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Original Article

Efficacy of mesotherapy in patients with acute and subacute neck pain: A randomized controlled trial

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ABSTRACT

Objectives: This study aims to investigate the effectiveness of mesotherapy in patients with acute or subacute neck pain compared to oral medications with the same active ingredients.

Patients and methods: In this randomized, single-blind study, 44 patients with acute to subacute neck pain (6 males, 38 females; mean age: 46.8±11.1 years; range, 23 to 65 years) were included between October 30, 2023, and June 30, 2024. These patients were randomly assigned to two groups. The first group received two sessions of mesotherapy solution, administered at seven-day intervals. The second group received oral meloxicam 15 mg once daily and thiocolchicoside 8 mg twice daily for seven days. Visual Analog Scale (VAS), Neck Disability Index (NDI), and cervical range of motion were evaluated before treatment and on the seventh and 14th days.

Results: There was no significant difference in demographic data, initial VAS scores, range of motion, and NDI scores between the two groups ($p>0.05$). Significant improvements in the VAS ($p<0.001$ and $p<0.03$, respectively) and NDI scores ($p<0.001$ and $p=0.016$, respectively) were observed within both groups. However, there was no significant difference between the groups ($p>0.05$). No significant difference was found within or between the groups in range of motion ($p>0.05$). In the first group, VAS scores significantly improved 30 mins after both sessions ($p=0.009$ and $p=0.038$, respectively).

Conclusion: We found mesotherapy to be as effective as oral combination therapy. Mesotherapy can be preferred as it allows the use of low-dose medication to relieve acute and subacute neck pain.

Keywords: Mesotherapy, muscle relaxants, neck pain, nonsteroidal antiinflammatory agents.

Nonspecific neck pain is defined as discomfort occurring in the lateral and posterior regions of the neck, without the presence of neurological or specific pathologies such as fractures, infections, or inflammation.[1] Acute nonspecific neck pain constitutes a significant public health issue, and if not properly controlled, acute neck pain can develop into chronic pain lasting for months or even years.[2] Similar to other musculoskeletal pain disorders; pain, inflammation, and functional impairment are treated with both pharmacological and nonpharmacological methods. However, systemic pharmacological treatments such as analgesics and anti-inflammatory drugs have limitations in usage, particularly in elderly patients and individuals with comorbidities requiring multiple treatments, due to some significant side effects and drug-drug interactions.[3,4] This situation increases the need for alternative treatment approaches. In this context, mesotherapy emerges as a potentially effective and reliable method for treating painful musculoskeletal syndromes. Mesotherapy is a minimally invasive technique involving the microinjection of active components into the dermis corresponding to the area to be treated.[5] This "micro-depot" results in slower drug release into surrounding tissues compared to parenteral applications, and various studies have shown that, after intradermal injections, the concentration of the drug remains high in local tissues for a longer duration than after intramuscular injections.[6,7] Additionally, using lower doses of active compounds with mesotherapy can provide a rapid

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onset of action and a prolonged effect.[7] According to the concept of "mesodermal modulation," the dermis is considered a new target organ. The local pharmacological effect is thought to be a combination of factors, including the chemophysical stimulation during microinjections, activation of specific trigger points, and additional neuroimmune mechanisms.[8,9]

