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Therapeutic effect of mesotherapy on pain in patients with knee osteoarthritis

Терапијски ефекат мезотерапије бола код пацијената са остеоартритисом колена

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SUMMARY

Introduction/Objective Knee osteoarthritis is a progressive, degenerative disease of the knee joint that can eventually lead to disability. Clinical mesotherapy is an intradermal therapy used for injecting diluted pharmacological substances into the superficial layer of the skin at multiple points. The objectives of this study were to determine the therapeutic effect of mesotherapy on pain in patients with knee osteoarthritis treated with a mixture of Zodol and Lidocaine, compared to patients with knee osteoarthritis treated with Lidocaine alone.

Methods Participants were randomly assigned into two groups. The experimental group, in which patients were treated with an injection containing a mixture of Lidocaine without adrenaline and of Zodol. The control group was treated with Lidocaine solution without adrenaline.

Results There is a statistically significant difference in pain intensity after the second dose of mesotherapy and one month after the fourth dose of mesotherapy. WOMAC scale values were significantly higher in patients in the control group. Also, there is a statistically significant difference in pain intensity after the second dose of mesotherapy and one month after the fourth dose of mesotherapy. The frequency of patients experiencing moderate and severe pain was significantly higher in the control group, while the frequency of patients reporting no pain or only mild pain was significantly higher in the experimental group.

Conclusion The therapeutic effect of mesotherapy on pain in patients with knee osteoarthritis in experimental group is more effective and longer-lasting compared to patients treated with Lidocaine alone.

Keywords: mesotherapy on pain; knee osteoarthritis; intradermal therapy

САЖЕТАК

Увод/Циљ Остеоартритис колена представља дегенеративну, прогресивну болест зглоба колена која на крају може довести до инвалидитета. Клиничка мезотерапија представља интрадермалну терапију која се користи за убризгавање разблажених фармаколошких супстанци у површински слој коже у више тачака. Циљеви истраживања били су утврдити терапијски ефекат мезотерапије бола код пацијената са остеоартритисом колена који су третирани мешавином зодола и лидокаина, у односу на пацијенте са остеоартритисом колена који су третирани само лидокаином.

Методе Проспективна студија, где су учесници насумично распоређени у две групе, прву чини радна група у којој су пацијенти третирани инјекцијом која је садржала смешу лидокаи-на без адреналина и зодола. Контролна група би-ла је третирана раствороа лидокаина,без адреналина.

Резултати Постоји статистички значајна разлика у интензитету бола после друге дозе мезотерапије и месец дана након четврте дозе мезотерапије. Вредности *Womac* скале су значајно више код пацијената у контролној групи. Такође, постоји статистички значајна разлика у интензитету бола после друге дозе мезотерапије и месец дана након четврте дозе мезотерапије. Учесталост пацијената који осећају умерен и јак бол је значајно већа у контролној групи док је учесталост пацијената који немају бол и који имају благи бол значајно већа у радној групи.

Закључак Терапијски ефекат мезотерапије бола код пацијената са остеоартритисом колена у експерименталној групи је ефикаснији и дуготрајнији него што је то случај са пацијентима који су третирани само лидокаином.

Кључне речи: мезотерапија бола; остеоартритис колена; интрадемална терапија

INTRODUCTION

Knee osteoarthritis is a degenerative joint disease that occurs as a result of progressive loss of articular cartilage. It most commonly affects older adults. It can be divided into two types: primary and secondary. Primary osteoarthritis occurs without any apparent cause, while secondary osteoarthritis can result from other conditions, most commonly including post-

traumatic and post-surgical states, rickets, gout, and others. Common clinical symptoms include knee pain, which develops gradually and worsens with activity, as well as stiffness and swelling of the knee. Treatment of knee osteoarthritis begins with conservative methods, and if these do not yield results, surgical treatment is considered [1]. Nonsteroidal anti-inflammatory drugs are the first line of treatment for knee osteoarthritis. However, patients who cannot take these medications or do not respond to them may try intra-articular corticosteroid injections, which usually relieve pain for several weeks. When it comes to non-pharmacological treatment, patient education, weight loss (for those who are overweight), and exercise play important roles. Exercises usually focus on strengthening the muscles of the lower limbs, which helps reduce pain and improve functional status [2].

