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Comparative Study of Arthrocentesis with Intra Articular Injection of Hyaluronic Acid versus Arthrocentesis Alone In Temporomandibular Dysfunction

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Abstract

Purpose: To compare the efficacy of intra-articular injection of hyaluronic acid (HA) with arthrocentesis versus arthrocentesis alone as a treatment modality in patients with temporomandibular joint dysfunction.

Materials and methods: A prospective randomized clinical study was done on forty subjects of 18–60 years of age reporting with TMJ dysfunction between December 2016 to July 2018 .Subjects were randomly allocated to study (arthrocentesis followed by intra-articular injection of sodium hyaluronate) and control groups (arthrocentesis

alone) and assessed for clinical parameters including masticatory efficacy, pain at rest and mastication, functional limitation on movement, subjective efficiency of treatment, tolerability of treatment, assisted and unassisted maximum mouth opening. Subjects were followed up postoperatively at 2 weeks, 1 month,3 months and 6 months and statistical analysis was carried.

Results: Single puncture arthrocentesis (SPA) in both groups showed increased incidence of TMD in age group of 20-30 years and female predilection. Statistically p value of >0.05 was noted in either group in terms of

masticatory efficacy, pain, functional limitation, mouth opening and subjective efficacy. Intergroup analysis showed no statistically significant difference in clinical parameters and with none of the patients presenting with any complications at the end of 6 months using paired t test.

Conclusion: In both groups, assessment of patient's subjective and clinical parameters showed improvement but there was no statistically significant improvement in arthrocentesis with sodium hyaluronate group when compared with arthrocentesis alone. Future studies with longer follow up, newer agents and larger cohort are suggested for overall comparative assessment of efficacy.

Keywords: arthrocentesis; functional improvement; sodium hyaluronate; TMD.

Introduction

Craniofacial region is a unique skeletomuscular complex from anatomically hosting master gland brain to functionally enabling basis of human interaction in terms of facial expression. One among its several uniqueness is Temporomandibular joint (TMJ) which is a compound diarthrodial synovial joint articulation of squamous part of temporal bone, condylar head, and its associated musculature. Functionally it comprises of two articulating surfaces with a specialised fibrous tissue the articular disk separating the joint into upper and lower compartments dictating and limiting the freedom of discontinuous articulation between two bones. 1,3,4,20

Temporomandibular disorder (TMD) is a collective term used for a number of clinical problems that involve the masticatory muscles, temporomandibular joint (TMJ), and /or associated structures with cardinal signs and symptoms of pain in the TMJ and muscles associated with it, limited mouth-opening along with joint sounds. TMD is a multifactorial disorder with multiple treatment modalities having a positive impact on patient's symptoms with

literature suggestive of management ranging from conservative treatment in form of soft diet ,correction of the occlusal interferences, analgesics, muscle relaxants, splint therapy to surgical management in refractory cases which comprises of minimally invasive surgical procedures like arthroscopy, arthrocentesis to advanced procedures like disc plication, repositioning, discectomy, condyloplasty and debridement of glenoid fossa. ^{2,3,5,17,23,25,32}

Arthrocentesis of the temporomandibular joint was introduced in 1991 by Nitzan et al. Since then it has gained widespread popularity among practitioners to treat TMDs. It is considered by many as the first-line surgical treatment for patients who do not respond to conservative treatment. 4,7,10,11,12,14,36,37,38 The procedure involves irrigation of the upper joint space and manipulation of the joint, which releases adhesions and thereby improves function. The conventional procedure uses 2 needles inserted through 2 separate puncture sites and these 2 needles must triangulate in the upper joint space to be efficient. One of the needles serves for the inflow of the lavage solution and the other as the outflow. 5,6,7,10,38 The procedure is technique sensitive with the blind insertion of the second needle often challenging to surgeon losing the right place during the procedure. So it may need manipulation and sometimes even multiple punctures often leading to extra-articular leak of the lavage solution which decreases the intra-articular pressure required for lysis of the adhesions causing post-operative pain and discomfort.7,4,9,16,38