Various studies exist in the literature regarding the use of mesotherapy for musculoskeletal pain. A systematic review and meta-analysis of seven studies by Paolucci et al.[10] demonstrated that mesotherapy was well-tolerated and effective in both acute and chronic musculoskeletal pain. A systematic review by Faetani et al.[5] reported that mesotherapy was more effective than systemic treatments in musculoskeletal pain, facilitating early rehabilitation and improving quality of life. However, due to heterogeneity in the drugs used, application techniques, session frequency, and total number of sessions, they concluded that more randomized controlled trials are needed to compare a standardized mesotherapy protocol with systemic treatments. Mammucari et al.[11] published International Consensus Guidelines on the safe and evidence-based practice of mesotherapy in 2025. In this guideline, studies comparing mesotherapy with systemic drugs were mostly conducted in emergency department settings and on patients with acute pain, likely because follow-up time points are more feasible in these cases to prevent bias related to the duration of oral medication use. There are only two randomized controlled trials and one case-control study comparing mesotherapy with oral treatment in patients with neck pain, which reported that mesotherapy holds promise for pain reduction and functional improvement.[2,12,13] In this context, there is a noticeable lack of studies evaluating the effectiveness of mesotherapy in patients with acute and subacute nonspecific neck pain. Furthermore, our review of the literature revealed that the number of studies comparing the effectiveness of oral therapy and mesotherapy is limited.

This study aimed to address this gap by comparing the effectiveness of oral therapy and mesotherapy in patients with acute and subacute nonspecific neck pain and to contribute to the literature on the effectiveness of mesotherapy in terms of pain, disability, and range of motion (ROM).

PATIENTS AND METHODS

The randomized, single-blind study was conducted with 44 patients (6 males, 38 females; mean age: 46.8±11.1 years; range, 23 to 65 years) admitted to the Physical Medicine and Rehabilitation outpatient clinic at the İstanbul Haydarpaşa Numune Training and Research Hospital between October 30, 2023, and June 30, 2024, with nonspecific neck pain lasting less than three months were included in the study. The inclusion criteria were as follows: patients aged between 18 and 65 years, neck pain lasting less than three months, Visual Analog Scale (VAS) score ≥4, ability to follow verbal instructions, with no cognitive deficits. The exclusion criteria were as follows: neck pain lasting more than three months, history of physical therapy applied to the neck region in the last three months, radiculopathy, fracture, infection, and inflammation of the neck region, neurologic deficit, history of drug allergy, use of anticoagulant medications, history of malignancy, psychiatric disorders, renal or heart failure, liver disease, history of gastric ulcer or bleeding, pregnancy, presence of infection, wounds, allergies, or burn-like lesions at the application site. Written informed consent was obtained from all participants. The study protocol was approved by the Istanbul Medipol University Clinical Research Ethics Committee (Date: 02.12.2021, No: E-37106781-000-205889). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Initially, 50 participants were selected based on inclusion and exclusion criteria and randomized into two groups: the mesotherapy group (Group 1) and the oral treatment group (Group 2). Randomization was performed using a computer-generated randomization program.[14] Each group consisted of 25 patients. One patient from Group 1 and three patients from Group 2 did not complete the treatments. After treatment, one patient from Group 1 and one patient from Group 2 missed their follow-up visits. As a result, six patients were excluded from the study. Group 1 had 23 patients, and Group 2 had 21 patients, totaling 44 patients who completed the study (Figure 1).

The patients' age, sex, educational level, occupational status, marital status, height, weight, comorbid systemic diseases, medications used, and symptom duration of neck pain were recorded. Body mass index values were calculated in kilograms per square meter.

Study protocol

Patients in the first group underwent two sessions of mesotherapy to the neck region, performed at

