

Comparison of the Efficacy of Mesotherapy and Intra-articular Steroid Injection in Patients with Chronic Shoulder Pain: A Randomized Clinical Trial

Ecem Pelin Kaymaz, **Sibel Süzen Özbayrak**, **Duygu Geler Külcü**

Department of Physical Medicine and Rehabilitation, Haydarpaşa Numune Research and Training Hospital, İstanbul, Türkiye

Abstract

Introduction: Chronic shoulder pain (CSP), commonly caused by rotator cuff disorders, adhesive capsulitis, instability, or arthritis, results in significant functional impairment, psychological distress, and decreased quality of life. Despite the use of physical therapy and intra-articular injections, treatment outcomes may be inadequate, necessitating alternative or adjunctive therapies. This study aimed to assess the efficacy of mesotherapy compared with corticosteroid injections in reducing pain, improving function, and increasing range of motion (ROM) in patients with CSP.

Methods: In this prospective, single-blind, randomized clinical trial, patients were allocated to either the mesotherapy group (Group 1) or the steroid injection group (Group 2). Group 1 underwent three weekly mesotherapy sessions targeting the shoulder, whereas Group 2 received a single intra-articular injection of 20mg triamcinolone hexacetonide. Pain intensity (Visual Analog Scale [VAS] at rest, during activity, and at night), functional disability (Shoulder Disability Questionnaire [SDQ]), and passive shoulder ROM were measured at baseline, 30 minutes, and 4 weeks post-treatment.

Results: Both groups experienced significant improvements in VAS, SDQ, and ROM scores ($p<0.05$). However, the mesotherapy group demonstrated significantly greater improvement across most clinical parameters than the steroid group ($p<0.05$).

Discussion and Conclusion: Mesotherapy is an effective treatment for chronic shoulder pain, offering comparable or superior benefits to corticosteroid injections. It should be considered a valid nonsurgical treatment alternative tailored to patient needs.

Keywords: Intradermal injection; mesotherapy; shoulder pain; steroid.

Shoulder pain accounts for approximately 16% of all musculoskeletal complaints, with rotator cuff tendinopathy (RCT) being the most common underlying cause [1]. RCT is a degenerative condition that arises from repetitive overuse of the shoulder without overt inflammation. It encompasses various subacromial pathologies, including rotator cuff tendinosis/tendinitis, subacromial bursitis, and shoulder impingement syndrome [2].

The management of chronic shoulder pain (CSP) remains a clinical challenge, typically involving physiotherapy, intra-articular injections, or surgical intervention. Among these, corticosteroid injections are widely used because of their affordability and effectiveness in alleviating pain and improving mobility across all stages of RCT [3]. However, their therapeutic benefit is often limited to the short term [4]. Moreover, corticosteroids may impair collagen synthesis

Correspondence: Sibel Süzen Özbayrak, M.D. Department of Basic Oncology, Oncology Institute, İstanbul University, İstanbul, Türkiye

Phone: +90 506 343 81 87 **E-mail:** sibels62@yahoo.com

Submitted Date: 12.09.2025 **Revised Date:** 17.09.2025 **Accepted Date:** 24.09.2025

Haydarpaşa Numune Medical Journal

OPEN ACCESS This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).



and contribute to tendon degeneration or rupture with repeated use [5]. In addition, systemic contraindications such as uncontrolled diabetes or hypertension may preclude their use in certain patients. These limitations underscore the need for alternative therapeutic options that offer longer-lasting efficacy and can be utilized in steroid-restricted cases.

Mesotherapy, first introduced by Dr. Michel Pistor in 1958, is a minimally invasive technique involving the repeated intradermal administration of pharmacological agents into the superficial layers of the skin [6]. The objective is to achieve both immediate and sustained local pharmacological effects using lower drug dosages compared with systemic administration, owing to delayed diffusion. Mesotherapy may be employed alongside other pharmacological and non-pharmacological treatments. Previous reports suggest its potential efficacy in reducing musculoskeletal pain, improving function, and enabling earlier initiation of rehabilitation—thereby enhancing patients' overall quality of life. In fact, mesotherapy has been found to be more effective than systemic therapy for localized pain and functional impairments associated with various musculoskeletal conditions [7].

Despite this, there is a paucity of research evaluating the effectiveness of mesotherapy in painful shoulder conditions, and to date, no studies have directly compared its efficacy with that of corticosteroid injections [8,9].

The aim of this study is to evaluate the efficacy of mesotherapy in reducing chronic shoulder pain, improving shoulder function, and enhancing range of motion in comparison with corticosteroid injections.

Materials and Methods

Study Design

This prospective, randomized, single-blind clinical study was conducted according to the ethical guidelines of the Declaration of Helsinki. The Local Ethics Committee approved the study, with reference number 05/27.03.2024. The study was registered in the "Clinical Trials Library for Protocol Registration and Results System" with the number NCT06610032.

