

A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PAIN RECEPTOR BLOCKING AGENT AND LUBRICATION SYSTEM ON PAIN IN CASE OF TEMPOROMANDIBULAR JOINT INTERNAL DERANGEMENT

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ABSTRACT

Examination of pain intensity after affected temporomandibular joint arthrocentesis and administration of pain receptor blocking agent or lubrication system in case of temporomandibular joint disorders with painful clicking and symptomatic temporomandibular joint. To compare between the effects pain receptor blocking agent and lubrication system on pain in case of temporomandibular joint disorders.

KEY WORDS: Clicking, temporomandibular joint, Arthrocentesis, painful temporomandibular joint, postoperative pain.

INTRODUCTION

A temporomandibular disorder involves different elements of the masticatory system despite being considered as a single disorder by many practitioners. It is a subgroup of craniofacial pain with problems that involve the temporomandibular joint, masticatory muscles, and associated head and neck musculoskeletal structures. Pain, limited or asymmetric mandibular motion and temporomandibular joint sounds are the frequent presentation of patients with temporomandibular disorder.

Currently management of temporomandibular disorders entail a combination of home self-care, counseling, physiotherapy, pharmacotherapy, jaw-appliance therapy, physical medicine, behavioral medicine and surgery. Structural anatomic pathology that is producing pain and dysfunction are usually treated by surgery. These surgical procedures may include; Arthrocentesis, arthroscopy, open arthroscopy and combined joint and reconstructive jaw procedure. Approximately 85 to 90% of temporomandibular disorder (TMD) constituting the vast majority of temporomandibular disorder whether articular

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or muscular that can be treated with noninvasive, non-surgical and reversible intervention. Surgical therapy may be considered, if the pain is substantial and the limitation of function is severe enough to interfere with daily life activities, and for patients with intra-articular disorders that don't respond to a reasonable course of non-surgical intervention – generally 3 to 6 months duration ^[1,2]. To treat temporomandibular joint pain and limited mouth opening, arthrocentesis is one of the minimally invasive techniques ^[3]. A consideration of the whole intra-articular situation requires, a comprehensive understanding. By counteracting the degeneration of tissues, arthrocentesis may act by allowing the elimination of hyper-viscus medium with catabolites and inflammatory cells ^[4].

Several drugs have been used intra-articularly in the temporomandibular joint of these drugs fentanyl significantly reduced pain intensity via intra-articular injection through post-operative pain control in comparison with intra-articular sodium hyaluronate injection after temporomandibular joint arthrocentesis. Morphine and Tramadol have been used intra-articularly with or without arthrocentesis for pain control postoperatively. Hyaluronic acid used in the treatment of temporomandibular joint disorders. Sodium hayluronate has been used in the form of injection with or without arthrocentesis for the treatment of internal derangement ^[23,24,33,37,38]. Determination of which has a better outcome whether injecting anti-inflammatory drugs or hyaluronic acid simultaneously with arthrocentesis to manage painful clicking temporomandibular joints, needed evaluation and this is the goal of the present study.

PATIENT AND METHODS

Twenty patients diagnosed with symptomatic painful clicking temporomandibular joint [3 males and 17 females] [group A involved one male and 9 females while group B involved 2 males and 8 females] were included in the study. Participants were randomly allocated into two equal groups using the flip coin method. In the group (I) "Curavisc"

patients received arthrocentesis with 50 cc lactate Ringer's solution and injected at the end with 20mg /2ml of (Curavisc) at the end of the surgical session. While in the group II (Epicotil) patients received arthrocentesis with 50 cc lactate Ringer's solution and injected at the end with 20mg/2ml of Epicotil at the end of the surgical session. All the selected patients should meet the definitely outlined inclusion criteria. No radiographic evidence supporting the case has been taken. Diagnosis is based on the clinical setting only.

The following measurements would be taken from each patient with the aid of manual divider and metallic ruler in addition to manual digital palpation of the involved affected musculoskeletal structures.

The following measurements had been recorded pre / post-surgical session:

MIO (maximal inter-incisal opening with the help of metallic ruler in mm) measuring MIO from upper-incisal edges to lower incisor edges. Pain Score of the affected and involved temporomandibular joint together with the muscular structures, measured on Verbal Numerical Rating Score (V.N.R.S).

From 0 no pain experience

TO 10 PAIN experienced at its worst level

The following muscles will be examined with the help of manual digital pressure including: Masseter. Temporalis. Medial Pterygoid. Lateral Pterygoid. Sternocleidomastoid Muscle. Trapezius Muscle. The affected temporomandibular joint was surgically lavaged (washed out) with 50cc. Lactated Ringer's solution with the help of Shepard cannula and at the end of the surgical session, either of the 2 drugs Curavisc or Epicotil was injected intra-articularly at amount of 20mg/2ml. All patients will be followed-up at the following time intervals. 2,4 and 12 weeks. Each patient involved in the comparative study will receive post-operative instructions that should be followed strictly. In case of severe postoperative pain, anti-oedematus agent and analgesics were prescribed to the participants.