Clinical mesotherapy

Therapeutic skin injections date back to ancient Chinese and Indian medicine. In 1958, Michel Pistor introduced the term "mesotherapy" to describe the inoculation of drugs into the superficial layer of the skin [3].

Clinical mesotherapy is an intradermal therapy used to inject diluted pharmacological substances into the superficial layer of the skin at multiple points, at a depth of 3–4 mm. Specifically, this involves the use of a short needle to deposit the drug into the dermis. The intradermal microdeposit modulates the drug's kinetics by slowing absorption and prolonging the local mechanism of action [3, 4, 5]. This technique involves infiltrating a small amount of the drug into the superficial layer of the skin, observing the painful area. When injected intradermally, the drug diffuses into the tissues and joints, remaining for a longer period than with intramuscular administration. The goal of mesotherapy is to achieve the therapeutic benefit with lower drug doses when other options have failed, cannot be used, or are unavailable [6]. Many localized pain syndromes benefit from mesotherapy; in fact,

mesotherapy is used to treat localized pain, resulting in improved quality of life [7]. Mesotherapy on pain is a safe method and has no adverse effects [4].

The mesotherapy technique involves the inoculation of the drug using a 4 mm (27G) or 13 mm (30–32G) needle. The angle of the needle depends on the area being treated. The technique requires medical and pharmacological knowledge and must be performed in accordance with disinfection protocols (appropriate disinfectants are necessary) using sterile single-use devices [3]. It should be noted that despite the widespread use of mesotherapy, certain uncertainties still exist, and further preclinical and clinical research is needed to define its role in clinical practice [6]. Although it has a wide range of applications, there is still no standardized protocol. For these reasons, every study conducted in the field of mesotherapy is highly valuable [8].

METHODS

The study was designed as a prospective randomized, double-blind study and was conducted at the Clinical Hospital Center Kosovska Mitrovica, in the Department of Physical Medicine and Rehabilitation, over a period of 8 weeks. The randomization code was generated used a computer- generated random number sequence, where participants was assigned in two groups in 1:1 ratio. The randomization list was prepared by an independent person not involved in participant selection. The approval for conducting this study was obtained from the Ethics Committee of the Health Center in Kosovska Mitrovica. A total of 59 patients were included in the study - 16 male and 43 female patients. Although a formal statistical power analysis was not conducted prior to the start of research, the number of participants was sufficient to perform the planned statistical analysis and to monitor changes in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and VAS scales at defined time points. The

experimental group consisted of 31 patients, while the control group included 28 patients. The average age of patients in the experimental group was 58.7 ± 14.5 years, and in the control group 60.3 ± 15 years. The study was conducted after obtaining written informed consent from all participants. All patients were diagnosed with knee osteoarthritis prior to the study. During medical history taking, attention was paid to possible allergic reactions to the medication and the use of anticoagulant therapy, which are absolute contraindications for performing this procedure. Pain was assessed using the Visual Analogue Scale (VAS) – before the start of the study, after the second dose, and one month after the fourth dose. Functional status was assessed using the WOMAC scale – at the beginning of the study, after the second dose, and one month after the fourth dose. The Visual Analogue Scale (VAS) is a tool used to measure pain intensity. The scale is typically a 10-centimeter (or 100-millimeter) line marked from 0 to 10 or 0 to 100. The far-left point represents no pain (0), while the far-right point represents unbearable pain (10 or 100). Patients mark the point on the line that corresponds to their current pain intensity. The WOMAC is a questionnaire used to measure osteoarthritis symptoms in patients with knee or hip osteoarthritis. The scale covers three domains: pain, stiffness, and functional limitations. Results are measured on a Likert scale from 0 to 4, where 0 indicates "none" and 4 indicates "extreme" symptoms. Higher scores indicate greater levels of pain, stiffness, and functional impairment.

