VAN TIP DERGİSİ Medical Journal

CLINICAL RESEARCH / KLİNİK ÇALIŞMA

Van Tıp Derg 30 (4):321-326, 2023
DOI: 10.5505/vtd.2023.15146

The Effect of Glucosamine, Hyaluronic acid, Methyl Sulfomethane (MSM), Chondroitin Sulfate, and Type 2 Collagen Treatment on Facet Joint Syndrome

Faset Eklem Sendromunda Glukozamin, Hyalüronik asit, Metil Sülfometan(MSM), Kondroitin Sülfat ve Tip 2 Kollajen Tedavisinin Etkisi

Abdulsamet Emet, Yunus Demirtas

Department of Orthopedics and Traumatology, Yuksek Ihtisas University, Liv Hospital, Ankara, Turkey

Abstract

Introduction: Facet joint syndrome is one of the leading causes of low back pain, which can result in disability and loss of workforce. In this study, the effect of combined nutrition therapy in the treatment of lumbar facet joint syndrome was investigated.

Materials and Methods: A total of 28 patients aged 25-50 years, who received combined treatment for at least 3 months with the diagnosis of lumbar facet joint syndrome after evaluation of MRI, were included in the study. Patients were invited to their last check-up and their pre-and post-treatment VAS scores and Roland-Morris scores were evaluated and compared.

Results: Of the total 28 patients included in the study, 15 were male and 13 were female. The mean age of male patients was 39.9±1.5 and the mean age of female patients was 42.6±1. The mean VAS score of all patients was 7.7±0.8 before treatment and 2.60±0.8 after treatment. A significant difference was found when the mean VAS scores of all patients were compared before and after treatment. The mean pre-treatment Roland-Morris(RM) score of all patients was 18.7±2 and it was 4.6±2.8 after treatment. A significant difference was found when the RM score of all patients was compared before and after treatment.

Conclusion: Combined supportive therapies seem to be effective in the treatment of lumbar facet joint syndrome.

Keywords: Back pain; osteoarthritis; facet joint syndrome; supplementation.

Özet

Giriş: Faset eklem sendromu, sakatlığa ve iş gücü kaybına yol açabilen bel ağrısının önemli sebeplerinden bir tanesidir. Lomber faset eklem sendromu yaygınlığı ise %5-90 arasında değişmektedir. Bu çalışmada lomber faset eklemin sendromunun tedavisinde kombine nütrisyon tedavisinin etkisi araştırıldı.

Gereç ve yöntem: Lomber faset eklem sendromu tanısı ile Kasım 2022-Ocak 2023 tarihleri arasında en az 3 ay kombine tedavi alan 25-50 yaş arası toplam 28 hasta çalışmaya dahil edildi. Hastaların Manyetik Rezonans Görüntüleri (MRG) değerlendirilerek Evre 1-2 hastalar çalışmaya dahil edildi. Hastalar son kontrollerine çağırılarak tedavi öncesi ve sonrası VAS skorları ve Roland-Morris skorları değerlendirilerek karşılaştırıldı.

Bulgular: Çalışmaya dahil edilen toplam 28 hastanın 15'i erkek, 13'ü kadındı. Erkek hastaların yaş ortalaması 39.9±1.5, kadın hastaların yaş ortalaması 42.6±1 idi. Tüm hastaların ortalama VAS skoru tedavi öncesi 7.7±0.8, tedavi sonrası 2.60±0.8 idi. Tedavi öncesi ve sonrası tüm hastaların ortalama VAS skorları karşılaştırıldığında anlamlı fark bulundu. Tüm hastaların tedavi öncesi ortalama Roland-Morris(RM) skoru 18.7±2, tedavi sonrası 4.6±2.8 idi. Tedavi öncesi ve sonrası tüm hastaların RM skorları karşılaştırıldığında anlamlı fark bulundu.

Sonuç: Lomber faset eklem sendromu tedavisinde kombine destek tedavileri etkin olarak gözükmektedir.

Anahtar Kelimeler: Bel ağrısı; osteoartrit; faset eklem sendromu; takviye.