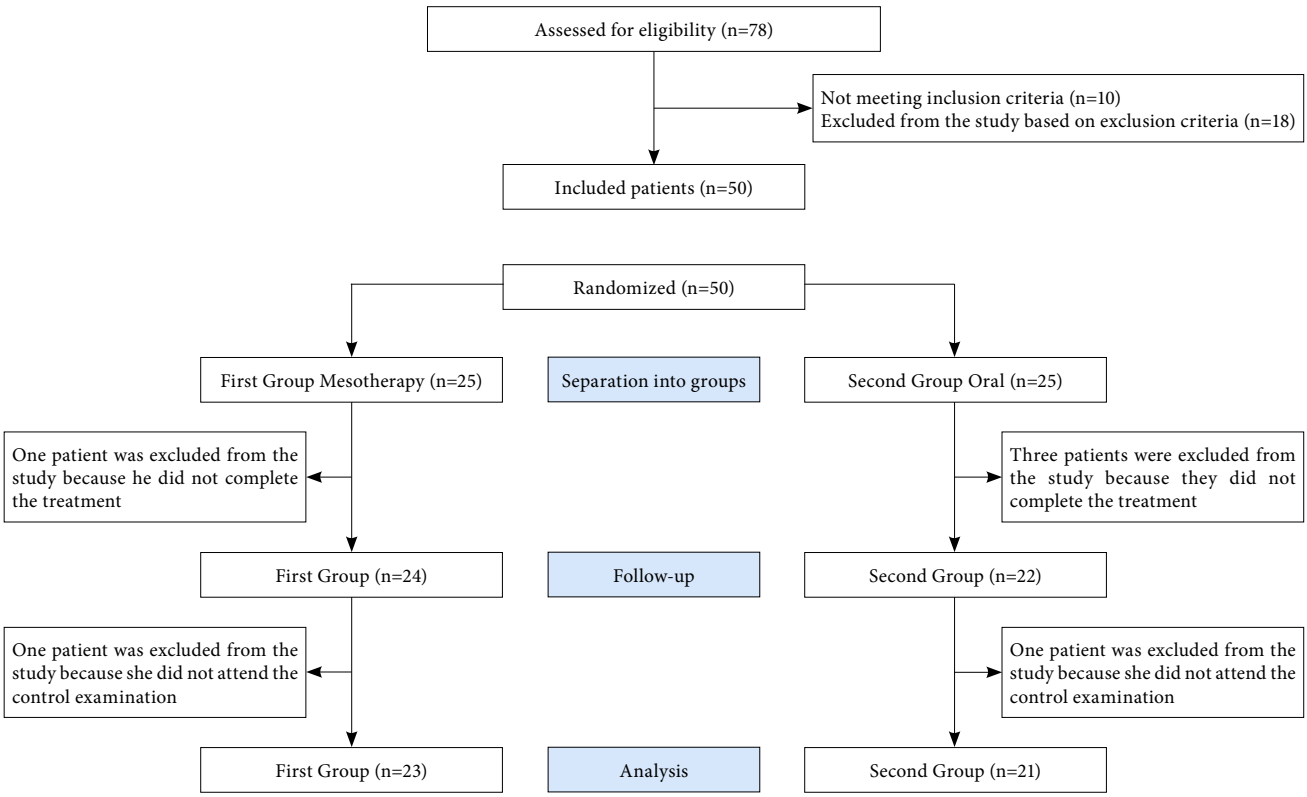

Figure 1. Flowchart of the study.

7-Day intervals. Intradermal mesotherapy was administered using the point-by-point technique at painful points in the neck with a 4-mm needle tip, injecting 0.1 mL per injection (Figures 2a, b). Subsequently, the nappage technique was used to apply mesotherapy in two bilateral rows along the cervical paravertebral muscles, extending from the occiput to the T1 vertebra.[6]

Figure 2. **(a)** Point-by-point technique, **(b)** nappage technique.

The solution used for the injections was prepared in the following sequence: 1 mL of 0.1% lidocaine, 1 mL of pentoxifylline, 1 mL of thiocolchicoside, and 1 mL of meloxicam diluted to one-fourth concentration. The injections were administered using a 30-gauge needle.[15] The obtained solution was used in varying amounts according to each patient's application area.

Patients were instructed to shower using only soap before their session and to avoid applying moisturizing cream, lotion, or perfume to the area before the procedure. After treatment, patients were advised to avoid showering for 12 h, protect the treated area from sunlight for 48 h, and refrain from physical therapy, heat applications, or applying creams or lotions to the treatment area for 24 to 48 h.

Patients in the second group were prescribed oral meloxicam 15 mg once daily and thiocolchicoside 8 mg twice daily for seven days.