Inclusion and Exclusion Criteria

The inclusion criteria for the study were as follows: age between 18 and 75 years, presence of shoulder pain for at least 6 months, a Visual Analog Scale (VAS) pain score of ≥ 4 , ability to understand and follow verbal instructions, and absence of cognitive impairment. The exclusion criteria included uncontrolled diabetes mel-

litus, complete rotator cuff tear, history of physical therapy to the shoulder within the past 3 months, corticosteroid or other injections to the shoulder within the past 3 months, previous upper extremity surgery, known allergy to any of the drugs used in the study, current use of anticoagulant therapy (e.g., warfarin, low-molecular-weight heparin), known coagulation disorders, use of oral or parenteral corticosteroids within the past 3 months, use of nonsteroidal anti-inflammatory drugs (NSAIDs) within the past 7 days, use of paracetamol within the past 48 hours, history of malignancy, diagnosed psychiatric disorders, rheumatologic conditions (e.g., polymyalgia rheumatica, rheumatoid arthritis, ankylosing spondylitis), renal failure, hepatic disease, heart failure, pregnancy, and the presence of infection, open wound, allergy, or burn-like lesions at the application site.

Sample Size Estimation

Sample size estimation was performed using G*Power software, version 3.1. Based on the statistical comparisons reported in a previously published study, an effect size (d)=0.80 was assumed for the percentage change in the VAS scores, with a standard deviation (SD)=1.44. Under these assumptions, the required minimum sample size for each group was calculated as $n=42$ to achieve a statistical power of 0.95 and a significance level (α)=0.05 [10]. To account for potential dropouts, it was planned to recruit 44 participants per group. As a result, a total of 88 individuals were enrolled in the study, of whom 84 successfully completed the study protocol.

Participant Recruitment

A total of 130 patients presenting with chronic shoulder pain were evaluated at the outpatient Physical Medicine and Rehabilitation Clinic between July and September 2024. Following the application of the predefined inclusion and exclusion criteria, 88 eligible participants were enrolled in the study. Participants were randomly assigned to two equal groups: the Mesotherapy Group (Group 1; $n=44$) and the Steroid Injection Group (Group 2; $n=44$). Randomization was performed using a computer-generated randomization algorithm [11]. Group allocation was conducted by an independent investigator not involved in the treatment administration or outcome assessments, and assignments were concealed in sealed, opaque envelopes. During the study period, two participants in Group 1 withdrew due to work-related reasons, and two participants in Group 2 were lost to follow-up at the one-month evaluation. A detailed patient flow diagram is provided in Figure 1. Prior to enrollment, all eligible participants who consented to take part in the study were informed in detail about

the objectives and procedures of the research. Written informed consent was obtained from each participant before any data collection began. All participants were instructed to maintain their usual lifestyle, including routine medication use and daily activities, without any modifications during the study period.

Procedures

The treatment protocol was designed based on the Treatment Algorithm published by the Italian Mesotherapy Association [12]. As a basic hygiene rule, patients were reminded to clean the shoulder where the injection would be administered with soap and water before the treatment day and not to apply any cream or lotion. All patients received local injections from the same physician to eliminate operator-related variability.

Mesotherapy Group

Intradermal mesotherapy was administered by an experienced and certified physician to the identified painful points of the shoulder. The procedure utilized a 5mL syringe fitted with 4mm, 30-gauge sterile disposable needles (Mesorelle, Biotekne SRL, Casalecchio di Reno, Italy).

At each treatment session, a pharmacological mixture was prepared consisting of the following components:

- 1mL of 1% lidocaine
- 1mL of pentoxifylline
- 1mL of thiocolchicoside
- 1mL of diluted meloxicam (1/4 dilution with 0.9% saline)

A total volume of 4mL of solution was used per session.

Prior to injection, the skin was disinfected with gauze soaked in chlorhexidine, and the area was allowed to dry and absorb the antiseptic for 5 minutes. The mixture was administered using the point-by-point technique, with 0.1mL injected per site at a depth of 1–3mm, at a 90-degree angle, and 2cm apart between injection sites, avoiding the formation of papules. Following this, a nappage technique was performed on the deltoid muscle at a 45-degree angle in a cage-shaped pattern (Fig. 2).

After the procedure, the skin was gently dried using sterile gauze, and a protective adhesive dressing was applied. Patients were observed for at least 20 minutes to monitor for any acute post-injection adverse reactions, such as dizziness, skin flushing, or localized bleeding. Additionally, patients were instructed not to wet the injection site for 24 hours post-treatment [13]. A total of three mesotherapy sessions were administered at weekly intervals to patients in Group 1.