All demographic data, post arthrocentesis clinical (subjective symptoms), V.N.R.S scores and injected drug effects were statistically analyzed.

Medications prescribed

- 1- Anti-eadematous and Ant-iinflammatory trade name (Alphintern) [chymotrypsin 300 E.M.U 14 micro ketals Trypsin 300 EA.U (5 micro ketals, Amoun pharmaceutical company.
- 2- Analgesic 400 md ibuprofen company Abott

Patients' selection

The 20 patients (3 males and 17 females) were allocated to one of the two groups using the flip coin method.

Group I: Curavisc®*, received arthrocentesis with 50 cc lactated Ringer's Solution* and injected at the end with 20mg/ 2ml of Curavisc at the end of the surgical session.

Group II: Epicotil® ** received arthrocentesis with 50 cc lactated Ringer's Solution*** and injected at the end with 20mg/ 2ml of Epicotil at the end of the surgical session. The selected patients should meet the following inclusion criteria:

Should not be below age of 18 years old (i.e.; as the patient should have passed his/ her growth spurt, and the procedure did not cause any form of growth disturbance and, he/ she would withstand the procedure). Should be free of any systemic affecting conditions (i.e.; the patient should be ASAI/ASAI). Should not have any pathology in

* curavisc® sodium hyaluronate sterile solution for intra-articular injection Made in Germany. Manufacturer IDT BiologicaGmbH (Curasen, Benleux B.V.)

** Epicotil® Tenoxicam Anti-rheumatic and anti-inflammatory agent For I.M or I.V injection Manufactured by; Egyptian International Pharmaceutical Industries CO.-E.I.P.I.Co.

*** Lactated Ringer's solution 500ml parental solution Manufactured by: Egypt Otsuka Pharmaceutical Co, S.A.E.

the affected temporomandibular joint other than (internal derangements, arthritis and arthrosis) (i.e.; temporomandibular joint pathology including cyst ankylotic masses, any mass lesions, Etc.). Should not undergo any open joint surgeries in the affected temporomandibular joint (i.e.; as the study objectives to treat via conservative surgical approach). Should not have taken any form of injection into the joint (i.e.; corticosteroids, local anaesthetics. botulinum toxin A, NSAIDs, opioids, etc.). The affected temporomandibular joint itself should be free from any chronic localized infection (i.e.; suppurating joint with sinus tract, etc.). The affected temporomandibular joint should be free of fractures as confirmed by patient's history, clinical examination; all patients should complain from painful clicking temporomandibular joint as confirmed by clinical setting only. No radiographic-evidence supporting the case has been taken; diagnosis is based on clinical setting only. All patients were subjected to in-depth explanation of their condition and informed consent has been signed from each patient describing the conditions. The surgical procedures and the outcomes noticed post-surgery. The following measurements would be taken from each patient with the aid of manual divider and metallic ruler in addition to manual digital palpation of the involved and affected structures. The following had been recorded: MIO (Maximal Inter-Incisor with the help of Metallic Ruler in mm). Pain score of the affected joint and involved muscular structures, on verbal numerical rating scale score (V.N.R.S) from 0 → no pain experienced, to 10 pain in its worst level). The muscles will be examined with manual digital pressure including: Masseter. Temporalis. Medial pterygoid. Lateral pterygoid. Sternocleidomastoid.

Trapezius. Lateral excursions towards contralateral side from affected side in mm. Degree of mandibular protrusion in mm. Presence absence of deflection/shift. All these will be recorded preoperatively in the diagnostic chart.

Surgical procedure

Under complete aseptic conditions, the surgery was performed. The surgical set includes:

Surgical drapes. Surgical gowns. Surgical towel clamps. Surgical containers. Complete Aseptic Technique.

Topical anesthesia (xylocaine 2% gel) or (Emla cream). Chlorohexidine mouth wash (Hexitol 2%). Localanesthetic agent Mepicaine (1,20,000). Levonordefrin as a vasoconstrictor)-or Articaine 3% (1:100,000 adrenaline). Dental aspirating syringes. Long needles 24,26 gauges. Alcohol 70%. Injected drug substance –lubrication system “Curavisc”. Pain receptor blocking agent “Epicotil”. I. V set. Plastic syringes of different sizes. Shepard cannula. Sterilized gauze “2x2”. Sterilized foil sheets. Surgical set. Each patient was draped according to the oral and maxillofacial surgery protocol “Complete aseptic technique. Squeezed gauze with Vaseline was inserted in the patient’s external auditory canal [Cotton placed in the patient’s ear]. The patient was asked to rinse his/her mouth with chlorohexidine 2% mouth wash. All the temporomandibular joint area was swabbed with chlorohexidine 2% M.W. The affected joint is palpated manually with the index finger by asking the patient to open and close the mouth several times to feel the position of the condylar head. Once the condylar head was felt, it is marked with surgical plastic pencil. Attempting at locating the depression in front of the condylar head



Drawing of the condylar head

by asking the patient to open and closing the mouth again several times. Once located, the depression is marked with plastic surgical pencil. To anaesthetize the joint, we use auriculotemporal nerve block type anesthesia (ATN block) technique only.

