

# COMPARISON OF EFFECTIVENESS OF PROLOTHERAPY AND CORRECTIVE EXERCISE PROGRAM VS PROLOTHERAPY AND ISOMETRICS STRENGTHENING ON PAIN AND FUNCTIONAL IMPROVEMENT IN SUPRASPINATUS TENDINOPATHY IN A TERTIARY CARE CENTRE

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<sup>A</sup> Study Design; <sup>B</sup> Data Collection; <sup>C</sup> Statistical Analysis; <sup>D</sup> Manuscript Preparation;

**Abstract Background** Regenerative injection therapies such as prolotherapy have gained importance in the recent years in non-surgical management of supraspinatus tendinopathy. The aim of the present study was to compare the efficacy of isometric rotator cuff strengthening versus corrective exercise program in the treatment of supraspinatus tendinopathy. **Material and Methods** Fifty patients aged 18–60 years were recruited with MRI diagnosed isolated supraspinatus tendinopathy or < 50% thickness tear and symptoms persisting for longer than 6 months. All patients were randomised into two groups: one prolotherapy with isometric rotator cuff strengthening exercise therapy (group ISE;  $n = 25$ ) and the other group also treated with prolotherapy injection followed by corrective exercise program (group CEP;  $n = 25$ ). Patients were examined at baseline, 3, 6, and 12 weeks. Improvement was assessed using a visual analog scale (VAS) for pain, and Constant Murley Score (CMS) for shoulder function. **Results** Significant difference ( $p < 0.001$ ) was found between the groups in the VAS and CMS at any follow-up period. **Conclusion**

Prolotherapy with CEP is more beneficial than prolotherapy with isometric strengthening exercise in supraspinatus tendinopathy. Improvement in pain and functional movements is more in the prolotherapy with CEP group than prolotherapy with ISE group.

**Key words:** supraspinatus tendinopathy, prolotherapy injection, corrective exercise program

## Introduction

Tendon overuse injuries (tendinopathies) constitute a major proportion of sports injuries. More than 50% of patients presenting with shoulder pain are diagnosed to be partial thickness supraspinatus tear or supraspinatus tendinosis (Kim et al., 2010). Clinical presentation of tendinopathy includes pain during/after exercise or associated with morning pain after waking up, and increased pain with increased load demonstrated in provocative manoeuvres. (Greis et al., 2015).

Non operative management is the primary treatment of supraspinatus tendinopathy without complete tear which includes rest, activity modification, exercise therapy like rotator cuff strengthening and non-steroidal anti-inflammatory drugs (Serafini et al., 2009). The role of inflammation continues to be a point of controversy for intervention related to tendinopathy. Cook and Purden (2009) investigated a variety of human tendons indicating that there are no inflammatory cells in degenerative tendons whereas another study reported an increase in presence of inflammatory cells in pathological tendons (Andarawis-Puri et al., 2015). It is hence prerogative that corticosteroid and non-corticosteroid medications may carefully be administered for pain relief (Dean et al., 2016), as chronic tendinopathies are mostly degenerative in nature, and as such, corticosteroids may have adverse effects on tendon healing (Gialanella & Prometti, 2011). Regenerative injection therapies like platelet rich plasma (PRP) are under usage, yet their effectiveness is a point to ponder (Sánchez-González et al., 2012). Dr. Hackett, was the first person to use prolotherapy, which is an injection technique (Munk et al., 1998). Prolotherapy has been identified as a regenerative injection therapy which is in line with other regenerative injection therapies such as PRP and other stem cell injections by the absence of a biologic agent (Rabago et al., 2013). Prolotherapy is being used for the treatment of various musculoskeletal conditions such as ligamentous laxity, osteoarthritis and tendinopathies like patellar, Achilles, tennis elbow. (Topol et al., 2016); (Ryan et al., 2011); (Ryan et al., 2010); (Reeves et al., 2016).