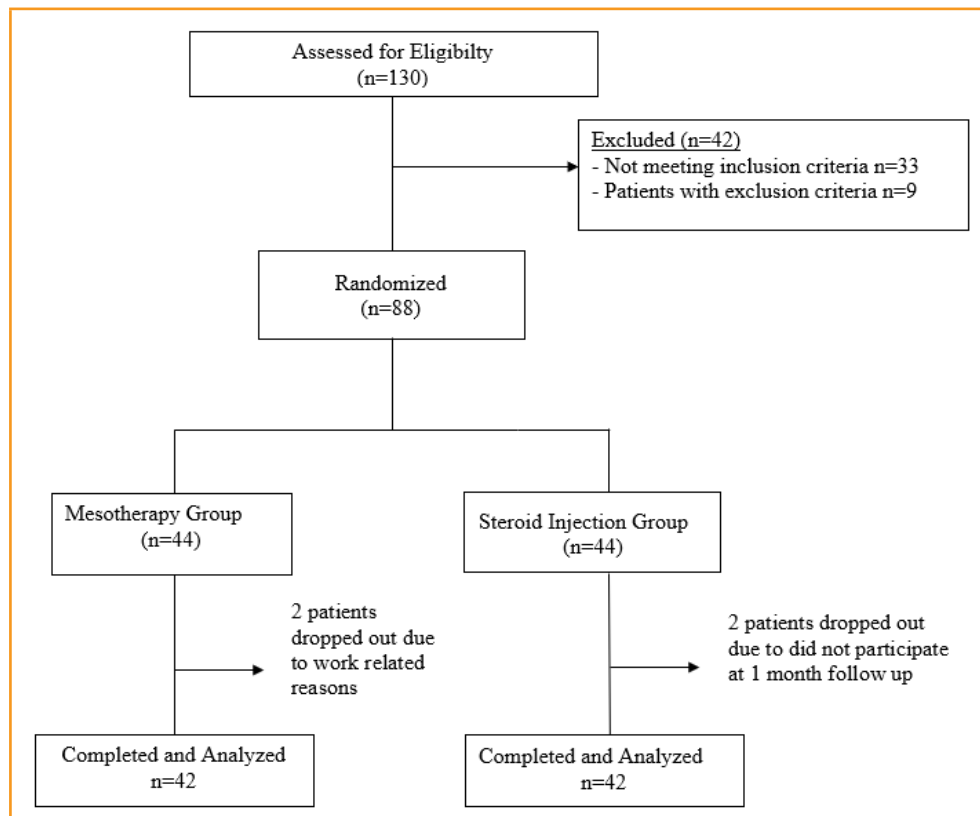


Figure 1. Patient flowchart.

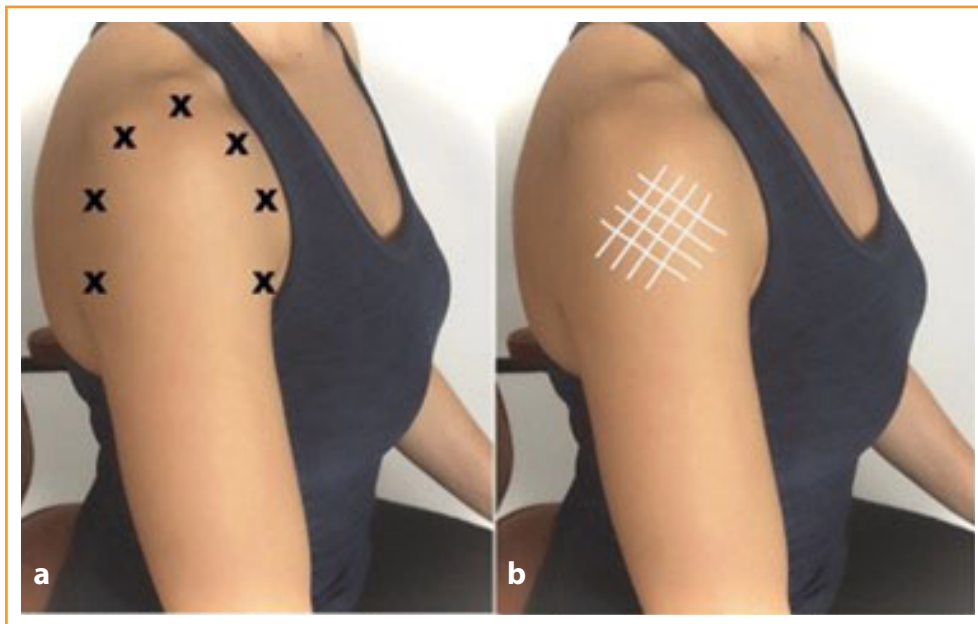


Figure 2. Injection sites used for mesotherapy. (a) point by point technique; (b) nappage technique.

Intra-articular Steroid Injection Group

In Group 2, a single intra-articular injection of 1mL (20mg) triamcinolone hexacetonide was administered. Injections were performed using the posterior approach as described by Russell and Cyriax [14]. During the procedure, the patient was seated on a chair facing away from the physician. A cross was marked on the skin 1cm inferior to the posterolateral corner of the acromion using the physician's thumbnail. The injection site was then sterilized with an alcohol swab.

The physician positioned the thumb over the posterior aspect of the acromion and placed the index or middle finger of the non-dominant hand on the anterior coracoid process. A 38mm, 21-gauge needle attached to a horizontally held syringe was inserted through the center of the marked cross and directed toward the coracoid process. Patients typically reported localized pain when the joint capsule was penetrated, often accompanied by mild resistance. Advancement of the needle was halted upon contact with the humeral head or the subacromial structures. The corticosteroid was injected slowly. Following the procedure, patients were monitored for at least 20 minutes to observe any acute post-injection adverse reactions.