With evolution of modification in technique researchers have ever since then tried various agents in arthocentesis with hyaluronic acid ,morphine, ketamine, dexamethasone, tenoxicam,

botulinum to name a few. 8,34,35,39,40,42,45. Apart from providing symptomatic relief studies have showed potent

anti-inflammatory action with added analgesic effect with use of NSAIDS especially Etodolac.^{34,35} With literature on TMJ disorders supporting the efficacy of hyaluronic acid injections to improve and restore normal lubrication in joints with disc position abnormalities and satisfactory inflammatory/degenerative processes. The present study aims to prospectively evaluate the effectiveness of arthrocentesis using SPA followed by intra-articular injection of sodium hyaluronate and arthrocentesis alone in temporomandibular joint dysfunction.

Materials And Methods

A prospective randomized clinical study was conducted in the department of Oral and Maxillofacial Surgery, AJ Institute of Dental Sciences after attaining ethical clearance from Institutional review board between December 2016 to July 2018 (IRB.No.) on forty patients clinically diagnosed with temporomandibular dysfunction. An informed consent was taken for partaking in the study for those who fulfilled the inclusion criteria. The cohort were randomly allocated to control (Group A) and study group (Group B) comprising of 20 subjects each. Study group comprised of subjects who underwent arthrocentesis using SPA followed by intra-articular injection of sodium hyaluronate and control group who underwent arthrocentesis with ringers lactate alone.

Inclusion criteria

- Age group: 18 to 60 years.
- More than 3 episodes of TMJ dysfunction refractory to non-surgical treatment.
- Clinically diagnosed with temporomandibular dysfunction.
- Chronic episodes of joint clicking, popping.
- Episodes of restriction in jaw movements/mouth opening (≥3).
- Informed consent for participation in study and follow up.

Exclusion criteria

- Patients allergic to agents used for the procedure.
- Systemic osteoarthritis disease.
- TMJ dislocation.
- Previous history of trauma to TMJ.
- Previous surgery of the affected joint.
- Systemically compromised patients (ASA 3, 4, 5).
- Pregnant and lactating women.

History was noted followed by clinic examination of TMJ for study parameters (Table 1) by the same maxillofacial surgeon preoperatively and postoperatively at an interval of 2 weeks,1 month, 3 month and 6 months. Patients received 3 therapeutic doses at day zero, 2 weeks and 1 month and parametric assessment was carried out.

Surgical Technique

The patients were placed in a semi-seated position with head turned to the unaffected side. A cotton pledget was placed in the auditory meatus to prevent entry of irrigation fluid. Pre-auricular region was prepared with appropriate antiseptic solution (Povidine iodine 10%). Holmlund-Hellsing canthotragal line (a straight line from the midpoint of the tragus to the lateral canthus) was marked using methylene blue and the point of puncture of the single needle device is located 10mm on this line (from the middle of the tragus) and 2mm below the canthotragal line.

Auriculotemporal nerve block was performed using 2% lignocaine hydrochloride with 1:200000 adrenaline. After five minutes, the anaesthetic solution was injected subcutaneously at the area of puncture and the needle was slowly redirected anteriorly and superiorly down to the zygomatic arch and the peri-capsular region was infiltrated. The upper compartment of the joint was penetrated and slowly distended with the anaesthetic agent to minimize discomfort. Through the marked puncture site, the single puncture device was directed anteriorly and

superiorly until contact is made with the zygomatic arch with close contact still maintained with the bone in this area and single needle is slid in the upper compartment (Figure 1.a, 1.b).

Group A: Arthrocentesis With Ringer Lactate Solution (Figure 2.a).