Outcome parameters

The researcher who evaluated the outcome parameters was blinded to the patient groups.

Visual Analog Scale

The VAS consists of a 10-cm long horizontal or vertical line, with verbal descriptors at both ends to indicate the severity of pain. The patient is asked to mark the point on the line that best represents their pain. The VAS value is then determined based on the distance (in centimeters) from the start of the line to the point marked by the patient. In our study, VAS was used to assess the pain felt in the neck by the patients.

Neck Disability Index

The Neck Disability Index (NDI) was designed by Vernon and Mior[16] to assess how neck pain affects daily living activities. The Turkish validity and reliability study of this questionnaire was conducted by Aslan et al.[17] The scale consists of 10 sections: pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleep, and leisure activities. Each section contains six items scored from 0 (no disability) to 5 (total disability). In our study, the NDI was used to determine the disability level due to neck pain.

Cervical range of motion

The ROM of the cervical joints, measured with a goniometer from a fixed anatomical landmark, is the most reliable method for clinically assessing neck movement.[18] The universally used goniometer measures cervical ROM in flexion, extension, lateral flexion, and rotation.[19] In our study, patients were asked to sit upright during the measurements. Flexion and extension were measured in the sagittal plane, right and left lateral flexion in the coronal plane, and right and left rotation in the transverse plane.

Patients were evaluated before treatment, on Day 7 (after treatment), and on Day 14 (follow-up). In the first group, VAS scores and joint ROM were additionally assessed before each session and 30 min after the session. Side effects were monitored, specifically focusing on gastrointestinal side effects, allergies, diarrhea, and drowsiness.

Statistical analysis

The sample size was calculated using the G*Power software version 3.1.9.7 software (Heinrich-Heine Universität Düsseldorf, Düsseldorf, Germany). Based on reference studies, the effect size for comparing different parameters (VAS, NDI) between groups was determined to be 0.9.[15] Using an effect size of 0.9 and setting the significance level at 0.05 to achieve 90% power, it was determined that a minimum of 20 participants per group (40 participants in total) would be required. Considering a 20% dropout, the study was initiated with 50 participants.

All analyses were performed using IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics (frequency, percentage, mean, standard deviation, median, minimum, and maximum) were calculated. The assumption of normal distribution was checked using the Shapiro-Wilk test, and homogeneity of variances was tested using Levene's test. In cases where the normality assumption was met, Student's t-test was used for comparing two independent groups. If the normality assumption was not met, the Mann-Whitney U test was applied. For comparing three or more independent groups the Friedman test was used when normal distribution was not observed. To identify the group or groups responsible for the significant difference, post hoc Bonferroni and adjusted Bonferroni tests were conducted. To test the relationship between categorical variables, Pearson's chi-square test was applied when the sample size assumption (expected value >5) was met, and Fisher exact test was used when the sample size assumption was not met. The statistical significance level was set at $p<0.05$.

RESULTS

There was no significant difference between groups in terms of demographic characteristics (p>0.05). The demographic data are presented in Table 1. No side effects were observed in Group 1. One patient in Group 2 experienced diarrhea on Day 7 of follow-up after treatment.

Visual Analog Scale scores

In Group 1, VAS values significantly decreased 30 min after each session (p=0.009 and p=0.038, respectively). In both groups, the initial values showed significant improvement when comparing Day 7 and Day 14. There was no significant difference between the values on Day 7 and Day 14. (Table 2). There was no difference between groups before treatment, on Day 7, and on Day 14.

Neck Disability Index scores

In both groups, the baseline values showed significant improvement when comparing Day 7 and Day 14. There was no significant difference between the values on Day 7 and Day 14. There was no difference between groups before treatment, on Day 7, and on Day 14 (Table 3).