Clinical Evaluation

Demographic data including age, gender, height, weight, and marital status were recorded for all participants. Additionally, comorbidities, current medical treatments, and the duration of shoulder pain were documented. The severity of shoulder pain at rest, during activity, and at night was assessed using the VAS. Functional status was evaluated using the Shoulder Disability Question-

naire (SDQ). Furthermore, passive range of motion (ROM) of the shoulder joint was measured in all directions—flexion, extension, abduction, adduction, internal rotation, and external rotation—using a standard goniometer. All assessments were performed at three time points: baseline (T1), 30 minutes post-treatment (T2), and 4 weeks after treatment completion (T3). Evaluations were conducted by a blinded assessor who was unaware of the patients' group assignments.

Visual Analogue Scale

The VAS is a unidimensional measure of pain intensity, scored on a scale from 0 to 10, where 0 indicates no pain and 10 indicates the worst possible pain. Pain scores are categorized as follows:

- 1–3: Mild pain
- 4–7: Moderate pain
- 8–10: Severe pain [15].

Shoulder Disability Questionnaire

The SDQ is a pain-related disability scale used to evaluate the functional status of patients with shoulder disorders. It consists of 16 items describing daily activities that may provoke shoulder symptoms within the preceding 24 hours. The Turkish version of the SDQ has been validated and shown to be reliable for clinical use [16].

Statistical Analysis

IBM SPSS Statistics 22 (IBM SPSS, Türkiye) was used for statistical analyses. The statistician who performed the evalua-

tion was blinded to the treatment groups. Descriptive data were expressed as percentages for categorical variables and as mean±standard deviation (SD) or median (minimum–maximum) for quantitative variables. The Kolmogorov–Smirnov test was used to assess the normal distribution of all parameters. Categorical variables were compared using the chi-square test. Independent t-tests or the Mann–Whitney U test were employed for between-group analysis where appropriate, whereas the Friedman test was performed for within-group analysis. Post hoc analysis was performed using the Wilcoxon signed-rank test with Bonferroni correction for significantly different values. Significance was evaluated at the $p < 0.05$ level.

Results

A total of 84 patients with chronic shoulder pain were included in the analysis, with 42 patients in each group. The mean age was 56.2 ± 11.7 years in Group 1 and 58.9 ± 9.7 years in Group 2. Female patients constituted the majority, accounting for 69% of the study population. There were no statistically significant differences between the groups regarding demographic characteristics ($p > 0.05$) (Table 1).

The mean duration of shoulder pain was 11.10 ± 5.3 months in Group 1 and 11.79 ± 4.3 months in Group 2. Pain was reported in the right shoulder by 52.4% of patients in Group 1 and 54.8% in Group 2.

Regarding the diagnosis of shoulder pathologies, in Group 1, 52.4% of patients were diagnosed with rotator cuff syndrome,

23.8% with adhesive capsulitis, and 23.8% with subacromial impingement syndrome. In Group 2, the respective rates were 38.1%, 31%, and 31%. Diabetes mellitus was present in 33.3% of Group 2 patients and 19% of Group 1 patients.

Both treatment modalities were well tolerated. Most patients reported a mild, transient burning sensation during needle insertion, which was not significantly bothersome. Bruising at the injection site occurred in five patients (three in Group 1 and two in Group 2), resolving spontaneously within a few days. No serious adverse events such as allergic reactions, dizziness, or infections were observed.

Baseline pain levels, range of motion, and functional scores demonstrated significant differences in some parameters (Table 2). Within-group analyses demonstrated statistically significant improvements across all evaluated parameters in both groups (Table 3). Post hoc comparisons revealed significant differences between baseline (T1) and 30 minutes

Table 1. Demographic variables of patients in group 1 and group 2

	Group 1 (n=42)	Group 2 (n=42)	p
Gender, n (%)			
Female	29 (69%)	29 (69%)	1
Male	13 (31%)	13 (31%)	1
	Mean±SD	Mean±SD	
Fisher's Exact Test			
Age (years)	56.2 ± 11.7	58.9 ± 9.7	0.3
Weight (kg)	71.8 ± 8.2	72.2 ± 10.2	0.9
Height (m)	165.5 ± 8.2	164.9 ± 8.0	0.7
BMI (kg/m ²)	26.2 ± 2.4	26.4 ± 2.4	0.5
Education n (%)			
Elementary school	16 (38.1%)	28 (66.7%)	0.08
Middle school	3 (7.1%)	3 (7.1%)	
High school	14 (33.3%)	6 (14.3%)	
University	89 (21.4%)	5 (11.9%)	
Pearson Chi-Square Test, Mann -Whitney U Test			

Group 1: Mesotherapy group, Group 2: Steroid Injection group, n: number; SD: Standard Deviation; BMI: Body Mass Index

