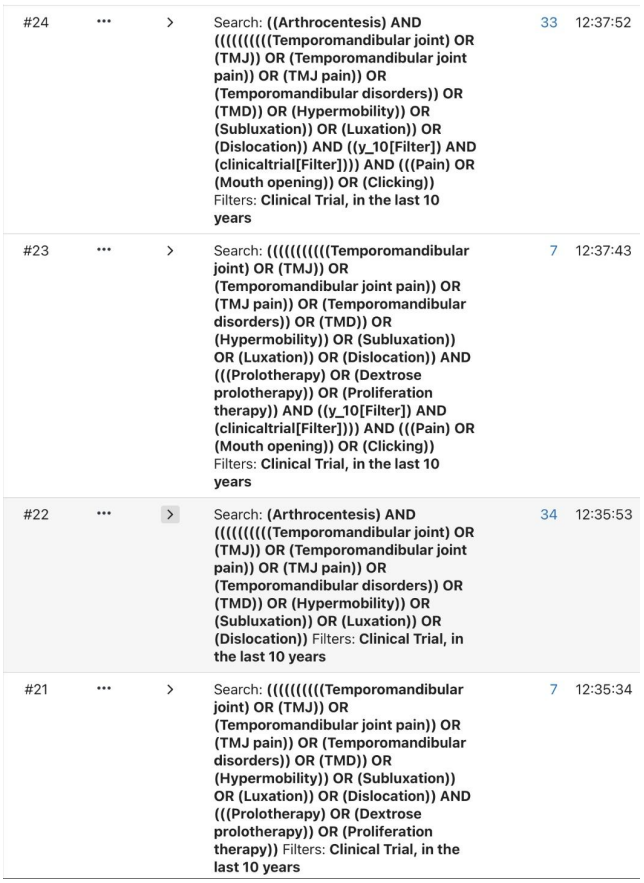
Advanced search of PubMed search engine was used using the following keywords:

Temporomandibular joint OR TMJ OR Temporomandibular joint pain OR TMJ pain OR (Temporomandibular disorders) OR (TMD) OR (Hypermobility) OR (Subluxation) OR (Luxation) OR (Dislocation) AND (Prolotherapy) OR (Dextrose prolotherapy) OR (Proliferation therapy) AND (y_10[Filter]) AND (clinicaltrial[Filter]) AND (Pain) OR (Mouth opening) OR (Clicking) AND (y_10[Filter]) AND (clinicaltrial[Filter]) OR (Arthrocentesis) AND (Temporomandibular joint) OR (TMJ)) OR (Temporomandibular joint pain)) OR (TMJ pain) OR (Temporomandibular disorders) OR (TMD) OR (Hypermobility) OR (Subluxation) OR (Luxation) OR (Dislocation) AND ((y_10[Filter]) AND (clinicaltrial[Filter])AND (Pain) OR (Mouth opening) OR (Clicking) AND ((y_10[Filter]) AND (clinicaltrial[Filter]). This search yielded 40 studies (Figures 1 A to Figure 1C).



Search	Actions	Details	Query	Results	Time
#25	•••	›	Search: ((((((((((Temporomandibular joint) OR (TMJ)) OR (Temporomandibular joint pain)) OR (TMJ pain)) OR (Temporomandibular disorders)) OR (TMD)) OR (Hypermobility)) OR (Subluxation)) OR (Luxation)) OR (Dislocation)) AND (((Prolotherapy) OR (Dextrose prolotherapy)) OR (Proliferation therapy)) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))) AND (((Pain) OR (Mouth opening)) OR (Clicking)) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))) OR (((Arthrocentesis) AND ((((((((((Temporomandibular joint) OR (TMJ)) OR (Temporomandibular joint pain)) OR (TMJ pain)) OR (Temporomandibular disorders)) OR (TMD)) OR (Hypermobility)) OR (Subluxation)) OR (Luxation)) OR (Dislocation)) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))) AND (((Pain) OR (Mouth opening)) OR (Clicking)) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))) Filters: Clinical Trial, in the last 10 years	40	12:38:30

Figure 1A: Image showing the PubMed search strategy.