A detailed medical history was taken from all patients, followed by a clinical examination and knee radiography. Participants were randomly assigned into two groups. The first was the experimental group, in which patients were treated with an injection containing a mixture of 1 mL of 1% Lidocaine without adrenaline (Lidocainechlorid, Galenika 1%, 35 mg/3.5 mL, Belgrade, Republic of Serbia) and 1 mL of Zodol (Zodol, 30 mg/mL, Hemofarm, Vršac, Republic of Serbia). The control group was treated with 1 mL of a Lidocaine solution without adrenaline (Lidocaine-hlorid, Galenika 1%, 35 mg/3.5 mL, Belgrade, Republic of Serbia). The

mesotherapy protocol involved the use of sterile, single-use 2.5 mL syringes with a 30G x 4 mm needle, inserted at a 90-degree angle against the skin. Each patient received injections once a week, for a total of 4 doses, with the fourth dose administered one month after the third. Patients were treated using the "point-by-point" technique, targeting painful areas around the knee.

Before enrolment in the stady and initiation of mesotherapy for pain menagment, participants were fully informed about the stady protocol and declared that NSAID therapy has been discontinued at least 10 days prior to treatment and that no medications from this group werw used trought the duration of the stady.

Descriptive methods and statistical hypothesis testing methods were used for the analysis of primary data. Among the descriptive statistical methods, measures of central tendency (arithmetic mean and median), measures of variability (standard deviation and range), and relative numbers were applied. For hypothesis testing, the Mann–Whitney test and the Friedman test were used. Statistical analysis was performed using the SPSS 21 software package. Statistical hypotheses were tested at a significance level of 0.05.

RESULTS

A total of 59 patients were included in the study - 16 male and 43 female patients. The experimental group consisted of 31 patients, while the control group included 28 patients. The average age of patients in the experimental group was 58.7 ± 14.5 years, and in the control group 60.3 ± 15 years.

There is a statistically significant difference in pain intensity according to the WOMAC scale after the second dose of mesotherapy and one month after the fourth dose. WOMAC scores were significantly higher in patients in the control group (Table 1).

Similarly, there is a statistically significant difference in pain intensity according to the VAS scale after the second dose of mesotherapy and one month after the fourth dose. The frequency of patients experiencing moderate and severe pain was significantly higher in the control group, whereas the frequency of patients with no pain or mild pain was significantly higher in the experimental group (Table 1).

There is a statistically significant difference in WOMAC scale values over time in patients in the experimental group. WOMAC scores decreased significantly over time (Table 2).

A statistically significant difference in WOMAC scale value over time was observe in patients in the control group. WOMAC scores decreased after the second dose, but increased again after the fourth dose (Table 3).

Also, a statistically significant difference was observed in the frequency of patients in the experimental group with varying pain intensity according to the VAS scale over time. The frequency of patients without pain increases over time. The frequency of patients with mild pain rises initially and then decreases, while the frequency of patients with moderate and severe pain decreases over time (Table 4).

There is a statistically significant difference in the frequency of patients in the control group with varying pain intensity according to the VAS scale over time. The frequency of patients with mild pain rises initially and then decreases, while the frequency of patients with

moderate pain stagnates then decreases, and the frequency of patients with severe pain decreases at first, but then increases over time (Table 5).

DISCUSSION

Mesotherapy is recognized as an effective alternative therapy for localized pain management [9], with studies demonstrating a reduction in neck and lower back pain by at least 50% compared to baseline levels [10]. In the context of acute conditions, Akbas et al. [11] observed that mesotherapy provides a statistically significantly greater reduction in pain intensity at 15 minutes, 30 minutes, and 24 hours post-treatment compared to intravenous dexketoprofen administration. These findings are further supported by Costantino et al. [12], who suggested that mesotherapy, using a combination of lidocaine, ketoprofen, and methylprednisolone, represents a valid alternative to conventional systemic administration of NSAIDs and corticosteroids for acute low back pain. Furthermore, it has been shown that mesotherapy can achieve therapeutic effects equivalent to systemic drug administration [13], but with a significantly more favorable safety profile. Specifically, Chen et al. [14] noted that mesotherapy resulted in fewer adverse effects, particularly regarding hemorrhage and WOMAC scores, when compared to traditional NSAID treatments.