Technique for Auriculotemporal Nerve Block

Pre-auricular area is prepared taking routine aseptic measures. Usually 27 or 26-gauge needle is inserted through the skin just anterior to the junction of the tragus and the ear lobe, the needle is then advanced behind the posterior aspect of the condyle in an anteromedial direction to a depth of 1 cm where the 1.5 ml of anesthetic solution is deposited after aspiration. If the true source of pain is the joint, then the pain should be eliminated or decreased within 5 minutes.^[32] Fig.12 Drawing of the condylar head. The affected area was then, checked for anesthesia by checking numbness of the following areas: Ear pinna, Temple area, Ear lobule, and the affected joint area. If all these areas, were numbed so, auriculotemporal nerve block anesthesia was profound. During the surgical procedure, the Shepard cannula device was used. It provides the following advantages:

Providing 2 entries with 2 portals with one single needle blade puncture “single lumen”. Being hygienic (minimum or absent trauma to the patient and tissues if inserted correctly through 2 attempts only). The patient was told that he or she would feel pressure only during cannula placement inside the joint space. There are 3 markings (graduations) on the cannula blade that ensues complete cannula entrance into the joint space upon its placement (complete placement by pushing the cannula through the 3 markings).

Technique of cannula placement and entrance inside the joint space

Again, palpate the condylar head through previously drawn marking, feeling the depression in front of the condylar head with the non-dominant hand index finger, with the dominant hand place the Shepard cannula in horizontal direction, from

inferior-medial-superior direction until it snugly fit inside the joint cavity. Ensure the cannula correct placement by asking the patient to open and close the mouth several times, the Shepard cannula will move up and down with the mouth movement denoting its correct placement. Then connect the I.V set in one of the cannula portals from one end and to the plastic syringe loaded with lactated Ringer's solution from the other end.



Shepard Cannula Placement

Observe, the free movement of the lactated ringer's solution from the other entry of the cannula in the form of drops collected in surgical kidney dish placed under the patient's chin and/ or fountain like motion of the solution from the other entry. During the lavage procedure, the patient was asked to move the mandible in the following directions:- Open/ closing, Lateral excursions and Protrusion-several times by manual manipulation of the mandible to break out fibrous adhesions present inside the joint cavity and ensure free mandibular movement. During lavage procedure, the index finger of the non-dominant hand will be placed all around the affected joint by compressing the joint to minimize flare up and fluid extravasation. The temporomandibular joint was lavaged with the minimum amount of lavage solution (50 cc). At the end of the arthrocentesis, one of the above-mentioned two drugs will be injected inside the joint cavity according to patient allocated group. Placing the index finger of the non-dominant

hand on the opened entry of the Shepard cannula during injection. Upon injection, of pain receptor blocking agent inside the joint cavity, the patient will feel severe pain for 3-5 seconds inside the temporomandibular joint space, then the pain would subside completely.