#24	•••	›	Search: ((Arthrocentesis) AND ((((((((((Temporomandibular joint) OR (TMJ)) OR (Temporomandibular joint pain)) OR (TMJ pain)) OR (Temporomandibular disorders)) OR (TMD)) OR (Hypermobility)) OR (Subluxation)) OR (Luxation)) OR (Dislocation)) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))) AND (((Pain) OR (Mouth opening)) OR (Clicking)) Filters: Clinical Trial, in the last 10 years	33	12:37:52
#23	•••	›	Search: ((((((((((Temporomandibular joint) OR (TMJ)) OR (Temporomandibular joint pain)) OR (TMJ pain)) OR (Temporomandibular disorders)) OR (TMD)) OR (Hypermobility)) OR (Subluxation)) OR (Luxation)) OR (Dislocation)) AND (((Prolotherapy) OR (Dextrose prolotherapy)) OR (Proliferation therapy)) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))) AND (((Pain) OR (Mouth opening)) OR (Clicking)) Filters: Clinical Trial, in the last 10 years	7	12:37:43
#22	•••	›	Search: (Arthrocentesis) AND ((((((((((Temporomandibular joint) OR (TMJ)) OR (Temporomandibular joint pain)) OR (TMJ pain)) OR (Temporomandibular disorders)) OR (TMD)) OR (Hypermobility)) OR (Subluxation)) OR (Luxation)) OR (Dislocation)) Filters: Clinical Trial, in the last 10 years	34	12:35:53
#21	•••	›	Search: ((((((((((Temporomandibular joint) OR (TMJ)) OR (Temporomandibular joint pain)) OR (TMJ pain)) OR (Temporomandibular disorders)) OR (TMD)) OR (Hypermobility)) OR (Subluxation)) OR (Luxation)) OR (Dislocation)) AND (((Prolotherapy) OR (Dextrose prolotherapy)) OR (Proliferation therapy)) Filters: Clinical Trial, in the last 10 years	7	12:35:34

Figure 1B: Image showing the PubMed search strategy.

#20	•••	Search: **((Pain) OR (Mouth opening)) OR (Clicking)**	908,261	12:26:28
#19	•••	Search: **Clicking**	20,658	12:26:18
#18	•••	Search: **Mouth opening**	8,506	12:26:11
#17	•••	Search: **Pain** "pain"[MeSH Terms] OR "pain"[All Fields] **Translations** **Pain:** "pain"[MeSH Terms] OR "pain"[All Fields]	882,156	12:26:04
#16	•••	Search: **Arthrocentesis** "arthrocentesis"[MeSH Terms] OR "arthrocentesis"[All Fields] OR "arthrocenteses"[All Fields] **Translations** **Arthrocentesis:** "arthrocentesis"[MeSH Terms] OR "arthrocentesis"[All Fields] OR "arthrocenteses"[All Fields]	1,142	12:25:56
#15	•••	Search: **((Prolotherapy) OR (Dextrose prolotherapy)) OR (Proliferation therapy)**	141,922	12:25:41
#14	•••	Search: **Proliferation therapy**	141,922	12:25:31
#13	•••	Search: **Dextrose prolotherapy**	155	12:25:21
#12	•••	Search: **Prolotherapy**	277	12:25:12
#11	•••	Search: **((((((((Temporomandibular joint) OR (TMJ)) OR (Temporomandibular joint pain)) OR (TMJ pain)) OR (Temporomandibular disorders)) OR (TMD)) OR (Hypermobility)) OR (Subluxation)) OR (Luxation)) OR (Dislocation)**	123,619	12:25:00
#10	•••	Search: **Dislocation**	78,901	12:23:27
#9	•••	Search: **Luxation**	44,666	12:22:27
#8	•••	Search: **Subluxation**	49,706	12:22:14
#7	•••	Search: **Hypermobility**	3,106	12:22:03
#6	•••	Search: **TMD**	11,993	12:21:31
#5	•••	Search: **Temporomandibular disorders**	19,828	12:21:09
#4	•••	Search: **TMJ pain**	9,090	12:20:51
#3	•••	Search: **Temporomandibular joint pain**	8,920	12:20:37
#2	•••	Search: **TMJ**	29,348	12:20:16
#1	•••	Search: **Temporomandibular joint**	28,654	12:20:07

Figure 1C: Image showing the PubMed search strategy.