The patients were asked to open the mouth and to shift the mandible to the opposite side to facilitate entry into the joint space. On entry to the superior joint space, 200 mL of Ringer's lactate is used to flush the joint under optimum pressure. During the lavage, the patient was asked to mobilize the mandible as much as possible, as well with the surgeon passively manipulating the joint to aid in the release of adhesions.

Group B: Arthrocentesis With Intra-Articular Injection Of Hyaluronic Acid (HA-KEM) (Figure 2.b)

Arthrocentesis is performed as described in the previous group and following which 0.5ml-1ml intra-articular injection of hyaluronic acid infused into the joint through one of the portal while occluding the other with a finger.

The device was completely withdrawn and a small sterile dressing was applied at the puncture site. Following procedure all patients were advised to restrict the joint movement, and soft diet for 1 week. Non-steroidal anti-inflammatory drugs (Tablet Etodolac) were prescribed for 5 days and followed up at an interval of 1 month, 3 month and 6 months. Comparative statistical analysis was carried out using paired sample students t test for intragroup and pooled students T test for intergroup respectively with p value of less than 0.05 considered statistically significant.

Results

In the study with subjects randomly allocated to study or control group majority of them in both the groups were in age group in the range of 20 to 30 years which was however statistically insignificant. Parametric assessment by the same examiner with baseline to each appointment during the treatment at an interval of 2 weeks, 1 month, 3 month and 6 month were suggestive of statistically significant difference at the end of 6 months in terms of clinical parametric assessment (Table 2, 3)(Figure 3.a-7). However, intergroup statistical assessment showed no significant difference but with well tolerated patient response in either groups and overall symptomatic improvement (Table 4).

Discussion

TMJ is unique in many respects, still subject to same disorders affecting other synovial joint and is second most common chronic musculoskeletal condition after chronic low back pain. 1,2,5 Temporomandibular disorders (TMD) represent a wide range of functional changes and pathological conditions affecting the TMJ itself, the associated musculature and ultimately all the other components of the oromaxillofacial complex. TMD occurs when there is a disturbance in the normal anatomic relationship between the articular disc and condyle that interferes with smooth movement of the joint and causes momentary catching, clicking, popping or locking. 5,6,8,44 Majority of subjects in both the groups were in the age group of 20-30 years accounting for 80% and 100% in group A and group B respectively however there was no intergroup statistical significance (p=0.054) which was in consonance in studies by other researchers. 1It is well established that TMD predominates in women and our study was in agreement with same accounting for 60% and 70% in group A and group B respectively with intergroup p value of 0.51.3

Over a period of time management of TMD ranges from conventional nonsurgical, non-invasive options ranging from biofeedback, modification of the diet, occlusal splints, physical therapy, pharmacotherapy, transcutaneous electrical nerve stimulation (TENS) to advanced surgical techniques in form of arthroscopy,

reconstruction arthroplasty (disk repositioning), meniscectomy, and repair of perforation of disk. 2,23,25,26,32,33

The effectiveness of viscosupplementation with sodium hyaluronate in humans for treatment of osteoarthritis such as knee, hip and shoulder long bones is scientifically proven but however efficacy of the same in TMJ was not dated till late 19th century. ^{30,31,48,49} This study was carried out individually to evaluate the synergistic effect of hyaluronic acid with arthrocentesis in comparison with arthrocentesis alone in the management of TMJ dysfunction.

The first thorough description of the indications, technique and therapeutic use of arthrocentesis dates back to 1592, when Fray Augustin Farfan described in his his work Tractado breve de medicina knee arthrocentesis. 48,49 Arthrocentesis of the temporomandibular joint was first described by D. W. Nitzan in 1991 as the simplest form of surgical therapy with the aim of washing out inflammatory mediators, releasing the articular disc and disrupting adhesions between the surface of the disc and the joint fossa by hydraulic pressure of the lavage solution. 4,6,8,13,36,38

