Prolotherapy - A venturing Treatment for Temporomandibular Joint Disorder

Sandeep Vankdoth¹, Shailender Reddy Adamala², Harshavardhan Talla³, Nimma Vijayalaxmi⁴, Gopaladas Madhulatha⁴
¹Post Graduate Student, Department of Oral Medicine and Radiology, Meghna Institute of Dental Sciences, Nizamabad, Telangana, India, ²Professor & Head, Department of Oral Medicine and Radiology, Meghna Institute of Dental Sciences, Nizamabad, Telangana, India, ³Reader, Department of Oral Medicine and Radiology, Meghna Institute of Dental Sciences, Nizamabad, Telangana, India, ⁴Senior lecturer, Department of Oral Medicine and Radiology, Meghna Institute of Dental Sciences, Nizamabad, Telangana, India

Prolotherapy, a regenerative injection therapy. Has been used to relieve joint pain and stabilize injured joints. Since the 1930s, this technique is used to strengthen and rejuvenate weak tendons, ligaments and also resolves the joint laxity, as a result patient’s problems with discomfort, pain and loss of function are resolved. This is done after identifying the areas of weakness by injecting naturally occurring therapeutic agents which stimulate the healing process by provoking the acute inflammatory response including the influx of stem cells which promote repair of damaged tissues. This low grade inflammatory response is temporary at the site of injection which synthesizes collagen and strengthens the cartilage by promoting fibroblasts. Growth factors are also produced at the site of injection which restarts the healing process that is never completed effectively. This article reviews the history of prolotherapy and its applications in dentistry.

**Keywords:** Proliferative therapy, Regenerative injection therapy, Sclerotherapy, Temporomandibular disorders, Tendinopathy

**INTRODUCTION**

Temporomandibular joint (TMJ) disorder (TMD), a commonly used term to describe disorders causing pain and dysfunction of TMJ. TMD includes the causative agents of facial pain, headache and tinnitus, ear pain, but it is difficult to obtain a effective treatment.¹ Symptoms commonly associated with TMD include pain at the TMJ, orofacial pain, chronic headaches and ear aches, including hyper- and hypo-mobility, locking of the jaw, dysfunction of the jaw, clenching or talking difficulty, clicking sounds while opening and closing of the mouth, but still some people have problems using their jaws without any pain.² It is the challenging for the practitioners to provide effective treatment in individuals suffering from chronic pain and while resorting for treatment that may complicate the problem and results in more suffering and disability.³

**DEFINITION**

Prolotherapy, as defined by Webster’s Third New International Dictionary, is “the rehabilitation of an incompetent structure, such as a ligament or tendon, by inducing the proliferation of cells.” The word “Proles” means growth. Prolotherapy injections cause proliferation or stimulation of growth of new, normal ligament and tendon tissue.⁴

Prolotherapy practice involves injections in the ligament and tendon insertions with a proliferant that stimulates proliferation of fibrous tissue, to repair and stabilize the fibro-osseous junction. Of late, in 2007, Reeves defined prolotherapy as, an injection of growth factors or growth factor production stimulants to grow normal cells or tissue.⁵

**JOINT PHYSIOLOGY**

As the tendons and ligaments flex to certain extent, they do not accept significant stretch in the strict meaning of the word. The fibrous tissue elongation can only be accomplished by rupture of a portion of the inelastic collagen fibers within the tissue. Ruptures can occur at any bony interface, which is penetrated at an oblique angle by fibrous strands. The resultant hypermobility of the injured joint allows excessive strain on the sensory nerves, that is felt as joint pain as a result of nociception at the fibro-osseous junction (FOJ). One example of this type of injury is an automobile collision, where shearing forces result from rapid differential acceleration of musculoskeletal components, as large amounts of vehicular kinetic energy is dissipated through the bodies of the vehicular occupants in fractions of a second. Concentration of stress at the FOJ and flexion of the fibrous strands make the FOJ particularly susceptible to rupture. Hyperfunction and para function are

**Corresponding Author:**
Dr. Sandeep Vankdoth, Department of Oral Medicine and Radiology, Meghna Institute of Dental Sciences, Nizamabad - 503 002, Telangana, India.
E-mail: mids.omr@gmail.com
also capable of causing tendon and ligament rupture and elongation, over a longer time span.