Table 2. Baseline variables of groups

	Group 1 (n=42) Mean±SD Median (Min-Max)	Group 2 (n=42) Mean±SD Median (Min-Max)	p
VAS			
Resting	6.1 ± 1.4 6 (3-120)	4.6 ± 2.7 5 (0-10)	0.008
Activity	9.0 ± 0.8 9 (7-10)	8.2 ± 1.3 8 (5-10)	0.004
Night	7.2 ± 2.0 7 (3-10)	6.3 ± 2.5 7 (0-10)	0.1
SDQ	72.4 ± 14.8 75 (37.5-100)	72.3 ± 12.5 75 (50-93.7)	0.8
Shoulder ROM			
Flexion	131.6 ± 26.4 125 (80-180)	156.3 ± 31.5 170 (90-180)	<0.001
Extension	19.7 ± 8.2 20 (10-40)	22.9 ± 8.8 22.5 (10-40)	0.07
Abduction	109.6 ± 309.9 100 (45-180)	151.0 ± 34.2 170 (90-180)	<0.001
Adduction	16.6 ± 6.4 20 (10-30)	20.2 ± 7.8 20 (5-30)	0.03
IR	47.1 ± 19.0 42.5 (10-90)	62.2 ± 17.5 70 (30-90)	<0.001
ER	41.6 ± 21.9 60 (40-90)	69.0 ± 23.7 80 (10-90)	<0.001
Mann Whitney U Test			

Group 1: Mesotherapy group, Group 2: Steroid Injection group, n: number, SD: Standard Deviation; Min: Minimum; Max: Maximum; VAS: Visual analogue scale; SDQ: Shoulder disability questionnaire; ROM: Range of motion; IR: Internal rotation; ER: External Rotation

Table 3. The improvement of clinical parameters within groups

	Group 1 (n=42) Mean±SD Median (Min-Max)	Group 2 (n=42) Mean±SD Median (Min-Max)
VAS Resting		
Pre-Treatment	6.1±1.4 6 (3-120)	4.6±2.7 5 (0-10)
30 minute	2.5±1.1 3 (0-5)	1.7±1.7 2 (0-7)
1 month	0.6±0.9 0 (0-3) p<0.001	0.9±1.3 0 (0-5) p<0.001
VAS Activity		
Pre-Treatment	9.0±0.8 9 (7-10)	8.2±1.3 8 (5-10)
30 minute	4.3±0.7 4 (3-6)	4.1±1.4 4 (1-7)
1 month	2.5±0.8 2.5 (1-5) p<0.001	3.0±1.3 3 (0-6) p<0.001
VAS Night		
Pre-Treatment	7.2±2.0 7 (3-10)	6.3±2.5 7 (0-10)
30 minute	3.0±1.3 3 (0-6)	2.4±1.8 2 (0-7)
1 month	1.0±1.0 1 (0-3) p<0.001	0.9±1.3 0 (0-5) p<0.001
SDQ		
Pre-Treatment	72.4±14.8 75 (37.5-100)	72.3±12.5 75 (50-93.7)
30 minute	28.2±8.1 28.1 (6.2-43.7)	34.8±15.9 31.2 (12.5-68.7)
1 month	11.3±5.8 12.5 (0-25) p<0.001	19.0±13.3 18.7 (0-56.2) p<0.001
Flexion		
Pre-Treatment	131.6±26.4 125 (80-180)	156.3±31.5 170 (90-180)
30 minute	157.6±14.1 160 (120-180)	165.1±22.3 180 (110-180)
1 month	172.7±8.9 180 (150-180) p<0.001	171.9±14.3 180 (130-180) p<0.001
Extension		
Pre-Treatment	19.7±8.2 20 (10-40)	22.9±8.8 22.5 (10-40)
30 minute	29.1±6.7 30 (20-45)	27.0±5.7 30 (15-40)
1 month	37.7±6.3 40 (30-50) p<0.001	30.8±6.5 30 (20-45) p<0.001

Table 3 (Cont). The improvement of clinical parameters within groups

	Group 1 (n=42) Mean±SD Median (Min-Max)	Group 2 (n=42) Mean±SD Median (Min-Max)
Abduction		
Pre-Treatment	109.6±30.9 100 (45-180)	151.0±34.2 170 (90-180)
30 minute	144.5±19.6 140 (80-180)	160.4±26.9 180 (100-180)
1 month	163.8±10.2 162.5 (140-180) p<0.001	166.9±19.9 180 (120-180) p<0.001
Adduction		
Pre-Treatment	16.6±6.4 20 (10-30)	20.2±7.8 20 (5-30)
30 minute	26.4±5.3 30 (15-40)	25.0±6.4 30 (10-30)
1 month	29.8±5.3 30 (20-45) p<0.001	27.15.5 30 (10-30) p<0.001
IR		
Pre-Treatment	47.1±19.0 42.5 (10-90)	62.2±17.5 70 (30-90)
30 minute	61.5±14.0 60 (40-90)	70.1±14.3 70 (45-90)
1 month	76.0±10.3 70 (60-90) p<0.001	71.9±14.3 70 (45-90) p<0.001
ER		
Pre-Treatment	41.6±21.9 30 (10-90)	69.0±23.7 80 (10-90)
30 minute	55.4±19.1 50 (20-90)	75.7±17.4 85 (40-90)
1 month	72.5±14.8 75 (40-90) p<0.001	77.1±16.7 90 (45-90) p<0.001
Friedman Test		
Group 1: Mesotherapy group, Group 2: Steroid Injection group, n: number; SD: Standard deviation; Min: Minimum; Max: Maximum; VAS: Visual analouge scale; SDQ: Shoulder disability questionnaire; ROM: Range of motion; IR: Internal rotation; ER: External rotation		

post-treatment (T2) (p<0.001), as well as between T2 and 4 weeks post-treatment (T3) (p<0.001) for all parameters.