Introduction

Low back pain is a complaint that causes a significant number of applications to orthopedics, physical therapy, and brain surgery outpatient clinics, as well as causing patients to be left out of the workforce and financial loss (1). Pain may occur due to discogenic, visceral organ, sacroiliacjoint, muscle, and trauma, as well as after degenerative processes (2). In the literature, low back pain is reported to occur at a rate of 5% each year, and some studies emphasize that the rate will increase by as much as 90% throughout one's lifetime (3, 4). Low back pain due to lumbar facet joint syndrome varies between 15% and 45% of all causes of pain (1, 4). Lumbar facet joint syndrome is a mechanical instability syndrome of the zygapophyseal joints in the lumbar spine due to degenerative and micro traumatic causes. Goldwait et al. was the first to state in 1911 that low back pain originates from the lumbar facet joints. Later, in 1933, Ghormley et al. suggested that there might be nerve compression due to hypertrophy of the facet joints and coined the

***Corresponding Author:** Abdulsamet Emet, M.D.And sok. 5B-13 Cankaya, Ankara E-mail: drsametemet@gmail.com
Orchid: 0000-0001-5415-218X, Yunus Demirtaş 0000-0002-4866-4127

Received:23.07.2023, Accepted:12.09.2023

term facet joint syndrome (5, 6). In the diagnosis of lumbar facet joint syndrome, three-dimensional(3D) radiographs, Magnetic Resonance Imaging (MRI), and Computed Tomography (CT), are used (7). After diagnosis, multimodal principles are applied as the first-line treatment method (8). In the acute period, analgesics and non-steroidal anti-inflammatory drugs are used, while in chronic patients percutaneous interventional procedures and surgical treatment are preferred. While there are studies in the literature on the use of glucosamine and MSM together with glucosamine in the treatment of facet joint syndrome, there are no studies on the combined treatment method that is safely used, particularly degenerative arthritis (9). In this study, it was aimed to investigate the effect of the combined treatment method on the treatment of lumbar facet joint syndrome.

Materials and Methods

A total of 33 patients, aged 25-50 years, who applied to the outpatient clinic between November 2022 and January 2023, had low back pain for at least 3 weeks and did not have a chronic disease, who received daily combined therapy (1440 mg Glucosamine, Chondroitin 840 mg, MSM 900mg, Aselbent Extract 300mg omega-3 300 mg, 180 mg vitamin C, 150 mg of magnesium, hyaluronic acid 60 mg, type-2 Collagen 30mg, Zinc 15 mg, Manganese 2 mg, 15 µg vitamin D3, *Vitendo Combo Tedafarma, Izmir, Turkey*) for at least 3 months, were included in the study. A total of 5 patients with spinal diseases other than facet joint syndrome (Discopathy, spondylolysis, spondylolisthesis, spinal stenosis) or rheumatic diseases were excluded from the study. MRI (Magnetic Resonance Imaging) classification system was used as the staging system (2). MRI sections of the patients were evaluated and classified by two different surgeons. Within this classification used, Stage 1-2 patients were included in the study. For each patient Non-steroidal anti-inflammatory drugs were given as a salvage intervention when combined nutritional therapy failed to relieve the patient's pain. Non-steroidal anti-inflammatory drugs were started to be used only when patients felt pain, they were not included in routine treatment. Combined treatment was supported by low back muscle exercises that they could do at home in all patients. It was learned that these exercises were performed regularly by the patients at their last control. The patients were not included in the regular physical therapy unit control. Patients were called to their last check-up and their pre-and post-treatment VAS scores and Roland-Morris scores were filled in and compared. The preparation used in this study is available as a food supplement in our country with the approval of the Ministry of Agriculture.

Ethical approval: The study began after receiving approval from the local ethics committee (Yuksek Ihtisas University, Liv Private Hospital 2023/006). Written informed consent was obtained from each patient.

Statistical analysis: The SPSS version 22 program was used for data analysis. All the data were expressed as means ± standard deviation (SD). Data were tested for normality using the skewness and kurtosis test, Kolmogorov–Smirnov or Shapiro–Wilk tests, histo- gram. Continuous variables presented as mean ± SD for normally distributed variables. The paired t-test was used for comparing the difference in VAS and RMS before and after treatment. The significance level was set at $p < 0.05$.

Results

Of the 28 patients included in the study, 15 were male and 13 were female. The mean age of male patients was 39.9±1.5 and the mean age of female patients was 42.6±1. When the patients were examined in terms of age distribution, no significant difference was found between male and female groups ($p>0.05$). The mean VAS score of all patients was 7.7±0.8 before treatment and 2.60±0.8 after treatment. The mean pre-treatment VAS score of male patients was 7.7±0.1, while it was 7.6±2.8 for female patients. The mean VAS score of male patients was 3±0.1 after treatment, while it was 2.1±0.1 for female patients. A significant difference was found in the pre-treatment and post-treatment VAS scores of all patients ($p=0.000$). The mean pre-treatment Roland-Morris (RM) score of all patients was 18.7±2 and it was 4.6±2.8 after treatment. While the RM score of male patients was 19±0.4 before treatment, it was 4.8±0.8 after treatment. The RM score of female patients was 18.3±0.6 before treatment and 4.3±0.8 after treatment. A significant difference was found when the pre-treatment and post-treatment RM score of all patients was compared ($p=0.000$) (Table 1). Of all patients, 14 were stage 1, and 14 were stage 2. Table 2 shows the comparisons of mean VAS and RM scores.