Arthrocentesis of the temporomandibular joint is a minimally invasive method of treatment bridging margin between conservative and surgical therapy with main objective to wash out inflammatory mediators, break adhesions, eliminate pain and improve joint mobility. Arthrocentesis eliminates restrictions on the disc and lateral capsule to wash out micro debris resulting from the breakdown of the articular surfaces, to irrigate the joint by enzymes and prostaglandins and to stimulate the normal lubricating action of the synovial membrane. In addition, the presence of fibrous adhesions in the superior joint space limits normal translatory function of the disc condyle complex. 9,13,21,22,23,25,38,44

Murakami and colleagues offered the first systematic description of TMJ arthrocentesis, which they termed manipulation technique after pumping and hydraulic pressure. The conventional procedure used 2 needles inserted through 2 separate puncture sites which were triangulated in the upper joint space with one needle serving for the inflow of the lavage solution and the other as the outflow. 23,29,38 Debate exists regarding the use of appropriate lavage solution with literature suggestive of various agents with Ringers lactate, Sodium hyaluronate to PRP to mention a few. Shinjo et al. suggested that lactated Ringer's solution is better tolerated than isotonic saline solution for cells derived from human meniscus tissue. Zardeneta et al. recommended a free flow of 100 ml Ringer's solution because denatured haemoglobin and various proteinases were recovered in this fraction, whereas Kaneyama et al. suggested that 300-400 ml should be used to wash out bradykinin, interleukin-6, and proteins. 36,38,39,40,41,42,43,44,45,47

It is often recognized that the conventional procedure is challenging based on the fact of blind insertion of the second (outflow) needle may be technically difficult. Multiple punctures through the temporomandibular joint capsule are often necessary often leading to extra-articular leak of the lavage solution and decreases the intra-articular pressure required for lysis of the adhesions. ¹⁵ An increased risk of facial nerve damage exists when repeatedly attempting to introduce a needle into the joint space after an unsuccessful primary needle insertion. In such cases, the single-needle method appears to be very beneficial in preventing complications. ^{7,10,11} Hence, researchers have introduced techniques of gaining access to the superior joint space via a single puncture site making the procedure easier for the surgeon and comfortable for the patient.

Nardini et al in their study first outlined the technique of conventional two needle arthrocentesis and then proposed their new technique of single needle arthrocentesis. The use of a single and more stable needle limited the traumatism of the intervention thereby reducing patients discomfort in the postoperative period. A Rahal et al developed a new device where two 18- gauge needles 1.5 inches long are each bent 30 degrees toward their respective opening and welded together in a Y fashion with the openings facing outward describing it to be a fast and easy-to-perform procedure with good safety and minimal invasion. 7,10

Gunay Yapıcı-Yavuz, Goksel Şimşek-Kaya, and Hayri Ogul aimed to comparative evaluate radiologically and clinically the effect of intra-articular injection of methylprednisolone, sodium hyaluronate or tenoxicam following arthrocentesis with that of arthrocentesis alone in patients with non-reducing disc displacement and concluded that either arthrocentesis alone or arthrocentesis with methylprednisolone acetate or sodium hyaluronate or tenoxicam intra-articular injections are similarly effective and promising methods in the treatment of TMJ with non-reducing disc displacement.⁴⁷

Hyaluronic acid (HA) is a normal product of joint tissues that is continuously released into the synovial fluid that serves as a lubricant, anti-inflammatory and adjuvant pain reliever enabling activation of the tissue repair process in the cartilage, with a normalizing action on the synthesis of endogenous acid by the synovial cells. ^{9,13,22,25}Sodium Hyaluronate (SH) has been proposed as an alternative therapeutic agent which is high viscous, high molecular substance plays an important role in joint lubrication and protection of the cartilage. In physiological conditions, hyaluronic acid plays an important role in maintaining intra-articular homeostasis by favouring the elasticity and viscosity of the synovial fluid thereby acting as a shock absorber. It has been hypothesized that abnormalities of the joint lubrication system may play a role in the onset of