Because baseline differences were observed in several variables between groups, the mean changes over time were compared. Group 1 exhibited significantly greater improvements in all parameters except for the SDQ score, VAS night pain severity, and shoulder extension range of motion (Table 4).

Table 4. The comparison of change of clinical variables throughout control visits

	Group 1 (n=42) Median (Min-Max)	Group 2 (n=42) Median (Min-Max)	p
VAS Resting 1-2	3 (1-8)	2.5 (0-10)	0.012
VAS Resting 2-3	2 (0-4)	0.5 (-1-3)	<0.001
VAS Activity 1-2	5 (3-6)	4 (1-7)	0.018
VAS Activity 2-3	2 (1-3)	1 (-1-4)	<0.001
VAS Night 1-2	4 (0-8)	3.5 (0-10)	0.628
VAS Night 2-3	2 (0-4)	2 (0-0-4)	0.022
SDQ 1-2	43.7 (12.5-75)	37.5 (13-68.75)	0.031
SDQ 2-3	18,7 (6.25-31.2)	15.3 (-6.25-37.5)	0.535
Flexion 1-2	20 (0-60)	2.5 (-15-50)	<0.001
Flexion 2-3	15 (0-30)	0 (0-40)	<0.001
Extension 1-2	10 (0-20)	0 (0-15)	<0.001
Extension 2-3	10 (0-25)	0 (0-25)	<0.001
Abduction 1-2	30 (0-85)	10 (0-50)	<0.001
Abduction 2-3	20 (0-85)	0 (0-50)	<0.001
Adduction 1-2	10 (0-20)	2.5 (0-20)	<0.001
Adduction 2-3	0 (0-15)	0 (0-10)	0.169
IR 1-2	15 (0-40)	10 (0-30)	<0.001
IR 2-3	10 (0-40)	0 (0-10)	<0.001
ER 1-2	10 (0-40)	0 (-10-35)	0.001
ER 2-3	20 (0-45)	0 (0-15)	<0.001

Independent Samples Mann Whitney U Test, Wilcoxon Signed Rank Test with Bonferroni correction

n: number; Min: Minimum; Max: Maximum; VAS: Visual analogue scale; SDQ: Shoulder disability scale; IR: Internal rotation; ER: External rotation

Discussion

Chronic shoulder pain and restricted ROM are common complaints across various age groups, resulting from a complex interplay of mechanical and biochemical factors. Many patients with this type of localized pain do not respond adequately to oral or topical pharmacological treatments, and physical therapy interventions may also prove insufficient. In such cases, intra-articular steroid injections or suprascapular nerve blocks are often considered treatment options. However, these interventions are not without risks and may be associated with various complications and adverse effects.

Mesotherapy represents a potentially safe alternative, particularly for patients who are unsuitable for long-term oral medications or for steroid injections due to comorbidities. From this perspective, unmanageable chronic shoulder pain may benefit from a localized treatment approach based on the principles of mesotherapy, which may also mitigate the side effects associated with other treatment modalities.

In this study, we aimed to evaluate the efficacy of mesotherapy injections compared with intra-articular steroid injections in patients with chronic shoulder pain, focusing on pain reduction, improvement in shoulder ROM, and enhancement of functional status.

The results obtained at the end of treatment and at the one-month follow-up demonstrated statistically significant improvements in all measured parameters in both groups. However, the magnitude of change over time was significantly greater in the mesotherapy group compared with the steroid injection group, except for the SDQ score and VAS night pain severity score.

Mammucari et al. [12] reported that intradermal injections into the superficial skin layers facilitate slow diffusion of the drug into the underlying tissues. Measurements of sodium ketoprofen concentrations in skin, muscles, and joints after local intradermal versus intramuscular (IM) administration showed higher and more sustained drug levels in the tissues adjacent to the injection site following intradermal delivery compared with IM injection. These findings were further supported by studies involving intradermal inoculation of procaine [17]. Similar observations in human studies confirmed that drugs injected intradermally (up to 4mm depth) maintain higher local concentrations, whereas injections at depths exceeding 10mm lead to rapid systemic absorption and shorter local tissue retention times [18].

A review of the literature on mesotherapy applications in musculoskeletal disorders reveals that conditions such as knee osteoarthritis, low back pain, chronic spinal pain, and

neck pain have been frequently investigated [19–24]. However, only a limited number of studies have examined the efficacy of mesotherapy specifically for shoulder pain [8,9].