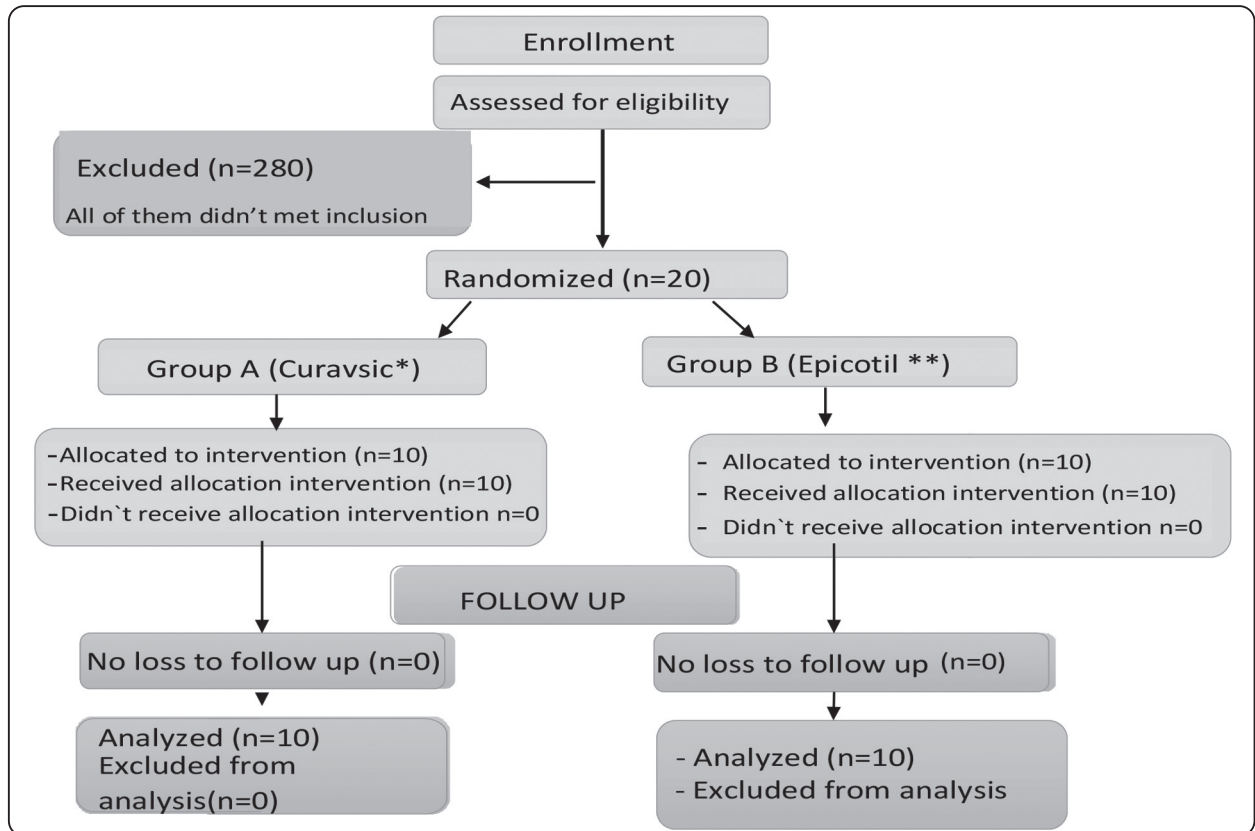
At the end, the patient is asked to open and close eyes to check for facial nerve integrity. Each patient would be given the following instructions post-operatively: Cold ice packs to be placed on the area of surgery for the following next 6 hours (20 mins on, 10 mins off). EATING soft crushed food for the next month; Keep mandibular movement to the minimum, avoiding aggressive jaw movement, avoiding shouting, in case of yawning, place the hand under the chin; and avoid eating gums. All patients were prescribed the following post operatively: Alpha chymotrypsin in the form of tablets. NSAIDs in the form of tablets (minimum amount). Both used for only one week. All patients will be followed up in the following time interval 2, 4, and 12 weeks. Post-operative data will be recorded in the diagnostic chart.



Fountain like action of the lavage solution during arthrocentesis

RESULTS

From 300 enrolled patients, 20 patients were included in the study. The flowchart of the patients through the study followed the CONSORT flow diagram is presented in the above Figure.



CONSORT flow diagram of the study

Demographic Data:

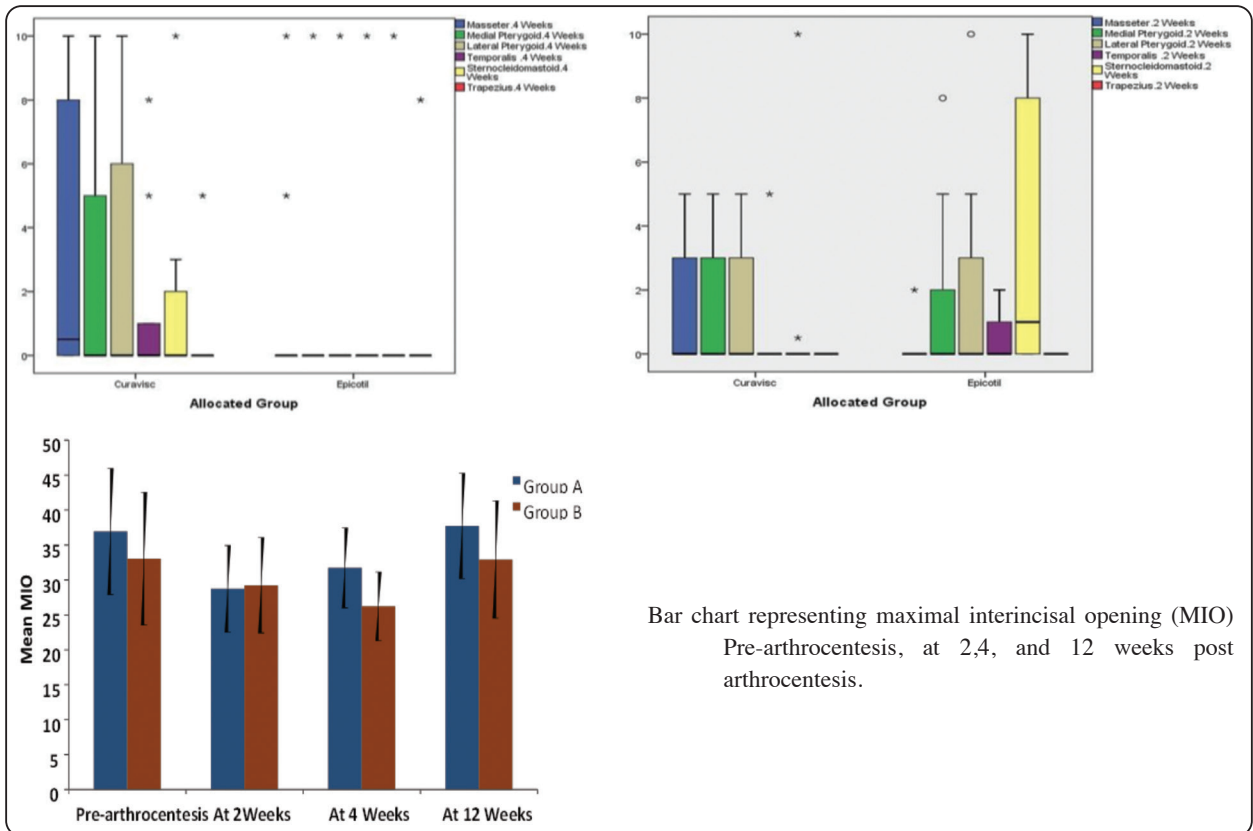
Data for age and gender are presented in Table (1) and Figures (22. 1a, 1b). 20 patients with temporomandibular Joint disorders participated in this study (3 males and 17 females). They were randomly divided into two equal groups (**Group A:** Curavisc; **Group. B:** Epicotil).