TMJ disorders, thus providing a rationale for the viscosupplementation with HA in patients with TMJ internal derangements and inflammatory-degenerative disorders. 9,41,44

Intra-articular injection of hyaluronic acid (HA) has recently become one of the favourite non-operative options for treating osteoarthritis and approved by the U.S. Food and Drug Administration in 1999. HA is a critical constituent of the healthy synovial fluid, which increases the viscosity of the synovial fluid and has a significant contribution to the joint homeostasis which facilitate gliding via layer formation on the cartilage and also soothes the pain and exerts an immunomodulatory effect on inflammatory cells. HA is acting as a shock absorbent to protect soft tissue from trauma. Besides, the function of protective effects on cartilage extracellular matrix have been reported by *in vitro* and *in vivo* studies, which could reduce the production and activity of pro inflammatory mediators and matrix metallo proteinases. 19,21,22

In this present study the 40 subjects who reported with history of pain and clicking sound of TMJ who underwent SPA with arthrocentesis alone and arthrocentesis with 1 ml hyaluronic acid significant improvement with respect to baseline levels were achieved in all outcome variables at end of 3rd month, however intergroup analysis was statistical insignificant in agreement with other studies. 14,18,44,46

On assessment of Functional limitation of jaw, our study is covenant to study by Machodo in showing no significant differences from baseline at end of 2 week and 1 month with mean value of 0.5(p=0.10 and 0.34). However at end of 3 and 6 months gradual improvement with mean score of 0.3 and 0.1 was noted respectively. The subjective efficacy of treatment was noted to improve with ascent of time with good subjective patient response of 2.7 and 2.8 respectively from baseline.

Intraoperatively both groups well tolerated the procedure with mean score of 1.6 and 2.1 respectively with statistically insignificant p value of thereby suggesting better patient compliance to SPA.

Interesting finding was noted was reported by Zardeneta et al wherein they conducted a similar study design and assessed both groups for symptomatic improvement in pain and checked for biomarkers. Significant symptomatic improvement was noted in both groups but decrease in biomarkers were noted in study group who received sodium hyaluronate. This suggested supporting evidence to anti-inflammatory properties of sodium hyaluronate and our study is in agreement with the same.⁴⁴

Nitzan hypothesized that persistent inability of the disc to slide as a result of extended pressure applied to the joint forces the synovial fluid away allowing the adherence of the disc to the posterior slope of the articular eminence which can be reversed by simple lavage thereby reestablishing normal maximal opening and our study is in agreement with the same. Our study showed increase in mouth opening and reduction in joint sounds in both the groups and highest was observed after 3 months thereby signifying need for longer follow-up for conclusive results. 6,24,37 None of the subjects in both groups presented with any complications thereby serving as a safe, economical therapeutic tool in refractory TMD cases.

Pain, joint tenderness and episodes of restriction in jaw movements was the most common clinical presentation in TMD. Combined treatment with arthrocentesis and NSAID is rational for an inflamed synovial joint in removing the inflammatory and associated mediators from the synovial space which alters the intra-articular pressure thereby reducing the synovial inflammation. ^{34, 35} Symptomatic improvement in pain was noted with use of Etodolac owing to its analgesic and anti-inflammatory action in agreement with other studies.

Arthrocentesis is a minimally invasive method routinely performed in day care basis with minimal complications in the treatment of TMD. The limitation of this study is limited sample size and non-blinded study. Thus, a study with large sample size and longer follow up is suggested for precise results.

Conclusion

The origin of arthrocentesis has become a subject of interest in the medical literature to provide symptomatic relief, especially in cases of traumatic synovitis. With passage of time researchers have studied use of TMJ arthrocentesis as a relatively less invasive alternative to reduce the inflammation in the joint space and to restore the function in TMD. In our study both the groups showed symptomatic improvement but statistically insignificant when compared with baseline. Future studies with longer follow up, newer agents and larger cohort are suggested for overall comparative assessment of efficacy.