TABLE 1
Distribution of demographic characteristics and relationships between them according to study groups

	Group 1 (n=23)					Group 2 (n=21)					
Variables	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*
Age (year)			43,8±9,9					49,7±12,3			0.088*
BMI (kg/m^2)			25,81±4,35					27,02±3,25			0.305*
Duration of neck pain (week)			4.8±3.0	4	1-11			6.1±4.0	8	1-11	0.311‡
Sex											1.000#
Female	20	87.0				18	85.7				
Male	3	13.0				3	14.3				
Marital status											0.701#
Married	18	78.3				18	85.7				
Single	5	21.7				3	14.3				
Educational status											0.457#
Primary school	6	26.1				7	33.3				
Middle school	1	4.3				1	4.8				
High school	7	30.4				7	33.3				
Bachelor	9	39.1				4	19.0				
Postgraduate	0	0.0				2	9.5				
Comorbidity											0.139**
No	16	69.6				10	47.6				
Yes	7	30.4				11	52.4				

SD: Standard deviation; BMI: Body mass index; # Fisher exact test; * Student's-t test; ** Pearson Ki Kare test; ‡ Mann Whitney U test.

TABLE 2
Distribution and comparison of VAS scores according to study groups and measurement times

	Group 1			Group 2			
VAS	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Before treatment	6.5±1.3	6	5-10	5.9±1.4	5	4-10	0.102‡
After 1st session	4.2±2.0	4	0-10	-	-	-	
Day 7 (after treatment)	3.48±1.97	3	6-8	3.86±2.15	3	0-8	0.546*
After the 2nd session	1.9±1.8	2	0-	-	-	-	
Day 14 (follow-up)	2.6±2.3	2	0-8	3.9±2.4	4	0-8	0.088‡
Test statistics		58.387			11.676		
p		<0.001†			0.003†		

VAS: Visual Analog Scale; SD: Standard deviation; † Friedman test; ‡ Mann-Whitney U test; * Student's t-test.

TABLE 3
Distributions and comparison of NDI scores according to study groups and measurement times

	Group 1			Group 2			
NDI	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Before treatment	16.3±5.4	16	6-33	14.5±6.6	13	2-30	0.299‡
Day 7 (after treatment)	9.57±4.7	9	0-17	10.86±6.77	11	1-28	0.463*
Day 14 (follow-up)	7.57±3.85	7	0-15	10.86±7.38	11	0-25	0.077*
Test statistics		37.012†			6.276		
p		<0.001			0.016		

NDI: Neck Disability Index; SD: Standard deviation; ‡ Mann-Whitney U test; * Student's t-test; † Friedman test.

TABLE 4
Comparison of baseline ROM values of groups

	Group 1			Group 2			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Flexion (°)	52.39±9.03	55	30-60	46.9±10.66	50	30-60	0.057
Extension (°)	55.87±13.54	55	30-75	53.1±14.1	55	20-75	0.509
Right lateral flexion (°)	37.17±5.61	35	30-55	31.19±8.79	30	15-55	0.003*
Left lateral flexion (°)	36.52±6.98	40	20-45	34.05±8.75	35	10-45	0.368
Right rotation (°)	64.13±19.11	70	30-85	54.29±18.59	55	20-85	0.105
Left rotation (°)	62.17±21.42	70	10-85	63.57±14.24	65	30-85	0.840

ROM: Range of motion; SD: Standard deviation; * p<0.05; ‡ Mann-Whitney U test.

Range of motion

The ROM angles were not significantly different at baseline, except for right lateral flexion angles (Table 4). No statistically significant differences were found in terms of flexion, extension, right lateral flexion, left lateral flexion, right rotation, and left rotation angles measured by a goniometer (p=0.346, p=0.262, p=0.063, p=0.252, p=0.175, and p=0.489, respectively) within and between groups (Figure 3).