Ease of application, and reduced time for rehabilitation are the reasons reported for the preference of prolotherapy, where no serious side effects were reported for prolotherapy when used for the above-mentioned conditions (Rabago and Nourani , 2017). However, the mechanism of action of prolotherapy is by causing local irritation with subsequent inflammation and tissue healing resulting in enlargement and strengthening of damaged ligaments, tendons and intra-articular structures (Lin et al., 2019). The primary objective of the present study was to assess the improvement in pain intensity and shoulder function in patients with supraspinatus tendinopathy at 3, 6 and 12 weeks as measured by VAS (visual analogue score) and CMS (constant murley score) scores respectively. In multiple clinical trials, hypertonic dextrose is the most commonly used prolotherapy solution (D'Lima, 2016). The proposed mechanism of action is transport of dextrose into human cells by using GLUTs 1–4 transport proteins, and this dextrose interacts with DNA to signal either cell growth or repair, Thereby, DNA expression changes, favouring the production of multiple cytokines (Laiguillon et al., 2015). Hence, prolotherapy could be identified as a useful option to treat the supraspinatus tendinopathy.

There are limited studies in literature comparing the prolotherapy and non-operative management in treatment of supraspinatus tendinopathy. Till date, only few randomised controlled studies were found evaluating the use of prolotherapy in supraspinatus tendinopathy, of which, three studies favoured prolotherapy (Bertrand et al., 2016), (Seven et al., 2017) and (Sari and Eroglu, 2020). One study deferred against prolotherapy (Cole et al., 2018) and one study was inconclusive. (Cook and Lewis, 2019). This apart, exercise therapy is a known line of treatment followed in the management of supraspinatus tendinopathy where mechanical loading of a tendon helps in its repair. Hence, loading a tendon in the form of isometric, concentric, and eccentric exercises should be considered in the rehabilitation program (Maeda et al., 2009). Appropriate loading forces induce a tensile stretch to tenocytes, and activate protein kinases. (Killian et al., 2012). Evidence regarding the efficacy of exercises in adults is substantial where exercises has been advocated to be cost-effective. Exercise regimen in conditions like rotator cuff tendinopathy is an effective modality in terms of pain reduction, improvement in work-ability, and potential improvement for return-to-work when compared to a control intervention or to a placebo. (Desmeules et al., 2016). Considering all these into account, we hypothesised that prolotherapy combined with a corrective exercise program helps in pain reduction and increasing range of movement in patients with supraspinatus tendinopathy. This study compares the efficacy of prolotherapy with isometric strengthening exercises (ISE) versus prolotherapy with corrective exercise program (CEP) in the treatment of supraspinatus tendinopathy.

## Material and Methods

This was a randomised controlled study conducted in Department of Sports Medicine and Sports Sciences (SISSM), Saveetha Medical College, Chennai, India. Ethical approval was taken prior to start of the study.

### **Sample size calculation**

In a study by Seven et al (2017), the observed mean value of VAS at 12 weeks after prolotherapy for chronic rotator cuff lesions was  $2.35 \pm 1.98$  and in control group was  $4.00 \pm 2.11$ , taking these values as reference, the minimum required sample size with 80% power of study and 5% level of significance was 24 patients in each study group. So, total sample size taken was 50 (25 patients per group).

### **Inclusion and exclusion criteria**

Patient selection was based on the following inclusion criteria: age of the patients above 18 years, pain in the shoulder of more than 6 months duration, with evidence of isolated supraspinatus tendinopathy in MRI (tendinosis or <50% thickness tears) with persistent pain despite conservative treatment given for more than 2 months, and consenting to be a part of this study. Exclusion criteria were the presence of any of the following: (i) patients with >50% thickness tears of the supraspinatus tendon on MRI (ii) associated tendinopathy of other rotator cuff muscles (iii) systemic inflammatory arthritis, including ankylosing spondylitis, rheumatoid arthritis or psoriatic arthritis (iv) patients with prior rotator cuff tear (v) history of diabetes mellitus or hypertension (vi) patients with infection, known malignancy, bleeding disorder or pregnant patients, and (viii) patients who had received previous corticosteroid injection or PRP injection in the same shoulder.