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Legend Figures

Figure 1.a: Armamentarium



Figure 1.b: SPA needle



Figure 2.a: Arthrocentesis in control group (Group A)



Figure 2.b: Arthrocentesis in study group (Group B)



Figure 3.a: Clinical Unassisted mouth opening in Group A at 6 months (25 to 39 mm)



Figure 3.b: Clinical Unassisted mouth opening in Group B at 6 months (26 to 40mm)



Figure 4.a: Functional limitation on jaw movement

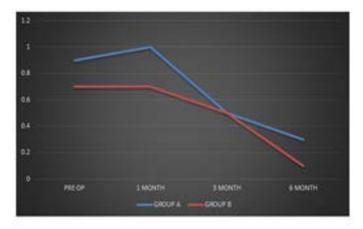


Figure 4.b: Masticatory efficiency

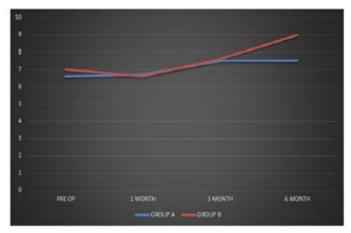


Figure 5.a: Mouth opening Unassisted (Group A)

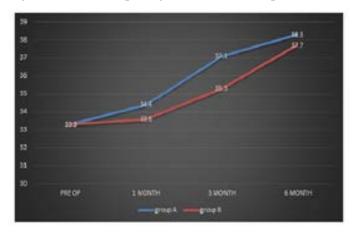


Figure 5.b: Mouth opening Unassisted (Group B)

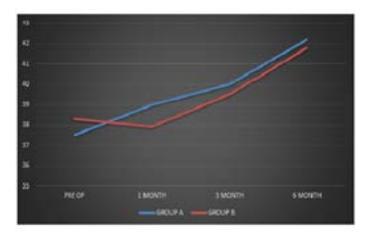


Figure 6: Pain at rest and function



PAIN AT REST

PAIN AT MASTICATION

Figure 7: Subjective efficacy in treatment



Table 1: Parameters for Assessment

1	Masticatory efficiency	Assessed by a visual analogue scale (VAS)							
		From o to 10, the extremes of which were eating only semi liquid food							
		and optimal masticatory efficiency of any kind of food.							
2	Pain at rest and mastication	Assessed by a visual analogue scale from 0 to 10.							
		$\begin{array}{ c c c c c c c c c c c c c c c c c c c$							
		No pain Mild, annoying Nagging, Distressing, Intense, Worst possible, pain uncomfortable, miserable dreadful, unbearable, troublesome pain horrible pain excrutiating pain pain							
		The extremes of which were no pain and pain as bad as the patient ever							
		experienced							
3	Functional limitation during	0- absent, 1 -slight, 2- moderate, 3 -intense, 4 -severe							
	usual jaw movement								
4	Subjective efficiency of	0- poor, 1- slight, 2- moderate, 3-good, 4- excellent							
	treatment								
5	Tolerability of treatment	0- poor , 1-slight, 2-moderate, 3-good, 4-excellent							
6	Maximum mouth opening	Non Assisted And Assisted In Millimeter							

Table 2: Intragroup Statistical Assessment (Group A)