Age and Gender distribution in both groups:

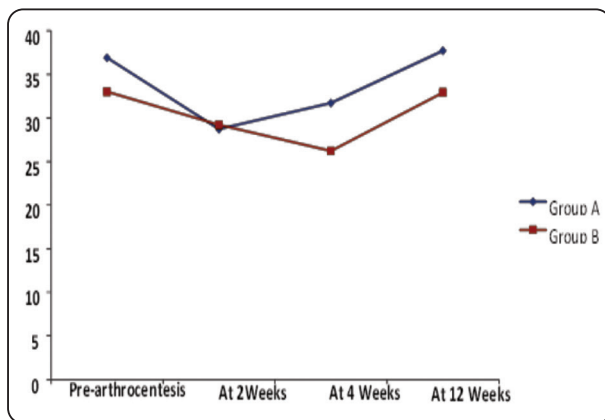
The mean age of patients in Group (A) was 26.4±6.6 years and range (18-40) while in Group (B) was 30.3±14.4 years and range (18-66). There was no significant difference between mean age values between both groups (p=0.447). Gender distribution in Group (A) involved one male and 9 females while in Group (B) involved 2 males and 8 females. There was no significant difference between both groups for gender (p=1.000). Results showed that age and gender distribution were non-significant in both drug groups. Epicotil drug (Group B) was significant in

alleviating joint tenderness while Curavisc (Group A) was non-significant in alleviating affected temporomandibular joint tenderness. Epicotil drug (Group B) was significant in alleviating affected muscle tenderness being reduced over time interval 2, 4, and 12 weeks than Curavisc (Group A) was non-significant in alleviating affected muscle pain.

Epicotil drug (Group B) and Curavisc drug (Group A) was both significant in mouth opening being increased overtime intervals. Protrusion of the mandible in postero-anterior direction was non-significant in both drug groups. EPICOTIL DRUG (Group B) and CURAVISC DRUG (Group A) both were not significant in terms of presence of deflection /shift during mandibular full range of motion measured at regular time intervals follow up in 2, 4, and 12 weeks post-surgical session. Epicotil drug (Group B) is much more significant than Curavisc (Group A). In lateral excursions improving free mandibular movement towards right side.



Bar chart representing maximal interincisal opening (MIO) Pre-arthrocentesis, at 2,4, and 12 weeks post arthrocentesis.



A collecting graph of the MIO between the 2 groups Pre- arthrocentesis and at 2,4, and 12 weeks Post arthrocentesis.

DISCUSSION

Temporomandibular joint is a synovial joint. Like any other synovial joint in the human body it can be washed-out (i.e. lavaged). Any synovial joint surgery is accompanied by post-operative pain. It has been hypothesized that any drug injected

intra-articularly inside the joint space act on specific drug receptors inside the temporomandibular joint to manifest its action on the pain inside the temporomandibular joint. Infiltrating drug substance into the joint cavity space after the surgical intervention has been one of the most widely used management modality for pain control postoperatively and to improve joint function. So, many intra-articular drug substances are used intra-articularly inside the synovial joint space to control pain, providing post-operative analgesia, to improve joint function, to minimize rescue supplemental analgesic consumption by the patient and to minimize and/or treating clicking of the patient. Of these substances are local anesthetic agents, steroids, celecoxib, prolotherapy, clonidine, fentanyl, neostigmine, tenoxicam, bupivacaine, levobupivacaine, tenoxicam, ketamine, ketamine-levobupivacaine, sodium hyaluronate, Botulinum toxin-A, and opioids. Since patient with pain after temporomandibular joint arthrocentesis

(lavage) cannot return to his/ her work early as delayed discharge and rehabilitation is one of the main consequences of post-operative pain. One cause of continuing pain is synovial impingement as stated by DAWES et al ^[32].