DISCUSSION

In this study, mesotherapy was compared to oral nonsteroidal anti-inflammatory drugs (NSAIDs) and muscle relaxants containing the same active ingredients in patients with acute to subacute nonspecific neck pain. Both groups showed significant improvements in VAS pain scores and NDI scores, with no significant difference between them. The observed pain reduction persisted through the 14th Day after treatment. However, no significant changes were observed in the ROM angles in either group.

Mammacuri et al.[11] recently published a guideline for mesotherapy in 2025. In this guideline, they referenced several studies on localized pain. Some studies analyzed the efficacy of mesotherapy by comparing it with systemic drug therapy, either intravenously or orally, while others compared it with placebo. As previously mentioned in a recent systematic review and meta-analysis,[5] demonstrating similar efficacy to systemic drugs is important for evidence-based medicine. The rationale for mesotherapy in pain management is to use less medication while achieving comparable effectiveness. Well-designed studies are necessary to substantiate this claim.

Kocak[20] compared a single session of mesotherapy, composed of tenoxicam, lidocaine, and thiocolchicoside, with intravenous ketoprofen in patients with trauma-related acute musculoskeletal pain. The mesotherapy group exhibited greater pain relief (VAS) with no reported side effects. However, in that study, Kocak[20] included a broader patient population with pain following acute musculoskeletal injuries without distinguishing specific regions