	Parameter	Mean	SD	P value	
1.	Age	20-30 (n=16)			
2.	Gender (M :F)	8:12			
3.	Clinical Evaluation				
a.	Masticatory efficiency				
	-Preop	6.6	1.08	0.34	
	-1 month	6.7	1.16	0.001	
	-3month	7.5	0.97	0.001	
	-6 month	7.5	0.98	0.001	Significant
b.	Pain (at rest)				
	Preop	4.5	2.8		
	-1 month	4.3	3.02	0.34	
	-3 month	3	1.70	0.006	
	-6 month	1	0.67	0.001	Significant
c.	Pain(at mastication)				
	Preop	7.1	1.44		
	- 1 month	6.6	1.9	0.001	
	-3 month	6.6	1.25	0.001	
	-6 month	1	0.67	0.001	Significant
d.	Functional limitation during usual jaw movement				
	Preop				
	-1 month	0.9	0.74		
	-3 month	0.5	0.67	0.34	
	-6 month	0.5	0.53	0.10	
		0.3	0.3	0.005	Significant
e.	Subjective efficiency of treatment				
	-1 month	1.5	0.52		
	-3 month	2.4	0.7	0.003	
	-6 month	2.7	0.53	0.003	Significant
f.	Tolerability of treatment (Intra op)	1.6	0.7	0.18	
g.	Maximum mouth opening				
	Preop (Assisted)	37.5			
	-1 month	39	4.50	0.09	
	-3 month	40.3	6.2	0.001	
	1	1	1	1	<u> </u>

-6 month	42.2	4.9	0.001	Significant
Maximum mouth opening				
Preop (Non assisted)	33	4.85		
-1 month	34.4	5.62	0.14	
-3 month	37.1	4.72	0.001	
-6 month	38.3	2.83	0.006	Significant

Table 3: Intra Group Statistical Analysis (Group B)

	Parameter				
1.	Age	20-30(n=20)			
2.	Gender (M: F)	6:14			
3.	Clinical Evaluation				
	Masticatory efficiency				
	-Preop	7	0.94		
	-1 month	6.6	1.17	0.103	
	-3 month	7.6	1.43	0.17	
	-6 month	9	0.94	0.001	Significant
	Pain (at rest)				
	Preop	3.3	3.2		
	-1 month	3.2	3.11	0.68	
	-3 month	2.3	2.002	0.05	
	-6 month	0.7	0.95	0.05	Significant
	Pain(at mastication)				
	Preop	6.8	0.79		
	-1 month	6.3	1.16	0.138	
	-3 month	4.6	1.71	0.001	
	-6 month	1.2	1.62	0.001	Significant

Functional limitation during usual jaw movement				
Preop				
-1 month	0.7	0.67		
-3 month	0.7	0.48		
-6 month	0.5	0.53	0.34	
	0.1	0.32	0.02	Signi ficant
Subjective efficiency of treatment				
-1 month	1.3	0.48		
-3 month	2.2	0.79	0.007	
-6 month	2.8	1.13	0.008	Significant
Tolerability of treatment (Intra op)	0.7	0.7	0.18	
Maximum mouth opening(Non assisted)				
Preop				
-1 month	33.3			
-3 month	33.6	4.64	0.39	
-6 month	35.3	5.44	0.003	Significant
	37.7	4.16	0.003	
Maximum mouth opening				
Preop(Assisted)	38.3	5.51		
-1 month	37.9	6.19	0.4	
-3 month	39.5	5.03	0.008	
-6 month	41.8	3.53	0.006	Signi ficant

Table 4: Inter Group Statistical Analysis

	Masticatory efficiency		Pain(at rest)	Pain (at mastica		Function limitatio usual jav moveme	n during v	Subje efficie of treatm	ency	Toleral of treat (intra o	ment	Maximum opening (Non assis		Maximum opening (assisted	m mouth
	A	В	A	В	A	В	A	В	A	В	A	В	A	В	A	В
Mean	7.07	7.55	3.2	2.37	5.32	4.72	0.55	0.5	2.2	2.1	1.6	2.1	35.7	35	39.75	39.37
SD	0.5	1.05	1.61	1.20	2.9	2.53	0.25	0.28	0.62	0.75	2.1	0.87	2.43	2.02	1.99	1.75
P	0.44		0.4	14	0.	.78	0.8	80	0.8	6	0.18	3	0.8	0	0.7	9
value	ie															