Patients were seeking treatment for the main complaint of pain and limitation of mandibular movement and clicking as concluded by Heba et al ^[24] while in this study patients were seeking treatment for the main complaint of pain and clicking. Diagnosis of temporomandibular disorders, which is the mainstay for evaluation of the disorder in order to establish proper treatment, was based upon MRI, according to A. Sipahi et al ^[33], whereas diagnosis in this group of patients was based on clinical setting only. Large number of patients was involved in the study to evaluate the effect of the used drugs properly in a comparative manner, so twenty patients with painful clicking joint underwent arthrocentesis using Hartman's solution (lactated Ringer's) solution in this study, whereas thirty patients with temporomandibular joint internal derangement underwent arthrocentesis using normal warm saline according to Arati et al ^[20].

This number of patients should be grouped so, Pushkar et al ^[34] in temporomandibular joint study divided patients into 2 groups based on type of anesthesia (sedation Vs General) and location of surgery (office Vs Hospital), while in this study, patients received local type anesthesia and the surgery was done in an office based setting. The pain assessment tool is of great importance for pain score determination. In this group of patients, pain score assessment tool was verbal rating numerical scale (VRNS), whilst Arati et al ^[20] in temporomandibular joint study assessed pain by using (VAS). Joint tenderness to palpation, associated muscle tenderness, Maximal interincisal opening (MIO), mandibular protrusion, presence and /or absence of deflection and/ or shift, lateral excursions toward both sides were documented pre-

operatively and post operatively in this group of patients, while Arati et al ^[20]. In temporomandibular joint study, assessed maximum inter-incisal opening (MIO), joint noises, and mandibular deviation were documented preoperatively and post-operatively. Patient position during surgery is important in order to accomplish the procedure in a suitable manner. For the patient positioning during the surgery, it was standardized by Mehra et al ^[34] in temporomandibular joint surgery study, where patients who received I.V sedation, were all positioned in an upright to semi upright sitting position in a routine surgical/dental chair in the office. Similarly, in this group of patient where all patients positioned in an upright to semi-upright sitting standardized position in a routine surgical/dental chair in the office. Another group of patients in a study by Mehra et al ^[34], in temporomandibular joint study was placed in a supine position on a standard O.R table.

The aseptic technique is of great value in the surgical procedure due to its benefits as it produces patients' comfort and decreases anxiety also it decreases the risk of surgical infection. In a study by Arati et al ^[20] under aseptic precautions, arthrocentesis was performed, another study by G. Dimitroulis et al ^[35] the ear and pre-auricular skin over the temporomandibular joint are prepared with topical antiseptic solution, and the area was isolated with sterile drapes, the same as for in a study by S. Matsa et al ^[36], the same is done in this group of patients complete aseptic technique according to the oral and maxillofacial protocol was used. The anesthesia type is an important factor in the procedure through which patient might not feel any pain or discomfort during the surgical procedure Mehra et al ^[34] performed the procedure under I.V sedation in an office setup or under G.A by using a secure airway (hospital) while, a group of patients received, in a temporomandibular joint study by Mehra et al ^[34] I.V sedation, another group in the same study received G.A. In a study by Mehra et al ^[34] after a successful I.V access, sedation was

initiated with midazolam and fentanyl, followed by propofol infusion through a pump, if a patient was combative intravenous ketamine was supplemented. Another group in the same previous study received general anesthesia in a hospital setting as follows, after midazolam administration in the preoperative area, fentanyl and propofol were used to induce general anesthesia and a secured laryngeal mask airway (LMA) was placed in all patients. G.A was maintained throughout this group of case, using sevoflurane inhalation anesthesia, while in this study for temporomandibular joint, the surgery was done by using local type anesthesia in the form of auriculotemporal nerve block only using commercial Mepicaine or Articaine 3%. Another study by G.Alpaslan et al, ^[37] performed arthrocentesis under local type anesthesia where the anesthetic agent was 3% carbocaine. In a study by Grossman E. et al ^[38] in temporomandibular joint surgery, used 2% lidocaine to block the auriculotemporal nerve followed by deep posterior branch and masseteric nerve branch, whereas S. Tozoglo et al ^[39] used in temporomandibular surgery local anesthesia by injecting it in a ring block fashion, in the form of local infiltrations given subcutaneously around the joint at the site of needle arthrocentesis puncture sites. There were several techniques used during temporomandibular joint arthrocentesis. In a study by G. Dimitroulis et al ^[35], 2 needle arthrocentesis technique has been used to wash-out the joint space, while in this study, Shepard cannula was used having the following advantages over the conventional 2 needle technique in that: Being hygienic. Less traumatic to the patient (i.e., single puncture). Decreased risk of infection (provided complete aseptic technique followed). Decreased risk of facial nerve injury (only single puncture). Decrease operation time. Patient feels comfortable. Decrease post-operative morbidity. In a study by K.-U. Rehman et al ^[40] stated that Shepard cannula has been used for more than 10 years for over 100 procedures with no complications". Arati et al. ^[20],

