Introduction
There are various causes of TMD such as disc degeneration, dislocation or erosion of surfaces of the condyle, fossa and articular eminence. The first-line approach for temporomandibular joint pain management usually includes resting the jaw, relaxing the jaw muscles, jaw exercises as recommended by a physiotherapist, eating a soft diet and ultimately surgery. Hence to seek out other alternative treatment like prolotherapy is not unusual for patients suffering from TMD. The principle on which prolotherapy works is that “injection of a specialized solution into weakened and injured ligaments, tendons or joints.”

The term prolotherapy was coined by George S. Hackett in 1950s from Latin word “prolo” which means “offspring” and thus we get the word “proliferate” which means “to grow rapidly”. Reeves has defined prolotherapy as “an injection of growth factors or growth factor production stimulants to grow normal cells or tissue.” Webster’s New Collegiate Dictionary defines prolotherapy as “the rehabilitation of an incompetent structure, such as ligaments or tendons, by the induced proliferation of new cells.”

The principle on which prolotherapy works is that “injection of prolotherapy solution at the sites of pain and weakness stimulates the natural healing mechanism of the body to repair and rebuild the injured tissue into more stronger and less painful structure than before.”

History
In the 5th century B.C., Hippocrates used prolotherapy for treating dislocated shoulders of soldiers on the battlefields with red-hot needle cautery to stabilize the joint. Dr. George Heaton in 1832, used the same concept for treatment of hernias, varicose veins and hemorrhoids, known as sclerotherapy, because the injection sclerosed or fibrosed the area. The technique of sclerotherapy was expanded by Earl Gedney in 1936 by injecting into temporomandibular joints. The concept of tendon pathology and ligament laxity was expanded to chronic musculoskeletal pain by George S. Hackett in 1939. Dr. George S. Hackett and his main student, Dr. Gustav A. Hemwall promoted prolotherapy for many years and the technique practiced by them became known as “Hackett-Hemwall technique” of prolotherapy. Various studies have been documented in literature that have given positive results for the use of prolotherapy in temporomandibular joint pain.

Table 1: Review of few studies that have shown significant effects of prolotherapy for temporomandibular joint pain.

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Outcome Measures</th>
<th>Results</th>
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<tbody>
<tr>
<td>Roy V Hakala et al</td>
<td>26 adults</td>
<td>TMJ pain, clicking</td>
<td>Pain and clicking disappeared in 45% of the patients</td>
</tr>
<tr>
<td>Ross A Hauser et al</td>
<td>3 Males 11 Females</td>
<td>Pain intensity, Range of motion, Disability, Quality of life</td>
<td>50% reduction in pain, improved range of motion, 72% reduced disability</td>
</tr>
<tr>
<td>Roy H et al</td>
<td>3 Adults</td>
<td>TMJ pain, clicking, headache</td>
<td>Clicking dissipated, pain decreased</td>
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Technique of prolotherapy
In prolotherapy technique, either a single injections or a series of injections are given at the site of pain, most of the times diluted with a local anesthetic. In order to achieve maximum ef-
fect of treatment with prolotherapy 2 to 6 treatment sessions are required over a period of 2-12 months. According to the standard protocol non-steroidal anti-inflammatory drugs should be restricted 1-2 days before treatment and 10-14 days after treatment. Post-injection intake of aspirin or any other anti-inflammatory drugs to relieve discomfort should be avoided. Active movements of the injured area enhance the healing of the ligament injury and hence it is advocated.1

**TMJ prolotherapy**

TMJ prolotherapy consist of injection of prolotherapy solution into the joint and the fibro-osseous junction of the ligament and capsular attachments on the zygomatic arch, mandibular neck and condyle. The aim of TMJ prolotherapy is basically to improve the stability of the temporomandibular joint by increasing the capsular and ligament strength.1

Since face and temporomandibular joint are highly innervated and sensitive areas, injections in these areas should be atraumatic. Injections are given into the posterior and anterior joint spaces which are marked after cleansing the skin anterior to the ear and palpating the lateral pole of the condyle while opening and closing the jaws.

**Figure 1a:** Palpation of TMJ fossa posterior to translated condyle

**Figure 1b:** Intra-auricular palpation of TMJ

The depth of the depression that forms anterior to the tragus of the ear as the condyle moves forward and downward is the target of the injection. This point is marked with pen.

**Figure 2:** Marked injection sites

A disposable bite block is then placed in the patient’s mouth between anterior teeth to keep the mouth open and prevent the condyle from closing back into the fossa and onto the needle. The needle is directed medially and slightly anteriorly and inserted at the marked point to avoid penetration into the ear. The prolotherapy solution is deposited here.2

**Figure 3:** Angle and depth for injection of posterior joint space

The anterior disc attachment, where the disc connects to the superior portion of the lateral pterygoid muscle is the second target. This target area is located at the same time when the posterior joint space is palpated, i.e., the location of the slight depression just anterior to the condyle when the mouth is closed, and this point is marked with washable ink. It becomes much more difficult to palpate this depression after the posterior joint recess has been injected, hence this point should be marked before injecting the posterior aspect of the joint.5