Cochrane search strategy

Cochrane trial for clinical registry was searched using following keywords- Temporomandibular joint, TMJ, hypermobility, subluxation, dislocation, prolotherapy, proliferation therapy, dextrose prolotherapy, arthrocentesis, pain score, maximum interincisal opening, clicking with Cochrane Library publication dates between 2001 to 2021, in Trials. This search yielded 1 study (Figure 2).

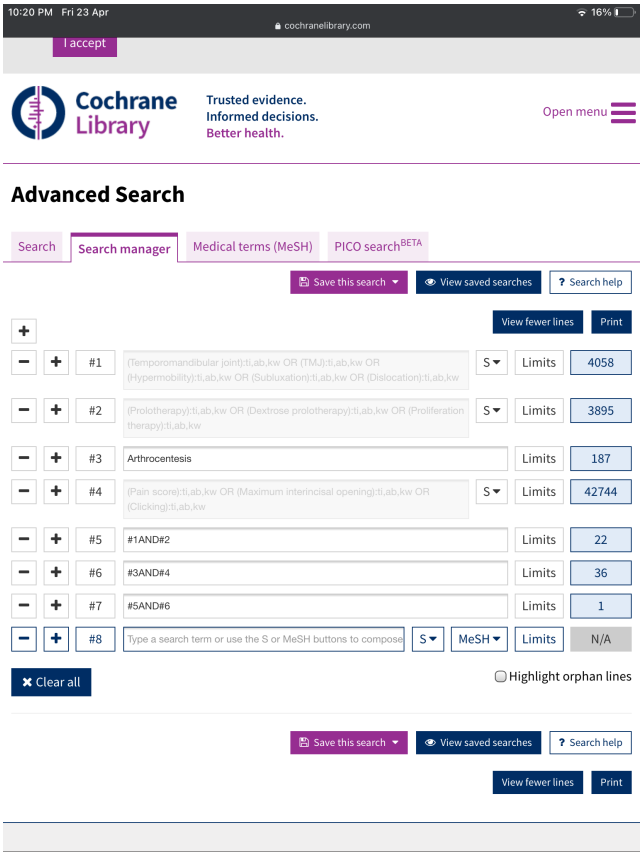


Figure 2: Image showing the Cochrane search strategy.

Google scholar search strategy

Google Scholar search engine was searched using the following keywords Temporomandibular joint, TMJ, hypermobility, subluxation, dislocation, prolotherapy, proliferation therapy, dextrose prolotherapy, arthrocentesis, pain score, maximum interincisal opening, clicking with year of publication range set as 2001-2021. This search yielded 8 studies.

Data collection and analysis

Selection of studies

One author (Shivangi Gaur) carried out the search strategy for the individual data bases. The total number of titles obtained were scanned and evaluated independently by two authors, SG and (Madhulaxmi M) to identify the relevant studies. The studies duplicated in the different data bases were excluded. In case of any disagreement between the two authors, final decision was obtained by discussion between the two authors. Abstracts of the studies were evaluated when complete information regarding the groups and participants included was not mentioned in the title. The abstract evaluation was carried out independently by two authors SG and MM to identify the final studies to be included based on the inclusion and exclusion criteria. Full text articles were evaluated when the abstracts did not provide adequate information regarding the groups

compared. Figure 3 gives the PRISMA flow diagram for the included studies (Figure 3). All the irrelevant studies were excluded and the reasons for the exclusion were noted in the characteristics of excluded studies (Table 1). The final studies included by the discussion of both the authors were further evaluated for the quality of studies following the guidelines given by Cochrane Handbook of systematic review. This was done independently by both the authors and any discrepancy was resolved by discussion between both the authors.