Sposito et al.^[8] evaluated improvements in ROM in patients with rotator cuff tendinopathy treated with mesotherapy. Their protocol involved a drug cocktail containing diclofenac or meloxicam, a coumarin derivative (melilotus extract with rutin), and a local anesthetic (procaine), occasionally combined with a vasodilator (buflomedil). Their findings suggested that mesotherapy is effective in managing rotator cuff tendinopathy by reducing pain, improving ROM, and enhancing overall upper limb function. Our results align with these findings; additionally, our study contributes further by comparing mesotherapy with intra-articular steroid injections—a well-established treatment for chronic shoulder pain—thus providing a more robust evaluation of mesotherapy's efficacy.

Cacchio et al.^[9] investigated the effectiveness of disodium EDTA mesotherapy for treating calcific tendinitis of the shoulder. Patients received weekly mesotherapy sessions for three weeks consisting of 1 mL disodium EDTA, 1 mL 1% procaine, and 3 mL injectable water. This was combined with pulsed-mode ultrasound therapy using a 15% disodium EDTA gel solution, administered five times per week over the same period. The control group received sham ultrasound therapy. Results demonstrated that disodium EDTA mesotherapy is a safe and effective treatment for calcific tendinitis, significantly reducing pain, improving shoulder function, and promoting the resolution of calcifications.

Chen et al.^[19] reported superior improvements in pain relief and functional outcomes, along with fewer side effects, in patients treated with mesotherapy compared with those receiving oral therapy. They also proposed that “acupuncture reflexological effects” might contribute as a confounding factor to the observed benefits. Another possible confounder is the mechanical distension of tissues following injection, which may activate cutaneous and subcutaneous receptors involved in the release of endorphins—endogenous molecules with potent analgesic properties [12].

The aforementioned factors may explain why, in our experience, mesotherapy injections demonstrated superior improvements across nearly all clinical parameters. Additionally, the increased frequency of clinic visits due to the three-session mesotherapy protocol might have contributed to patients feeling more closely monitored and cared for, potentially introducing a bias favoring greater improvement in the mesotherapy group.

The primary strength of our study lies in being the first randomized controlled trial to directly compare the efficacy of intra-articular steroid injections—considered the gold

standard treatment—with shoulder mesotherapy in patients with chronic shoulder pain.

Nonetheless, our study has several limitations. First, the relatively small sample size; second, the short duration of follow-up. Zhang et al.^[25] reported that intra-articular steroid injections for frozen shoulder provided pain relief primarily in the short to medium term (1 to 6 months), with diminishing benefits over longer follow-up periods. Given the possibility that a similar decline in effectiveness may occur with mesotherapy, future studies assessing the long-term outcomes of both treatment modalities would be valuable.

Conclusion

In conclusion, mesotherapy appears to be a valuable option in the rehabilitation field for musculoskeletal pain, offering advantages such as less invasiveness, few or no side effects, and easy reproducibility. Moreover, owing to its safety profile, it may be considered a first-line therapeutic approach for chronic shoulder pain. Future randomized controlled trials are warranted to establish more uniform treatment protocols and to evaluate long-term efficacy. Our goal was to provide a treatment alternative with effectiveness comparable to steroid injections while being safer for the patient and easier for the clinician to apply.

Ethics Committee Approval: The study was approved by Istanbul Medipol University Ethics Committee (No: 05, 27.03.2024). Clinical Trials Library for Protocol Registration and Results System” with the number NCT06610032.

Informed Consent: Written informed consent was obtained from each participant before any data collection began.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Use of AI for Writing Assistance: Not declared.

Authorship Contributions: Concept – E.P.K., S.S.Ö.; Design – E.P.K., S.S.Ö.; Supervision – D.G.K.; Fundings – E.P.K., S.S.Ö., D.G.K.; Materials – S.S.Ö., D.G.K.; Data collection &/or processing – E.P.K., S.S.Ö., D.G.K.; Analysis and/or interpretation – E.P.K., D.G.K.; Literature search – E.P.K., S.S.Ö., D.G.K.; Writing – E.P.K., S.S.Ö.; Critical review – D.G.K.

Peer-review: Externally peer-reviewed.

References

1. van der Windt DA, Koes BW, de Jong BA, Bouter LM. Shoulder disorders in general practice: incidence, patient characteristics, and management. *Ann Rheum Dis* 1995;54:959–64. [CrossRef]