Collagen generally heals incompletely and elastin does not heal at all (tendon and ligament constituents). Therefore, ligament rupture can be defined as a permanent injury. Continuous function on injured joints complicates and aggravates the injury. The TMJs present with a particular concern, as it is difficult or impossible to immobilize the joint, except with surgical inter maxillary fixation bars and wires that hold the teeth in firm contact. Even with the teeth in contact and without chewing, swallowing of saliva happens approximately 600 times each day with 60 pounds of force applied to the jaw. Bruxism may increase the force level to 250 pounds. This force can account for the common observation that TMJ injuries worsened with time and continued use of the injured joints.

**HISTORY**

Hippocrates treated athlete’s shoulder instability by initiating healing through inflammation and strengthening of the capsule of the shoulder, by a red-hot needle 2500 years ago. In the late 1900s before surgery became available, injections of irritant solutions were performed to repair TMJ dysfunction. The promotion of healing in early attempts was called as “sclerotherapy,” implying formation of scar. In the 1930’s Louis W. Schultz, described the strengthening method of the TMJ capsule by irritant solutions. Often, to stop permanently the clicking, pain, and hypermobility of the TMJ joint a series of 3-5 injections were given.

**Solutions used in Prolotherapy**
The agents used in prolotherapy are of four types. They include osmotic agent, inflammatory mimetic, chemical irritant and physical irritant.

Osmotic agent about 12.5% of dextrose solution is commonly the used osmotic agent which is prepared by diluting 50% dextrose with 1% methyl paraben as a preservative, water, and lidocaine. It helps in the prevention of iatrogenic infection. One part of 50% dextrose; two parts of 1% lidocaine; one part of bacteriostatic water is used. Dextrose is a corn product and should not be used for patients who are allergic to corn. Dextrose along with a very small amount of local anesthetic and saline is very effective and is the cheapest.

**Inflammatory Mimetic**
Sodium morrhuate mimics the activity of intracellular inflammatory agents, which attracts the macrophages, granulocytes to the injection site acting as an inflammatory mimetic, which is derived from fatty acids in the fish oil.

**Chemical and Physical Irritant**
They act either by foreign body reaction or by cell wall damage/alteration by attracting macrophages and granulocytes to the injection site. Phenol and pumice flour serves as the chemical and physical irritants.

Platelet-rich plasma (taken from your own blood and concentrated), autologous blood and some other chemicals can also be used as proliferent solutions (Table 1, Figures 1 and 2).

**Technique**
The preferred position of the patient for this technique is supine or reclined posture, to provide stability to head

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**Table 1: Classification of proliferant solution and mechanism of action**

<table>
<thead>
<tr>
<th>Irritants</th>
<th>Phenol - P2G (phenol, glycerin, and dextrose)</th>
<th>Directly alkylate the proteins on the surfaces of cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particulates</td>
<td>Pumice</td>
<td>Attract the macrophages</td>
</tr>
<tr>
<td>Osmotic shock agents</td>
<td>Hypertonic dextrose (12.5-25%)</td>
<td>Act by dehydrating cells at the injection site</td>
</tr>
<tr>
<td>Chemotactic agents</td>
<td>Sodium morrhuate, cod liver oil</td>
<td>Attract inflammatory cells</td>
</tr>
<tr>
<td>Growth factors</td>
<td>RBC-rich plasma</td>
<td>Stimulates proliferation</td>
</tr>
<tr>
<td>RBC: Red blood cell</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Figure 1:** Proliferant solutions (www.charmaustin.com)

**Figure 2:** Injection site for the proliferants (www.practicalpainmanagement.com)
and to decrease the risk of syncope. The head is turned to the opposite side away from the injection site. Before administering injection, the anatomic landmarks are marked. The procedure consists of drawing up 12.5% of 50% dextrose, 0.75 mL of bacteriostatic water and 1.5 mL of 2% lidocaine into a 3 mL syringe for each TMJ. As the condyle translates forward and down the depression that is formed immediately anterior to the tragus of the ear is the target area for injection. A disposable bite block is placed between the anterior teeth to keep the patient from closing the condyle back into the fossa. The needle is penetrated at the marked point and to avoid the penetration into the ear it is directed medially and slightly anteriorly. Slight aspiration is done to confirm that the needle tip is not in a vessel, and 1 mL of solution is deposited.