in a study, the mean pre-operative pain was high and the pain decreased at 1 year follow up interval post-operatively, while in this group of patients, joint tenderness score was statistically significant post-operatively being reduced overtime at 2, 4 and 12 weeks follow-up intervals. In a study by Arati et al, ^[20] mean maximal mouth opening increased at 1-year follow-up interval post-operatively, whereas in this group of patients maximal inter-incisal opening increased at 2, 4, and 12 weeks follow-up interval period.

Many drugs have been used intra-articularly after the surgical procedure, Mehra et al ^[34], used at the end of the surgical procedure, 5mg of steroid (kenalog) in combination with 5 ml of 0.5% plain Marcaine per joint were flushed through the ports prior to needle retrieval. Local side effects of the intra-articular injection of gluco-corticosteroids such as destruction of articular cartilage, infection, and progression of already recognized joint disease, have been reported.

However, the cause of these deleterious effects had not been fully explained and adequate controls are lacking, while in this study either of the two drugs Curavisc (20mg/2ml) or Epicotil (20mg/2ml) was administered intra-articularly through one of the two ports prior to needle retrieval. In the same study by Mehra et al ^[34], post-surgical instructions and prescriptions included the use of a flat maxillary splint, soft diet, and self-administered (range of motion exercises) of the lower jaw.

While in this group of patients, each one would be given the following instructions post - operatively:- Cold ice packs to be placed on the area of surgery for the following next 6 hours (20 minutes on, 10 minutes off). Eating soft crushed food for the next month; and Keeping mandibular movement to the minimum, avoiding aggressive jaw movement, avoiding shouting, in case of yawning place under the chin.; and 4- Avoiding chewing gum, all patients were prescribed the following postoperatively:-

Alpha chymotrypsin in the form of tablets. NSAIDs in the form of tablets (minimum amount). Both were used for only one week. Post-operative complications after the surgical procedure could occur. In a study by Grossman E. et al^[38] in temporomandibular surgery study, there may be temporary affection of the zygomatico temporal branch of the facial nerve caused by local anesthesia injection or the edema itself or post-surgical trauma, while in this study no facial nerve affection has been reported. For the drug substance injected intra-articularly after the surgical procedure, opioids agonists have powerful anti-inflammatory properties when injected intra-articularly in a study by Heba et al^[24] and by exerting its action in the periphery via opioids receptors, while in this study, when injecting pain receptor blocking agent and/ or lubrication system, they had a powerful anti-inflammatory properties and they exert their action in the periphery via their corresponding receptors.

Another study by S. Tozoglu et al^[39] claimed that the anti-inflammatory effects of intra-articular corticosteroids on synovial tissues have been well documented. They were useful for alleviating pain, swelling, and dysfunction in patients with inflammatory diseases of the joints such as rheumatoid arthritis and gouty arthritis, as well as in those with primarily non-inflammatory joint diseases such as osteoarthritis. There were many glucocorticoid preparations such as cortisone, hydrocortisone, betamethasone, methylprednisolone acetate, triamcinolone acetonide, and triamcinolone hexacetonide,

Methylprednisolone and triamcinolone (40mg/1 ml) preparations are long-acting and may be preferable. In a study by S. Tozoglu et al^[39], suggested intra-articular injection of morphine (10 mg in 1 ml) as a long-acting analgesic in patients with continuing pain in the temporomandibular joint, and evaluated the analgesic effects of bupivacaine, fentanyl, morphine, and saline after arthrocentesis. They found that both bupivacaine (1 ml of 0.5% solution) and fentanyl (25 mg in 1 ml) relieved pain for only

8-12 h, saline (placebo) had no analgesic effect, and morphine (10 mg) was most effective and relieved pain for several days or weeks. Although fentanyl is a more potent analgesic agent than morphine, they thought that it was more rapidly eliminated from the joint capsule because of its high lipid solubility, while in this study lubrication system and pain receptor blocking agent had been used after joint arthrocentesis.