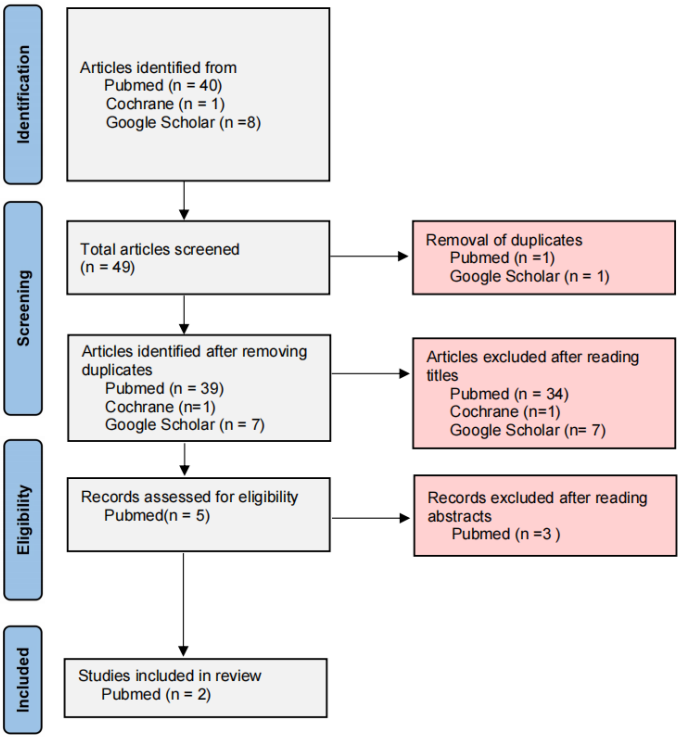


Figure 3: Prisma flowchart showing included studies.

Table 1: Characteristics of excluded studies.

S.No	Study	Reason for exclusion
1	Taşkesen F et al.	Ahead of print online article

Data extraction and management

Data for the included studies were evaluated for the characteristics of the study. Following characteristics were included:

- Author and year of study.
- Journal.
- Study design.
- Sample size.
- Type of groups.Outcome assessed.
- Results.
- Conclusion.

The variables observed are mentioned in (Table 2). A detailed evaluation of the variables observed in the study was noted by their mean values and statistical significance.

Table 2: Variables of interest.

Variables of interest	
Clinical parameters	TMJ pain
	Maximum interincisal opening
	Dislocation Incidences post treatment
	Clicking Sounds

Assessment of the quality of included studies

The quality of the included studies was assessed using the guidelines given by the Cochrane Handbook of systematic review. The parameters used to evaluate the included studies are as follows:

- Random sequence generation (Selection bias).

- Allocation concealment (Selection bias).
- Blinding of participants and personnel (Performance bias).
- Blinding of outcome assessment (Detection bias).
- Free of Incomplete outcome data assessment (Attrition).
- Free from baseline imbalance (Reporting bias).
- Adequate reliability.

Individual parameter was assessed for high risk, low risk and unclear risk (Table 3). The final risk of bias of individual study was determined as low risk if all the studies showed low risk for the individual parameters. In case of high risk or unclear risk for one or two parameters, moderate risk was considered for the included study. If more than 2 parameters showed high risk or unclear risk, the included study showed to have a high risk of bias.

Table 3: Criteria for the assessment of risk of bias.

S.No	Criteria	Inference
1	Adequate random sequence generation	Yes : Random number table, computer random number generator, stratified or lock randomization, low tech-coin toss, shuffling cards, envelopes, throwing dice
		No: Quasi random- date of birth, day of visit, ID or record number, alternate allocation
		Non-random- choice of clinician or participant, availability
		Unclear
2	Allocation concealment	Yes : Central allocation, sequentially numbered, sealed, opaque envelopes, identical containers
		No : Random sequence known to staff in advance, envelope or packing without any safe guard, random predictable sequence
		Unclear
3	Blinding participants and personnel	Yes : Blinding and unlikely that blinding could have been broken, No blinding but outcome cannot be influenced
		No: No blinding, incomplete or broken blinding and outcome likely to be influenced
		Unclear
4	Blinding of outcome assessment	Yes : Blinding and unlikely that blinding could have been broken, No blinding but outcome cannot be influenced
		No: No blinding, incomplete or broken blinding and outcome likely to be influenced
		Unclear
5	Incomplete outcome data assessment (attrition, exclusion	Yes: No missing data. Reason for missing data not related to outcome and missing data balanced across the group
		No : Reason of missing data influencing the outcome
		Unclear
6	Free from baseline imbalance	Yes: Protocol is available and all the pre-specified outcome is reported.
		Protocol is not available but all the outcome of interest are reported
		No : Outcome are not reported as pre-specified or outcome are reported incompletely
		Unclear
7	Adequate reliability	Yes : Study free of any other source of bias
		No:Non-randomized studies, blocked randomization in unblinded trials.
		Unclear
	Risk of bias in the included studies	A) Low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met.