**Mechanism of action**

Injection into the injured structure leads to stimulation of healing process. Therefore, to understand the mechanism behind prolotherapy, basic knowledge of healing process is necessary.11 Inflammation is an essential component of soft tissue healing as it initiates the process of healing, which is followed by proliferative stage in which there is proliferation of fibroblasts, endothelial cells and myofibroblast and the new tissue that ultimately results after the remodeling stage looks and functions very closely to the original tissue before injury. Since NSAIDS has the ability to inhibit the healing response, they are contraindicated during prolotherapy, whereas prolotherapy re-initiates the inflammatory process.6

Although the exact mechanism of action for prolotherapy has not clearly been established, but the three most commonly used prolotherapy solutions in clinical practise have been hypothesized to act via three different pathways, i.e., hypertonic dextrose acts by osmotic rupture of local cells, phenol-glycerine-glucose (P2G) acts by local cellular irritation, and morrhuate sodium acts by chemotactic attraction of inflammatory mediators-and sclerosing of pathologic neovascularity associated with tendinopathy. Another possible mechanism suggested is the potential of prolotherapy to stimulate the release of growth factors that favours soft tissue healing.7

**Types of Prolotherapy**8-10

Growth Factor Injection Prolotherapy: In this type of prolotherapy, growth factor i.e. a complex protein, is given in injection which specifically begins growth of a certain cell line, for example erythropoietin. This type of prolotherapy is currently in early stages of study for sprain (fibroblast growth), strain and arthritis
(cartilage cell growth) and will substantially advance in the near future. However, it will be a more expensive treatment option than the other two types of prolotherapy.

Growth Factor Stimulation Prolotherapy: In this technique, growth factor stimulant, for example non-inflammatory dextrose (10% or less) is given in injection. Human cells produce growth factors such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factor-beta (TGFβ), basic fibroblast growth factor (bFGF) and connective tissue growth factor (CTGF), even when exposed to 0.3% dextrose.

Inflammatory Prolotherapy: In this type of prolotherapy, solutions such as 12.5%-25% dextrose, phenol-containing solutions and sodium-morrhuate containing solutions are given through injections that causes activation of the inflammatory cascade to produce growth factors. It is likely to be the most cost effective form of prolotherapy in the future as it stimulates the body’s own natural wound healing cascade and hence is unexpensive.

Growth Factors
- Epidermal growth factor (EGF)
- Platelet-derived growth factor (PDGF)
- Transforming growth factor beta (TGFβ)
- Basic fibroblast growth factor (bFGF)
- Connective tissue growth factor (CTGF)
- Growth Factor stimulating agents which act by attracting the inflammatory cells.

Particulates
Particulates are irritants of a different type, for example pumice flour. These are small particles of size approximately one micron, which act by attracting the macrophages. As the macrophages reach the injection site and ingest the pumice granules, these macrophages secrete polypeptide growth factors which ultimately results in fibroplasias and new collagen deposition.

Osmotic Shock
Osmotic Shock is the main characteristic of this type of proliferants. Mechanism of action of these agents is dehydration of the cells at the injection site, as they causes a net flow of water into the injection site by removing water from living cells. Concentrated glucose, glycerine and zinc sulphate are some of the examples of osmotic agents.

Chemotactic agents
Sodium morrhuate, which is the sodium salt of the fatty acid component derived from cod liver oil, is the only member in this group of proliferants currently. It contains precursor to some chemotactic agents which act by attracting the inflammatory cells.

Growth Factors
Growth factor like RBC-rich plasma helps to stimulate proliferation.

Possible indications for prolotherapy may include one or more of the following:
- Knee osteoarthritis
- Low back pain
- Achilles tendinopathy
- Neck strain
- Shoulder dislocation
- Sacroiliac joint dysfunction
- Costochondritis
- Lateral epicondylitis
- Fibromyalgia
- Pain from whiplash injury
- Plantar fasciitis

Contraindications
Contraindications for patients to receive prolotherapy injections may include:
- Patient on anticoagulant medication
- Bleeding disorders
- Local abscess
- Known allergy to prolotherapy agent
- Acute infections such as cellulitis
- Septic arthritis
- Relative contraindications include:
  - Acute fracture
  - Acute gouty arthritis

Complications
Temporary change in dental occlusion is the most common side effect. The condyle rest lower in the fossa and the posterior teeth may not occlude fully; until the 2ml of injection solutions dissipates from the joint. Another complication can be seen as minor bruising at the site of injection for one or two days, especially in fair-skinned patients. One of the rare complications can be partial paralysis of the lower eyelid, which may occur when the local anesthetic solution diffuses forwardly.

Prolotherapy in India
Prolotherapy clinics in India are located in few cities which includes:
- Ahmedabad
- Coimbatore
- Gurgaon
- Kochi
- Mumbai
- New Delhi
- Noida

Conclusion
A long term solution is provided by prolotherapy unlike other treatment modalities which provides only palliation. As surgical intervention is considered as the terminal treatment option for TMD, it is appropriate to consider prolotherapy as an alternative treatment modality. Temporomandibular joint prolotherapy is being performed since more than 70 years and it still continues to demonstrate its effectiveness and safety over longer periods. Although many studies on temporomandibular joint prolotherapy are in seminal stages resulting in less data availability, it may become a safe and effective treatment option for temporomandibular disorder in future.