In a study by, MANFREDINI et al^[41] 5 weekly with 2-needles arthrocentesis plus low M.W.H.A and 5 weekly single-needle arthrocentesis plus low M.W.H.A. had been performed, while in this study, only a single session arthrocentesis plus lubrication system or pain receptor blocking agent was used. Low doses of intra-articular morphine injected on the completion of knee joint surgery can produce post-operative analgesia via activation of local opioid receptors in the knee joint as recorded by Oral EG et al^[42]. The phenomenon of post-operative pain as a consequence of many surgical procedures have also been well documented and applied to spine surgeries by EISENACH et al^[45]. A multimodal analgesia approach has become a standard of care in the current pain practice, for example addition of NSAIDs [non-steroidal anti-inflammatory drugs (Epicotil) to opioids for post-operative analgesia can reduce opioids consumption by about 20-30% by Oral EG et al^[42]. According to the current study, no survey has been made for the evaluation of Epicotil in temporomandibular joint intra-articular injection, post joint lavage. Tenoxicam (Epicotil), and NSAIDs is extremely suitable for postoperative pain analgesia, it has demonstrated both analgesic efficacy and anti-inflammatory effect on the upregulated expression of prostaglandin E2 [PGE2], interleukin (IL)-6, and interleukin 8 (inflammatory mediators) in response to surgery by DAWES et al^[32] and by Arati et al^[20]. This is probably important, as IL-6, IL-8, and PG2 has been implicated in the pain pathogenesis. Addition of tenoxicam (Epicotil) to morphine has

a great effect in controlling post-operative pain rather than using morphine alone in spine surgery the same as for in this research for temporomandibular joint surgery, where Epicotil controls pain and provide relief. Opiates such as morphine tramadol have peripheral and central analgesic effects, and there is evidence of opiate receptors presence at terminals of afferent peripheral nerves.

Administration of opiates, tenoxicam, and any drug used intra-articularly post-joint surgery might provide analgesic effect due to the presence of this drug receptor at the terminals of afferent peripheral nerves inside the joint space by H. Hosseini et al ^[43]. The peripheral effect of narcotic like analgesics could explain why the intra-articular administration of morphine and tramadol could provide a satisfactory pain relief state as well as fewer systemic adverse effects by Oral EG et al ^[42]. Regarding morphine and tramadol availability and accessibility in the market, as long as these drugs remain inaccessible to the large majority of people around the world, patients will not be able to derive the health benefits to which they are entitled by H. Hosseini et al, ^[43] as it remains impractical to control pain due to its limited access ^[43]. Concerning the route of drug substances administration, thorough pre-clinical testing of central nervous system (CNS) therapeutics includes a consideration to routes of administration and agent bio-distribution in assessing therapeutic efficacy. Between the two major classifications of administration, local vs. systemic, systemic delivery approaches are often preferred due to ease of administration. However, systemic delivery may result in suboptimal drug concentration being achieved in the CNS, and lead to erroneous conclusions regarding agent efficacy. Local drug delivery methods are more invasive, but may be necessary to achieve therapeutic CNS drug levels as proved by Serwer et al ^[44]. The same is applicable to the temporomandibular joint where the drug is administered locally to address pain not systemically (e.g. via I.V. route). So, to

prove that morphine or any drug administered intra-articularly to provide for postoperative analgesia following knee surgery acted peripherally locally not (Centrally) at various time intervals, post drug venous blood samples were taken to determine plasma levels of the used drugs and its primary metabolite, namely morphine-3-gluconide and morphine-6 glucuronide measurable amount of morphine glucuronide were found in the plasma of some patient whereas morphine-6 glucuronide was detected in only other patient. So, the plasma levels of the injected drugs were lower than that regarded for sufficient post-operative analgesia in all but few patient, (i.e. The drug titer is inside the joint space, indicating a possibility of peripheral analgesia as stated by H. Hosseini et al ^[43]). No need for venous blood samples to assess plasma concentration of the injected drugs, as these drugs are injected locally inside the joint cavity as concluded by H. Hosseini et al ^[43]. In study by Eisenach et al ^[45] proved that Epidural morphine sulphate has proven analgesic efficacy and superiority over systemically administered morphine for improving postoperative pain.

The same is for as joint surgery administration of opiates, tenoxicam, any drug used intra-articularly post joint surgery might provide analgesic effect due to the presence of this drug receptor (e.g., opiate receptors) at the terminal of afferent peripheral nerves inside the joint space. Morphine has lower lipid solubility, which account for its slow rate of absorption into the circulation from a low blood flow to the articular area. It has been proposed that glucosylation of morphine intra-articularly may produce morphine-6- glucuronide which has a longer half-life that may account for more prolonged effect ^[43] according to H. Hosseini. Furthermore, this study was intended to provide local analgesic effect by injecting the drug locally than systemically (intravenously), without producing any systemic adverse effect for the drug being used.

CONCLUSION

Addressing the injected drugs locally inside the joint “intra-articularly” proved good prognosis on the following time intervals 2, 4, and 12 weeks post surgically. **EPICOTIL DRUG (PAIN RECEPTOR BLOCKING AGENT)** was much more reliable and proved much more significant result and excellent prognosis than **CURAVISC (LUBRICATION SYSTEM)** While clicking shift/deflection disappeared with both drugs.

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