(B) Moderate risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were partially met.

(C) High risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met

RESULTS

Study selection

The systematic search from the electronic databases of PubMed revealed 40 studies, Cochrane library revealed 1 study and Google Scholar revealed 8 studies. No studies were obtained from hand searching. After removal of duplicates 47 studies were identified. After title scanning, 5 studies were identified. After abstract scanning 3 articles were eliminated as they did not meet the inclusion criteria. Full text articles for the other 2 studies were obtained for more detailed evaluation. The bibliography of these full text articles was scanned to include studies apart from the electronic databases. No relevant studies were found from the cross-reference. A total of 2 studies met the inclusion and exclusion criteria of the intended research.

Study characteristics

Characteristics of the included studies were mentioned and the Outcome of these studies were assessed using clinical parameters (Tables 4 and Table 5).

Refai et al [35] had a placebo controlled, prospective, randomized, double-blind clinical study design where twelve patients with painful subluxation or dislocation of the TMJ were assigned to the two groups. Patients in the interventional group received four injections of dextrose solution (2 mL of 10% dextrose and 1 mL of 2% mepivacaine) for each TMJ, each 6 weeks apart, whereas patients in the placebo group received four injections of placebo solution (2 mL of saline solution and 1 mL of 2% mepivacaine) for each TMJ, each 6 weeks apart. Outcome measures were assessed at each appointment just before the procedure and 3 months after the last injection. The outcome measures were a verbal scale for pain on palpation of the joint, clicking sound, maximal mouth opening (MMO),and frequency of luxations (number of episodes of locking per month). Both groups exhibited significant improvement in pain on palpation of the TMJ and frequency of luxations however there was no significant change in clicking sound. Only MMO showed a statistically significant difference between the groups throughout the post treatment phase. There was a significant reduction in MMO in interventional group in the 12th post operative week. However, the placebo group showed no significant difference in MMO throughout the study periods. For the last 2 periods of observation intervals, the placebo group exhibited statistically significantly mean MMO values than the interventional group. By the 12th postoperative week, the percentages of decrease in MMO were significantly greater in the interventional group.

Dolwick et al [42] recruited only female patients unsuccessfully treated with conventional treatment modalities. 24 patients that were recruited and randomly allocated to one of the two groups, either experimental or placebo group. In both groups, after local anesthesia was injected TMJ arthrocentesis was done. Joint lavage was done with 100 mL Ringer's lactate solution by a single investigator. Depending upon the group allocation group, triamcinolone acetonide (steroid) or Ringer's lactate solution (placebo) was injected into superior joint space. Patients were blinded to the study and were evaluated at baseline, 2, 6 and 12 weeks after arthrocentesis using VAS for primary outcome pain measures (pain intensity, pain unpleasantness, and chewing pain). Significant decrease in VAS pain scores were found between the baseline and post-treatment observation period for both the groups. The study group had statistically significantly less pain on chewing at 6-12 weeks as compared to placebo group. Mean maximum mandibular opening with/out pain were significantly higher in study group during the post treatment observation period than at baseline, whereas the placebo group exhibited higher mouth opening at 6 weeks. At the end of 12 weeks more patients in the study group (75%) had normal mandibular opening without pain (38 mm) as compared with the placebo group (20%). The proportion of patients with more than 50% improvement in pain on chewing in the study group (90%) was significantly higher than that in the placebo group (<40%) (Figures 4 and Figure 5).