Totally 14 patients were excluded among the 64 patients. In those, 9 patients were involved with other rotator cuff muscles and 5 patients already received PRP injection previously in the same shoulder.

### **Randomisation and groups**

After enrolment, the patients were randomly divided into ISE and CEP groups by using bowl method without replacement technique. The patient had to pick a card from the bowl containing 1 to 50 numbers (25 odd & 25 even numbers). The picked card was not replaced to ensure equal numbers in both groups. Both groups received the same dose of prolotherapy injection. Group ISE received prolotherapy (25% dextrose) injection followed by isometric rotator cuff strengthening exercises given, whereas Group CEP also received the prolotherapy (with 25% dextrose) followed by the corrective exercise program (Table 1) given.

### **Procedure for prolotherapy injection**

In sitting position, the affected shoulder was disinfected under strict aseptic precautions using 1% povidine iodine and spirit. By palpating posterior joint line of the shoulder, soft spot was identified 1 cm below and lateral to the acromian process. Using a 27G needle, 5–7 ml of prolotherapy solution (25% dextrose) and 1–2 ml of lidocaine (local anaesthetic) was injected in the subacromial space by the sports medicine physician. Post injection, icepack was used for pain control. Only paracetamol tablets (maximum 3 tablets a day) of 500 mg strength were allowed to the patient as rescue analgesic after injection for a maximum period of 10 days on need basis.

### **Rehabilitation protocol**

After prolotherapy, group ISE advised for isometric rotator cuff strengthening, 12 repetitions\* 3 sets with holding duration of 8–10 seconds for each repetitions. In group CEP, corrective exercise program by Lindell. C., 2017 was advised (Table 1). Force couples occur when the resultant force of two opposing muscle groups achieves a given moment. The rotator cuff acts as a force couple around the joint, with co-activation of agonist and antagonist muscles, as well as coordinated activation of the agonist and inhibition of the antagonist muscle (Lugo et al., 2008). This helps in producing the torques and accelerations necessary for using the glenohumeral joint. Deltoid, rotator cuff and upper trapezius-serratus anterior acts as force couples (Cools et al., 2014).

**Table 1.** Corrective Exercise Program

S No	Exercise	Reps	Sets
1	90/90 scapular stabilization in prone position	12	3
2	Overhead carries (kettlebell)	12	3
3	Sidelying external rotation with dumbbell	12	3
4	Bosu ball push ups	12	3
5	Dynamic scapular stability drill with slider	12	3

### **Follow up and outcome measures**

The patients were assessed at the time of enrolment, and at 3, 6 and 12 weeks follow up to assess the level of pain and functional status. The patients were asked to rate their pain on VAS - a subjective scale where 0 indicates no pain and 10 indicates worst possible pain. To measure the functional outcomes, CMS was used. It ranges from 0-100. It has 4 components. 1. pain (15 pts), 2. activities of daily living (20 pts), 3. strength (25 pts), 4. range of motion (40 pts). Score of <30 = unsatisfactory, 30–39 = fair, 40–59 = good, 60–69 = very good and >70 = excellent.

### Statistical analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean  $\pm$ SD and median. Normality of data was tested by Kolmogorov-Smirnov test. Quantitative variables were compared using unpaired t-test for normally distributed or Man Whitney test for non-normally distributed data and qualitative variables were compared using Chi- square test. A *P* value of  $<0.05$  was considered statistically significant.

## Results

CEP Group participants had pain and shoulder improvement, as described by VAS and CMS scores in as compared with ISE Group. Baseline characteristics for the two are given in the Table 2. No significant difference was found in the baseline characteristics between the study groups mentioned in the Table 2.