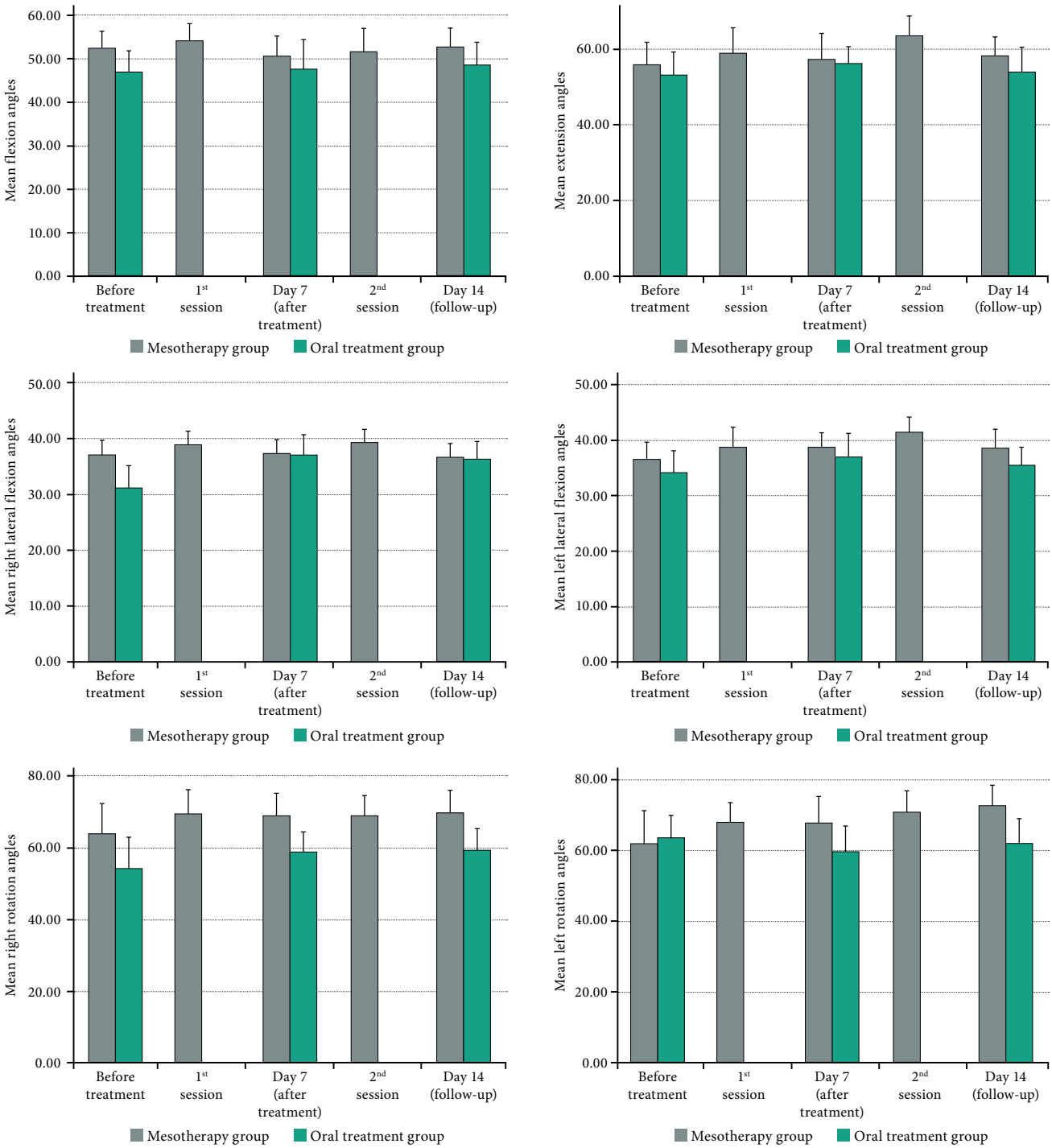

Figure 3. Cervical ROM angles of the groups over time.
ROM: Range of motion.

such as neck, shoulder, or lower back pain in the emergency department. Another study by Akbas et al.[21] investigated the efficacy of mesotherapy by comparing intravenous therapy with single-session mesotherapy in patients with low back pain in the emergency setting, finding similar results. Two other studies compared mesotherapy to placebo in acute low back pain[22,23] with one session, demonstrating superior outcomes over placebo. In acute painful conditions, analyzing the effect of a single session

is reasonable. We opted for two sessions because oral treatments typically last seven days, and equal follow-up duration without any treatment has been thought to be necessary to prevent bias. The recent guideline concluded that despite the number of examined studies, the quality of some of them was not adequate to draw strong conclusions or to develop standardized protocols specifying the number of sessions for certain conditions.[11] These studies also showed the immediate efficacy after 10 min to 120 min of mesotherapy application.[20,21] The immediate effect of mesotherapy was evaluated by assessing VAS scores 30 min after each session in our study, revealing a significant improvement similar to the results of those studies. It should be suggested that the efficacy of mesotherapy should start immediately and last for a longer duration than systemic drug administration.

Other studies on mesotherapy in chronic conditions involved three to nine sessions, primarily for low back pain and osteoarthritis, with follow-up periods of three to six months.[7,24-26] For example, Chen et al.[26] administered diclofenac twice daily for three months. Such prolonged durations of oral drug use pose a higher risk of side effects; therefore, we focused on acute cases. On the other hand, research on neck pain in this field is limited. Thus, evaluating the effect of mesotherapy in acute to subacute nonspecific neck pain was deemed more appropriate.

Studies investigating mesotherapy efficacy in patients with chronic neck pain, comparing either placebo (saline injections) or dry mesotherapy with 4-mm needles, have shown mesotherapy to be superior to control groups, particularly regarding VAS pain scores.[12,27] The number of sessions ranged from three to seven, typically weekly or twice weekly. Due to the retrospective design and methodological limitations, comparing these prior results with our study's findings may not be appropriate. Braueneis et al.[24] conducted a randomized study examining the effects of muscle relaxants or anti-inflammatory mesotherapy in patients with chronic neck or back pain and found both groups effective.

Only one case-control study evaluated the effects of mesotherapy on ROM angles in patients with bilateral cervicobrachial pain due to trapezius muscle spasm lasting at least 15 Days (10 patients).[1] They applied mesotherapy over eight sessions (twice weekly for the first two weeks, then weekly for the following four weeks) and observed significant improvements. However, our study did not find significant changes in ROM angles. Methodological differences, such as lack of control groups and broad symptom duration, may account for this discrepancy.