Table 4: Characteristics of included studies.

S. No	Author and Year	Study design	Sample size and Age group	Study Groups		Outcomes assessment
				Intervention	Control	Variables Evaluated
1	Dolwick et al, 2020	Prospective, randomised, double blind, placebo controlled	24 female patients only divided into two equal groups	12 patients allocated to steroid group	10 patients allocated to placebo group (2 patients lost to follow up)	VAS pain scores for resting pain intensity,resting pain unpleasantness, current chewing pain

						at baseline, 2,6,12 weeks post treatment Maximum mandibular movement with/out pain at baseline,2,6,12 weeks post treatment Mean pain on muscle palpation at baseline, 2,6,12 weeks post treatment TMJ sounds at baseline,2,6,12 weeks post treatment
2	Refai et al, 2011	Prospective, randomised, double blind, placebo controlled	12 patients divided into two equal groups	6 patients allocated in active group received 4 injections of dextrose solution (2 mL of 10% dextrose and 1 mL of 2% mepivacaine) for each TMJ, each 6 weeks apart	6 patients allocated in placebo group received 4 injections of placebo solution (2 mL of saline solution and 1 mL of 2% mepivacaine) for each TMJ, each 6 weeks apart	Verbal scale expressing TMJ pain on palpation, maximal mouth opening (MMO), clicking sound, and frequency of luxations (number of locking episodes per month) were assessed at each injection appointment just before the injection procedure and 3 months after the last injection

Table 5: Characteristics of included studies.

S. No	Author and Year	Journal	Results	Conclusions
1	Dolwick et al, 2020	Journal of Maxillofacial Surgery	Significant reduction in VAS scores for both groups. The steroid group had significantly less chewing pain at 6 and 12 weeks than the placebo group. Mean maximum mandibular openings without pain or with pain were significantly greater at all post-arthrocentesis time points than at baseline in the steroid group, whereas the placebo group had a larger mandibular opening at 6 weeks. At 12 weeks, significantly more patients in the steroid group (75%) had a nearly normal mandibular opening without pain (38 mm) compared with the placebo group (20%). In addition, the proportion of patients with a greater than 50% improvement in chewing pain in the steroid group (90%) was significantly higher than that in the placebo group (<40%).	The results of this randomized controlled trial support steroid supplementation after TMJ arthrocentesis to achieve longer-lasting pain management and increased pain-free mandibular mobility.
2	Refai et al, 2011	Journal of Maxillofacial Surgery	By the end of the study, each group showed significant improvement in TMJ pain on palpation and number of locking episodes and insignificant improvement in clicking sound. With the exception of the MMO, there were no statistically significant differences throughout the study intervals between the active and placebo groups. The active group showed a significant reduction in MMO at the 12th week postoperatively. Differences compared with mean baseline value remained significant at the end of the follow-up period. On the other hand, the placebo group showed an insignificant	Prolotherapy with 10% dextrose appears promising for the treatment of symptomatic TMJ hypermobility, 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 sizes and long-term follow-up is needed.

difference in MMO throughout the study periods. For the last 2 intervals, the placebo group showed statistically significantly higher mean MMO values than the active group. By the end of the 12th postoperative week, the percentages of decrease in MMO were significantly greater in the active group.