The efficacy of this method extends to chronic syndromes as well. In patients with chronic lumbar syndrome and chronic thoracic spine pain, studies by Pires et al. [15] and Koszela et al. [16] both demonstrated that mesotherapy with type I collagen yields statistically significant improvements compared to lidocaine alone. Similarly, Ranieri et al. [17] reported reduced pain intensity and functional improvement in patients with bilateral cervicobrachial syndrome following a six-week treatment protocol.

In our study, the application of a Zodol and Lidocaine mixture produced superior results in symptom reduction for knee osteoarthritis compared to lidocaine monotherapy. This aligns with the research by Narangerel et al. [18], who found that a combination of Meloxicam and Lidocaine significantly outperformed physiological saline, with positive effects appearing within four weeks and lasting up to three months. These results are consistent with the conclusions of Reza Farpour and colleagues [19], who identified Piroxicam mesotherapy as an effective and safe procedure for patients with mild to moderate knee osteoarthritis. Collectively, these data underscore the clinical value of mesotherapy as a targeted, potent, and safe intervention for both spinal disorders and osteoarthritis-related pain.

CONCLUSION

The therapeutic effect of mesotherapy on pain in patients with knee osteoarthritis treated with a mixture of Lidocaine and Zodol is more effective and longer-lasting compared to patients treated with Lidocaine alone.

Conflict of interest: None declared.

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Table 1. Pain according Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and visual analogue scale (VAS) in experimental and control group

Parameters	Experimental group n (31)	Control group n (28)	p
WOMAC scale at the start of the study, median (range)	68 (28-90)	67 (34-96)	0.843
WOMAC scale after the second dose of mesotherapy, median (range)	33 (0-64)	55 (20-96)	< 0.001
WOMAC scale one month after the fourth dose of mesotherapy, median (range)	16 (0-64)	66 (26-96)	< 0.001
VAS scaleat the start of the study, n (%) No pain Mild pain Moderate pain Severe pain	/ 1 (3.2) 14 (45.2) 16 (51.6)	/ 0 (0) 16 (57.1) 12 (42.9)	0.602
VAS scale after the second dose of mesotherapy, n (%) No pain Mild pain Moderate pain Severe pain	5 (16.1) 17 (54.8) 9 (29) 0 (0)	0 (0) 6 (21.4) 16 (57.1) 6 (21.4)	< 0.001
VAS scale one month after the fourth dose of mesotherapy, n (%) No pain Mild pain Moderate pain Severe pain	20 (64.5) 9 (29) 2 (6.5) 0 (0)	0 (0) 2 (7.1) 13 (46.4) 13 (46.4)	< 0.001

Table 2. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale in experimental group over time

Experimental group	**n (31)**	**p**
Start of the study, median (range)	68 (28–90)	< 0.001
After the second dose, median (range)	33 (0–64)	
After the fourth dose, median (range)	16 (0–64)	

Table 3. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale in control group over time

Control group	**n (28)**	**p**
Start of the study, median (range)	67 (34–96)	< 0.001
After the second dose, median (range)	55 (20–96)	
After the fourth dose, median (range)	66 (26–96)	

Table 4. Visual analogue scale (VAS) in experimental group over time

Experimental group	**n (31)**	**p**
Start of the study, n (%)		
No pain	/	
Mild pain	1 (3.2)	
Moderate pain	14 (45.2)	
Severe pain	16 (51.6)	
After the second dose, n (%)		
No pain	5 (16.1)	
Mild pain	17 (54.8)	< 0.001
Moderate pain	9 (29)	
Severe pain	/	
After the fourth dose, n (%)		
No pain	20 (64.5)	
Mild pain	9 (29)	
Moderate pain	2 (6.5)	
Severe pain	/	

Table 5. Visual analogue scale (VAS) over time

Control group	**n (28)**	**p**
Start of the study, n (%)		
No pain	/	
Mild pain	/	
Moderate pain	16 (57.1)	
Severe pain	12 (42.9)	
After the second dose, n (%)		
No pain	/	
Mild pain	6 (21.4)	< 0.001
Moderate pain	16 (57.1)	
Severe pain	6 (21.4)	
After the fourth dose, n (%)		
No pain	/	
Mild pain	2 (7.1)	
Moderate pain	13 (46.4)	
Severe pain	13 (46.4)	