2. Desmeules F, Boudreault J, Dionne CE, Frémont P, Lowry V, MacDermid JC, et al. Efficacy of exercise therapy in workers with rotator cuff tendinopathy: a systematic review. *J Occup Health* 2016;58:389–403. [CrossRef]
3. Kwong CA, Woodmass JM, Gusnowski EM, Bois AJ, Leblanc J, More KD, et al. Platelet-rich plasma in patients with partial-thickness rotator cuff tears or tendinopathy leads to significantly improved short-term pain relief and function compared with corticosteroid injection: a double-blind randomized controlled trial. *Arthroscopy* 2021;37:510–7. [CrossRef]
4. Buchbinder R, Green S, Youd JM. Corticosteroid injections for shoulder pain. *Cochrane Database Syst Rev* 2003;2003:CD004016. [CrossRef]
5. Browning DG, Desai MM. Rotator cuff injuries and treatment. *Prim Care* 2004;31:807–29. [CrossRef]
6. Mammucari M, Maggiori E, Russo D, Giorgio C, Ronconi G, Ferrara PE, et al. Mesotherapy: from historical notes to scientific evidence and future prospects. *ScientificWorldJournal* 2020;2020:3542848. [CrossRef]
7. Faetani L, Ghizzoni D, Ammendolia A, Costantino C. Safety and efficacy of mesotherapy in musculoskeletal disorders: A systematic review of randomized controlled trials with meta-analysis. *J Rehabil Med* 2021;53:jrm00182. [CrossRef]
8. Sposito M, Rivera D, Riberto M, Metsavaht L. Mesotherapy improves range of motion in patients with rotator cuff tendinitis. *Acta Fisiátrica* 2019;18; 196–9. [CrossRef]
9. Cacchio A, De Blasis E, Desiati P, Spacca G, Santilli V, De Paulis F. Effectiveness of treatment of calcific tendinitis of the shoulder by disodium EDTA. *Arthritis Rheum* 2009;61:84–91. [CrossRef]
10. Seven MM, Ersen O, Akpancar S, Ozkan H, Turkkan S, Yıldız Y, et al. Effectiveness of prolotherapy in the treatment of chronic rotator cuff lesions. *Orthop Traumatol Surg Res* 2017;103:427–33. [CrossRef]
11. Research Randomizer. Available at: www.randomizer.org. Accessed Feb 10, 2026.
12. Mammucari M, Gatti A, Maggiori S, Sabato AF. Role of mesotherapy in musculoskeletal pain: opinions from the Italian society of mesotherapy. *Evid Based Complement Alternat Med* 2012;2012:436959. [CrossRef]
13. Kocak AO. Intradermal mesotherapy versus systemic therapy in the treatment of musculoskeletal pain: A prospective randomized study. *Am J Emerg Med* 2019;37:2061–5. [CrossRef]
14. Cyriax J, Russell G. *Textbook of orthopaedic medicine*. Vol 2. 9th ed. London: Bailliere Tindall; 1977. p.164–6.
15. Campbell WI, Lewis S. Visual analogue measurement of pain. *Ulster Med J* 1990;59:149–54.
16. Çiftçi B, Uzunkulaoğlu A, Öke Topçu D. Validity and reliability of the Turkish version of the shoulder rating questionnaire in patients with shoulder pain. *Acta Orthop Traumatol Turc* 2021;55:208–12. [CrossRef]
17. Binaglia L, Marconi P, Pitzurra M. The diffusion of intradermally administered procaine. *Giornale di Mesoterapia* 1981;1:15–28.
18. Herreros FO, Moraes AM, Velho PE. Mesotherapy: a bibliographical review. *An Bras Dermatol* 2011;86:96-101. [Article in English, Portuguese] [CrossRef]
19. Chen L, Li D, Zhong J, Qiu B, Wu X. Therapeutic effectiveness and safety of mesotherapy in patients with osteoarthritis of the knee. *Evid Based Complement Alternat Med* 2018;2018:6513049. Erratum in: *Evid Based Complement Alternat Med* 2018;2018:5327589. [CrossRef]
20. Saggini R, Di Stefano A, Dodaj I, Scarcello L, Bellomo RG. Pes anserine bursitis in symptomatic osteoarthritis patients: a mesotherapy treatment study. *J Altern Complement Med* 2015;21:480–4. [CrossRef]
21. Paolucci T, Piccinini G, Trifan PD, Zangrando F, Saraceni VM. Efficacy of trigger points mesotherapy for the treatment of chronic neck pain: a short term retrospective study. *Int J Phys Ther Rehab* 2016;2:113. [CrossRef]
22. Yang XN, Geng ZS, Zhang XL, Zhang YH, Wang XL, Zhang XB, et al. Single intracutaneous injection of local anesthetics and steroids alleviates acute nonspecific neck pain: A CONSORT-perspective, randomized, controlled clinical trial. *Medicine (Baltimore)* 2018;97:e11285. [CrossRef]
23. Cui JZ, Geng ZS, Zhang YH, Feng JY, Zhu P, Zhang XB. Effects of intracutaneous injections of sterile water in patients with acute low back pain: a randomized, controlled, clinical trial. *Braz J Med Biol Res* 2016;49:e5092. [CrossRef]
24. Ferrara PE, Ronconi G, Viscito R, Pascuzzo R, Rosulescu E, Ljoka C, et al. Efficacy of mesotherapy using drugs versus normal saline solution in chronic spinal pain: a retrospective study. *Int J Rehabil Res* 2017;40:171–4. [CrossRef]
25. Zhang J, Zhong S, Tan T, Li J, Liu S, Cheng R, et al. Comparative efficacy and patient-specific moderating factors of nonsurgical treatment strategies for frozen shoulder: an updated systematic review and network meta-analysis. *Am J Sports Med* 2021;49:1669–79. [CrossRef]