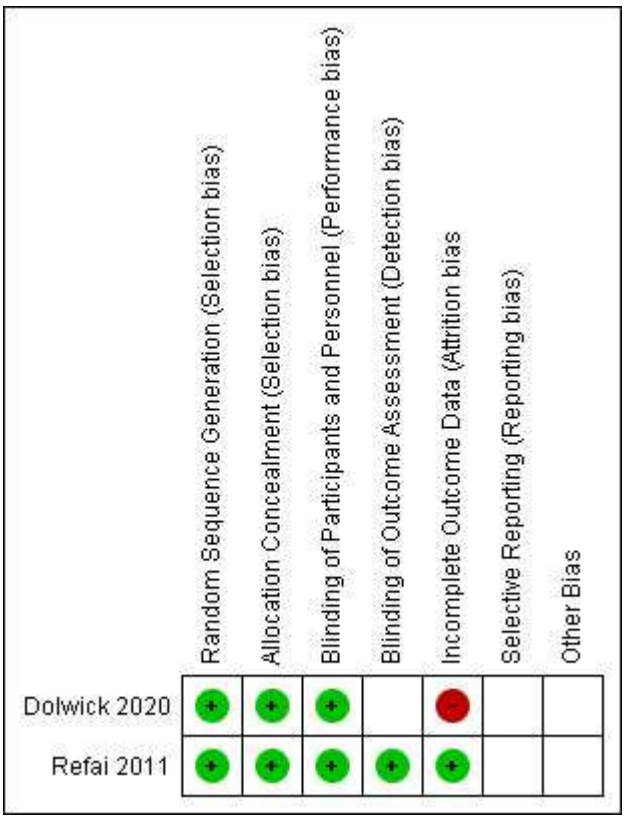


Figure 4: Risk of bias summary: Judgement about each risk of bias item for each included study.

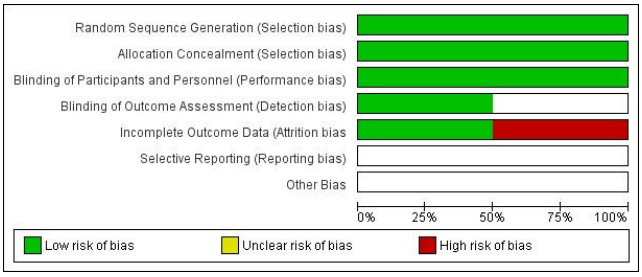


Figure 5: Risk of bias graph: Judgement about each risk of bias item presented as percentage among included studies.

DISCUSSION

The purpose of this systematic review was to identify the efficacy of prolotherapy and arthrocentesis for management of TMJ disorders was first described in the scientific literature in 1937.The first published article on prolotherapy, short for "proliferation injection therapy" and now also known as regenerative injection therapy (RIT), focused on treating the TMJ. The basic principle of prolotherapy is to inject a substance that will cause a low-grade inflammatory process within the joint, drawing in fibroblasts that strengthen the attachments of tendons and ligaments. The process stabilizes the joint, improves the range of motion in a hypomobile joint, helps prevent dislocation in a hypermobile joint, and relieves pain.

The face and TMJ are highly innervated and sensitive areas. Injections in this area must be as atraumatic as possible. To this end, we routinely use a 30-gauge, one-inch needle. We also use a dextrose solution whenever possible, as it causes less post-injection soreness than fish oil or pumice, and pumice is difficult to express through a 30-gauge needle. Compounding pharmacies can provide pre-mixed solutions, but we mix our solutions directly in the syringe. This consists of drawing up 0.75mL of 50% dextrose, 0.75mL of bacteriostatic water, and 1.5mL of 2% lidocaine into a 3-mL syringe for each TMJ. Using a 25-gauge needle to draw up the solutions speeds the process, then the needle is changed to 30-gauge and the syringe is shaken and the air expressed. The result is a dextrose concentration of approximately 12.5%. The 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.

Since TMJ disc displacement usually is anterior, our priority is to accomplish repair of the extended or torn posterior disc attachment. We locate the posterior joint space by cleansing the skin immediately anterior to the ear with alcohol and palpating the lateral pole of the condyle as the patient opens and closes. The target is the depth of the depression that forms immediately anterior to the tragus of the ear as the condyle translates forward and down. This can be marked with a washable felt-tip pen, if desired. Then, a disposable bite block is placed between the patient's anterior teeth to keep the patient from closing the condyle back into the fossa and onto the needle. The injection needle penetrates the skin at the marked point and is directed medially and slightly anteriorly to avoid penetration into the ear. Surface skin and connective tissue is deceptively thick in this location and the needle usually penetrates to, or nearly to, its full one-inch length before encountering the medial wall of the fossa. Slight negative pressure is exerted on the plunger to confirm that the needle tip is not in a vessel, even though no vessels of any size are expected to be encountered within the fossa. One mL of Prolotherapy solution is deposited here.