The second target is an area, where the disc connects to the superior portion of the lateral pterygoid muscle, which is often in spasm in chronic disc displacement. Strengthening of the tendinous attachment of the muscle to the disc is achieved by injecting the solution. The anesthetic component of the solution allows the disc to reposition itself over the condyle and often produces an immediate reduction in TMJ clicking. A schedule of 12 weeks is performed at an interval of 2, 4 and 6 weeks. 

**Mechanism**

The biological process of wound healing is initiated by inflammation.

The three types of prolotherapy are:
1. Growth factor injection prolotherapy: Injection of a growth factor that specifically begins growth of a certain cell line (example: erythropoietin).
2. Growth factor stimulation prolotherapy: Injection of certain substances causes the body to produce growth factors. Example: Non-inflammatory dextrose (10%).
3. Inflammatory prolotherapy: The inflammatory signals that result from solutions have a growth factor stimulation effect, but they cause a more vigorous response. Example: 12.5-25% dextrose, sodium-morhuate-containing solutions and phenol-containing-solutions. It is an inexpensive medical technique for stimulation of the natural wound healing cascade.

**Indications for Prolotherapy**
1. A tendinous or ligamentous injury.
2. Pain in the joints under load during function.
3. Failure of oral appliances.
4. In refractory cases where conservative management have failed.
5. Patients in whom surgical management is not possible.
6. To enhance recovery as an adjuvant to other treatment procedures such as oral appliances.

**Contraindications**
Allergy to the components of prolotherapy solution, an active state of infection, patient on anticoagulant medication a healing disorder, a condition associated with excessive bleeding, e.g. hemophilia. A malignant condition, existence of parafunctional habits, local abscess, bleeding disorders, septic arthritis.

**Potential Complications**
Post-injection complications likely result from faulty injection technique than from the proliferant solutions. However, before administration of any medicament, the patient must be screened for allergy to any of the injected substances.

With TMJ prolotherapy, some of these potential complications include
1. Discomfort during the procedure,
2. Temporary anesthesia that may extend as far as the eye and cause ptosis
3. Extravasation with external bleeding and/or visible facial bruising
4. Anxious patients occasionally report dizziness and are

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**Frequency of Injection**

Early prolotherapy injections were given at weekly intervals, but there was no evidence of benefit from more frequent injections. A common prototypical schedule is to inject at 2nd, 4th, and 6th-week Intervals, over a total of 12 weeks. Fibrous tissue proliferation may continue as long as several months following the injections.
at risk of syncope, which can be minimized by supine positioning of the patient during the procedure.\textsuperscript{15,14}

\textbf{Side-Effects}

After injection of the proliferent solution into the articular space, condyle and mandible inferiorly, which produces a temporary posterior open bite. This change in occlusion along with the local anesthetic effect incurs a risk that the patient may bite the tongue or buccal mucosa unknowingly. The occlusal changes may be permanent. Nausea, bruising light-headedness, treatment stiffness from injection seldom lasts more than 48 h, infection, pneumothorax, temporary tingling or numbness, a temporary increase in pain.\textsuperscript{15}

\textbf{Post injection Problems}

Specific postinjection instructions include:

1. Asking the patient to take semisoft diet until the posterior occlusion reestablishes, usually in 2-3 days, and to avoid rubbing, scratching, or irritating the anesthetized zone.
2. Eye drops may be necessary in cases of ptosis, for a few hours or until the eyelids regain motility.
3. Speech may be altered until the anesthetic effect subsided.
4. Since prolotherapy effects are dependent upon re-establishing a localized inflammation, ice and anti-inflammatory medications must be avoided for at least several weeks after the injections.
5. Acetaminophen and opioid analgesics may be prescribed for the post-injection discomfort and to help manage coexistent pain disorders.
6. A signed informed consent form is advisable to the patient.

\textbf{Future Prospective}

In the future the chemotactic factors and polypeptide growth factors produced by genetic engineering technology will become available for use, by recruiting the fibroblasts directly to an injured ligament by avoiding the discomfort of an inflammatory response.\textsuperscript{16,17}

\textbf{CONCLUSION}

Prolotherapy is a treatment method that provides a long-term solution rather than just palliation prolotherapy is a low-risk injection technique that uses the body’s self-healing mechanisms to improve structure and function by strengthening ligaments and tendons. Prior to resorting to long-term narcotic therapy or surgical intervention prolotherapy can be considered in appropriate patients. Although very less data is available on this modality and many studies are in the seminal stage, prolotherapy may yet be considered, a safe and effective treatment for TMJ pain in the future.

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