Our study focused on patients with acute and subacute pain, excluding chronic cases, and limited treatment to two sessions. The absence of ROM improvement suggests that medication alone, regardless of administration method or session number, may be insufficient to restore ROM in acute or subacute neck pain. A longer follow-up might have yielded different results regarding ROM angles. Koszela et al.[28] investigated the role of rehabilitation following spinal mesotherapy, emphasizing that rehabilitation is an essential step after mesotherapy to improve mobility; initiating exercise therapy after pain relief underscores its importance.

The studies investigating the efficacy of mesotherapy for neck pain, as far as we are aware, are limited to those we have discussed. Many of these studies have methodological issues, such as comparing mesotherapy solutions with different active ingredients, being retrospective, or using a single drug rather than a proper drug cocktail as defined by mesotherapy. Studies on mesotherapy for other musculoskeletal pain conditions are also limited, with fewer focusing on knee osteoarthritis and low back pain. These studies also have some methodologic flaws, such as a lack of detail on application techniques, comparisons of different NSAIDs via different routes or saline, and the use of corticosteroids for mesotherapy, which is not suitable for intradermal use.[7,21,25,26,29] These limitations highlight the need for well-designed studies that can effectively demonstrate the efficacy of mesotherapy. Given the methodology of our study, we believe it will make a significant contribution to the literature. Comparing the effects of the same active ingredients administered via mesotherapy versus the oral route is valuable for demonstrating the efficacy of mesotherapy. In our study, both groups received the same NSAID (meloxicam) and muscle relaxant (thiocolchicoside), allowing for a more direct comparison of treatment methods. It is important to note that conclusions about the superiority of mesotherapy based on studies using different active ingredients and administration routes, such as ketoprofen versus tenoxicam, may not be entirely accurate.

According to our literature search, there is only one well-designed study that evaluated the efficacy of mesotherapy on knee osteoarthritis.[15] In this randomized, single-blind study, one group received mesotherapy with 20 mg piroxicam and 2 mL of 2% lidocaine, while the other received 10 mg piroxicam orally. Both groups were given lifestyle changes and exercises. Significant improvements in VAS, the Western Ontario and McMaster Universities Arthritis Index (WOMAC), and Oxford Knee Score (OKS) scores were observed in both groups, with the mesotherapy group showing better results in WOMAC and OKS scores. This study had a larger sample size and longer follow-up, which are its strengths compared to our study.

Since there has been no previous study comparing mesotherapy and oral systemic treatments using the same active ingredients (NSAIDs and muscle relaxants), we believe our findings contribute to the literature. Based on our results, we can suggest that both mesotherapy and oral administration of the same NSAID and muscle relaxants have similar effects. Mesotherapy can be safely preferred in patients with comorbidities such as gastrointestinal, renal, and cardiovascular diseases, where systemic use of NSAIDs and muscle relaxants might be undesirable due to side effects.

One limitation of this study was the use of only two sessions for mesotherapy. Another limitation was the lack of long-term follow-up beyond 14 Days after treatment. A longer treatment duration or extended follow-up might have shown an effect on cervical joint ROM.

In conclusion, mesotherapy and oral treatment with the same active ingredients (NSAIDs and muscle relaxants) had the same effects in patients with acute and subacute neck pain. No side effects were observed during the treatment process, and mesotherapy was found to be a safe treatment option. The current literature shows that there are very few well-designed studies on pain management through mesotherapy, highlighting the need for further research. Advanced studies are required to determine the most effective active ingredient, optimal number of sessions, and ideal follow-up duration.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea, critical review: D.G.K., N.M.; Design: D.G.K.; Control: E.P.U., D.G.K.; Data collection, materials, analysis: D.G., B.G., E.P.U.; Literature review: D.G., E.P.U.; Writing: D.G., D.G.K., B.G.; references: D.G., B.G., E.P.U., D.G.K.

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