The second target is the anterior disc attachment, where the disc connects to the superior portion of the lateral pterygoid muscle. This muscle often is foreshortened or in spasm in cases of chronic disc displacement. Injecting the Prolotherapy solution here can strengthen the tendinous attachment of this muscle to the disc at the same time the anesthetic component anesthetizes and elongates the muscle, which can allow the disc to reposition itself over the condyle and often produces an immediate reduction in TMJ clicking. We locate this target area at the same time we palpate the location of the posterior joint space, note the location of the slight depression just anterior to the condyle when the mouth is closed, and mark this point with washable ink. Marking this point before injecting the posterior aspect of the joint is advisable, as it becomes much more difficult to palpate this depression after the posterior joint recess has been injected. For this injection, the bite block is removed and the patient is instructed to close gently, moving the condyle back into the fossa. We insert the needle at the marked point, again directing the tip medially and angulated slightly anteriorly to, or nearly to, its full one-inch length. Aspiration is performed and another 1mL of Prolotherapy solution is injected here.

Most TMD patients have some chronic masseter tension and pain with resultant strain on its attachment to the zygomatic arch. The third mL of Prolotherapy solution is used to address this problem. We palpate the masseter attachment along the inferior border of the zygomatic arch at the same time that we palpate and mark the posterior and anterior aspects of the condyle, and mark the area of the masseter that is most tender to palpation. Asking the patient to clench the teeth makes the masseter stand out, and the area that is most rigid to palpation is usually the most tender as well. The patient is told to relax the jaw, and the final mL is injected directly into this area, again at or near the full one-inch length of the needle.

The injection sites are wiped with alcohol, which removes the washable ink as well, and a pulse is taken for the medical record and to confirm that the patient has relaxed and is ready for discharge.

Our standard program is to repeat the injections three times, at two-week, four-week, and six-week intervals. This totals four injection appointments over twelve weeks. We palpate the joints for pain and noise, and palpate the affected muscles for pain, at each appointment. We also measure the range of jaw motion interincisally and record all these findings. Patients typically report some improvement after the first injection appointment but often have some increased discomfort shortly before the second appointment. The following appointments generally produce more benefit, quieter joints, and symptom relief without rebound. We expect the healing process to continue for at least twelve more weeks and schedule a final recall three months out.

Dextrose is a corn product and must not be used in patients with a corn allergy. Also, an alternative local anesthetic must be used in patients who are allergic to lidocaine.

At the one-inch depth of needle penetration, the areas described above have no major blood vessels and intravascular injections are not a significant risk with this technique, especially if aspiration is performed before each injection. Some authorities have stated that the lumen of a 30-gauge needle is too small to admit red blood cells, but clinical experience in injecting other, more vascular areas has shown that blood can easily be drawn up through this small needle. On rare occasion, the local anesthetic will diffuse forward and partially paralyze the lower eyelid. When this happens, it is immediately apparent and the patient is told to make a conscious effort to blink that eye frequently for the next hour or so, until the anesthetic effect diminishes, to lubricate the eye and prevent a corneal abrasion. Fair-skinned patients may display some minor bruising for a day or two but this is more common if the operator has difficulty locating landmarks and moves the needle laterally after insertion. The most common side effect is a temporary change in the dental occlusion. Until the 2mL of injection solutions dissipates from the joint, which may take one to four days, the condyle will rest lower in the fossa and the posterior teeth may not fully occlude. It is important to warn the patient that this is likely, and to be careful to chew food carefully and thoroughly before swallowing.

CONCLUSION

TMJ hypermobility is a debilitating disorder. However within the limitations of this review there is evidence that the concomitant use of prolotherapy with arthrocentesis may be superior in the management of TMJ hypermobility as compared to their individual use. The authors suggest formulation of well-designed randomised controlled trials to formulate a step ladder like treatment protocol for the management of TMJ hypermobility. This will help to achieve optimum amelioration of the quality of life of the individual.

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