**Table 2.** Baseline characteristics

	ISE Group	CEP Group	P value
Age	34.7 $\pm$ 10.0	34.6 $\pm$ 10.3	0.9
Sex (males:females)	16:9	19:6	1.0
Laterality (right:left)	17:8	17:8	0.4
VAS-day 0	7.0 $\pm$ 1.2	6.7 $\pm$ 1.2	0.4
Constant score-day 0	69 $\pm$ 8.3	68.4 $\pm$ 8.5	0.7

Pain intensity for both groups measured at 3, 6 and 12 weeks after intervention. In the within-group comparisons, ISE group as well as CEP group achieved a significant improvement in the VAS scores at 3, 6 and 12 weeks ( $P = <0.05$ ), when compared to baseline values, except for the CMS score at 3 weeks, for which the *P* value for comparison to baseline value was 0.06 (Tables 3 and 4, Figures 2 and 3). The baseline value of VAS in the ISE group was 6.7  $\pm$ 1.2, which improved to 3.4  $\pm$ 1.3 at 12 weeks (Table 3). The baseline value of VAS in the CEP group was 7.3  $\pm$ 1.2 which improved to 4.0  $\pm$ 1.2 at 12 weeks. Similarly, the baseline and 12 weeks value of Constant score in the ISE group were 68.3  $\pm$ 8.5 and 84  $\pm$ 5.8 respectively, and in the CEP group were 69.0  $\pm$ 8.2 and 82.3  $\pm$ 7.1 respectively ( $P < 0.05$ ).

**Table 3.** VAS at each follow-up

	IES Group		CEP Group B		
	Mean $\pm$ SD	P value for comparing to day 0	Mean $\pm$ SD	P value for comparing to day 0	P value for comparison of group A vs group B
Day 0	7.4 $\pm$ 1.3		6.7 $\pm$ 1.2		0.4
3 weeks	5.6 $\pm$ 1.0	$<0.01^*$	5.6 $\pm$ 1.1	$<0.01^*$	0.4
6 weeks	4.9 $\pm$ 1.1	$<0.01^*$	4.8 $\pm$ 1.0	$<0.01^*$	0.9
12 weeks	4.0 $\pm$ 1.2	$<0.01^*$	3.4 $\pm$ 1.3	$<0.01^*$	0.2

VAS- visual analog scale

\* Statistically significant *P* value, with significance set at 0.05; SD- standard deviation.

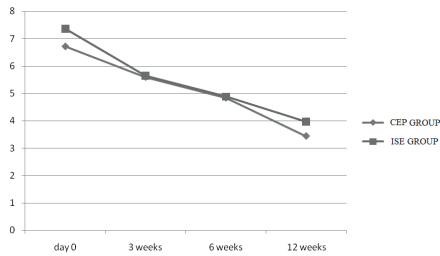


Figure 1. VAS score at each follow up

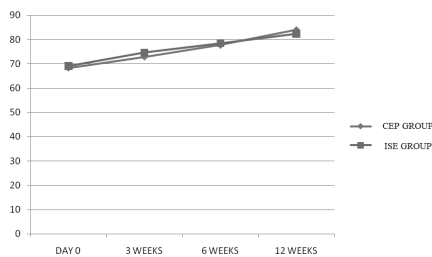


Figure 2. CMS score at each follow up

In the between group comparison, there was no significant difference between the ISE group and CEP group in the VAS and CMS. (Tables 3 and 4). The numerical values and the improvement in (Figures 1 and 2) suggest the benefits of CEP with prolotherapy is more than the isometric with prolotherapy group. None of the patients experienced any serious complications like bleeding, cellulitis or infection. Only 4 patients experienced moderate pain which was managed by paracetamol on need basis and local application of ice packs.

Table 4. CMS score at each follow-up for prolotherapy and corrective exercise program

	ISE Group		CEP Group		P value for comparison Of group A vs group B
	Mean $\pm$ SD	P value for Comparing to day 0	Mean $\pm$ SD	P value for comparing to day 0	
DAY 0	69.0 $\pm$ 8.3		68.4 $\pm$ 8.5		0.7
3 WEEKS	74.6 $\pm$ 7.8	0.019*	73.0 $\pm$ 8.3	0.061	0.5
6 WEEKS	78.5 $\pm$ 7.1	0.00*	77.8 $\pm$ 6.5	0.00*	0.7
12 WEEKS	82.4 $\pm$ 7.1	0.00*	84.0 $\pm$ 5.8	0.00*	0.1

\* Statistically significant P value, with significance set at 0.05; SD – standard deviation

## Discussion

In the present study, prolotherapy with corrective exercise program (CEP) showed improvement in pain (VAS) and function (CMS) at 3, 6 and 12 weeks as compared to baseline in the management of supraspinatus tendinopathy (SST).

Although there was no statistical significance, prolotherapy with addition of CEP has clinical significance in terms of pain score and functional score.

Cole et al (2018). compared prolotherapy with the corticosteroid and concluded that prolotherapy offered no additional benefit in supraspinatus tendinopathy). However, some authors reported significant improvements with prolotherapy as well. Lin et al. (2018) found improvement in shoulder pain (VAS) and shoulder function (SPADI) as compared to a placebo group. One study reported improvement in pain with prolotherapy in patients with painful rotator cuff tendinopathy, after 9 months of follow up, compared with blinded saline injection (Bertrand et al., 2016). Similarly, Lee et al (2015), in a retrospective comparison, showed significant improvement in VAS, SPADI and AROM with prolotherapy, and thus showed improvement in pain and disability, improvement in isometric strength of shoulder, and AROM of shoulder.

Our study identified prolotherapy as a useful injection technique because it is relatively safer as compared to the complications of local corticosteroid injections, where Nicholas et al. (2005) reported such as tendon rupture/weakening, subcutaneous fat atrophy, and skin hypopigmentation as the few common complications following corticosteroid injection.

Similarly, minor complications like pain, light headedness, allergy or infection were reported for prolotherapy in the literature. Dorman (1993) found a very low complication rate was found for prolotherapy with only 6 out of 272 subjects reporting any complications.

Further, the complication was restricted to only transient increase in pain for 1-2 days. (Catapano et al., 2020). In the present study, we did not observe any complication other than pain in 4 out of 25 patients (16%). The pain was managed by need based paracetamol and application of ice packs.

Further, studies have explored the effect of isometric exercises in the treatment of tendinopathy, in particular, its acute analgesic role. Exercise regimens, referred to as tendon loading programs, remain the most effective conservative approach in the treatment of tendinopathy where tendon loading exercises have shown beneficial effects in patients with chronic achilles tendinopathy and patellar tendinopathy (Millar et al., 2021).

Supraspinatus tendinopathy has shown greater improvement with a progressive loading program, rather than complete rest, with other treatment modalities used as adjuncts mainly targeted at achieving pain relief (Cardoso et al., 2019).

In the present study, prolotherapy with isometric rotator cuff strengthening exercise (group ISE) was compared with prolotherapy plus corrective exercise program (group CEP). Group B participants in our study underwent prolotherapy followed by a corrective exercise program consisting of selective muscle activation of the force couples [90/90 scapular stabilization, overhead carries, side lying dumbbell-external rotation] followed by the plyometrics (Lindell, 2017), we found that the combination of prolotherapy along with the CEP is beneficial on the supraspinatus tendinopathy.

The duration of follow up for our study was 3 months, which we felt was sufficient. However, for the condition under consideration, treatment is expected to result in improvements within this period and longer follow up may lead to better assessment of results. The age of the participants (18 to 60 years) in this study could have played a significant role in the result of this study, as it is possible that the efficacy of prolotherapy injection may produce different results in different age groups in rotator cuff tendinopathy. Similarly, sample size was not large enough to permit any subgroup analysis based on age, pain and other characteristics. It is however possible that inclusion

of a pain-relieving modality and with a larger sample size could lead to more prominent subgroup analysis in the near future. Further research might enlighten the accurate benefits of such combination of techniques.

## Conclusion

Regenerative injection techniques such as prolotherapy is found beneficial for pain management in supraspinatus tendinopathy. Prolotherapy combined with a corrective exercise program showed better pain reduction and increased range of movement. Moreover, combining prolotherapy with a corrective exercise program enhanced the overall functional independence of the participants. However, a long-term follow-up may show further benefits of such techniques towards pain and range of movement.

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