Table 1: The mean VAS and RM scores of the patients by gender

	Gender	N	Mean ± standard deviation
VAS Pre-T*	Male	15	7.7±0.5
	Female	13	7.6±1
VAS Post-T*	Male	15	3±0.7
	Female	13	2.1±0.6
RM Pre-T*	Male	15	19±1.8
	Female	13	18.3±2.2
RM Post-T*	Male	15	4.8±3.1
	Female	13	4.3±2.7

***Pre-T:** Pre-treatment, **Post-T:** Post-treatment*

Table 2: Comparison of VAS and RM scores before and after treatment

	Mean ± standard deviation	P-value*
pre-post treatment VAS score	5.1±1	p=0.000
pre-post treatment RM score	14.1±3	p=0.000

** paired t-test*

Discussion

In this study, it was found that combined therapy in the treatment of lumbar facet joint syndrome was beneficial in the short term in relieving the pain of the patients and maintaining their daily life activities. Adding this treatment to patients' standard conservative treatment modality as additional supplementation provides an improvement in patients' recovery process. After definition of facet joint syndrome nearly a hundred years ago, treatment for this syndrome has evolved to the present day (5). As a first line of treatment, conservative treatment is the most commonly used modality. Besides percutaneous minimally invasive interventions, surgical modalities are employed in cases where pain control cannot be achieved. In the acute period, analgesics, myorelaxants, and bed rest are used in the treatment. In cases where there is no response to these treatments, opioid agents may be preferred in treatment (10, 11). After the acute period has passed, physical therapy techniques applied at the appropriate time play a key role in the treatment of patients. For this purpose, manipulations, stretching exercises, strengthening exercises of the abdominal and gluteal muscles, as well as manipulation of the paravertebral muscles, increase the circulation of the disc and facet and show clinical effects (12). For patients that do not respond to these treatments, facet joint injections or radiofrequency ablation significantly contribute to the relief of pain and the patient's return to social life (13, 14). The aim of all these treatment modalities is to relieve pain. Nutritional support in the treatment of osteoarthritis has been a controversial issue in the literature for a long time. Cartilage degeneration and the lack of healing capacity have prompted all researchers to investigate the factors affecting cartilage metabolism and recovery. For this purpose, researchers evaluated the effects of glucosamine, chondroitin sulfate, type 2 collagen, and MSM on osteoarthritis (15). These compounds, whether endogenously produced or obtained from dietary

sources, have garnered considerable attention for their potential to modulate the pathophysiological processes underlying OA. Their purported mechanisms of action include the preservation of cartilage integrity, reduction of inflammation, and attenuation of pain. Glucosamine is a precursor for glycosaminoglycan (GAG) synthesis, a major component of cartilage. It enhance cartilage repair and stimulate chondrocytes to produce more collagen and proteoglycans, essential for cartilage structure and function (16). Secondly, Hyaluronic acid possess anti-inflammatory properties, reducing the production of inflammatory mediators (17). Also, Methyl Sulfomethane (MSM) reduce inflammation by inhibiting the production of inflammatory cytokines, such as IL-6 and IL-1β, act as an antioxidant, protecting joint tissues from oxidative damage and modulate pain transmission by influencing nerve signal conduction (18, 19). Thirdly, Chondroitin Sulfate enhance water retention in cartilage, contributing to its shock-absorbing properties (20). In the article published by Hocberg et al. in 2013 on chondroitin sulfate, they emphasized that it reduces proinflammatory cytokines, regulates cartilage metabolism/catabolism balance, and affects apoptosis. Moreover, the researchers argued that with these effects, it reduces the use of analgesics and improves the symptoms of osteoarthritis. Furthermore, they reported that it also has an effect on cartilage volume. They also emphasized that it is involved in the treatment algorithm for hip, knee, and hand osteoarthritis (21). There is a consensus in most meta-analyses that it delays osteoarthritis and improves symptoms (21-23). It has been suggested that these nutritional supports may also be effective in facet joint degeneration. In the literature, however, there are few studies on this subject. The most studied molecule for this purpose is associated with glucosamine and MSM. In a study by Tant et al., 32 of a total of 36 patients were able to complete the study, and they found a significant improvement in functional scores and VAS scores in all patients who used glucosamine for 12 weeks in all patients (24). Reena et al. concluded, however, that there is controversy regarding whether glucosamine can prevent the development of lumbar osteoarthritis and chronic low back pain (25). There is no study in the literature on the effectiveness of combined preparations in the treatment of lumbar facet joint syndrome. In this study, combined preparations used for 3 months improved the post-treatment VAS and RM scores compared with the pre-treatment scores. This suggests that there is a combined effect of Type-2 Collagen, Hyaluronic Acid, Chondroitin Sulfate as well as Glucosamine, which supports cartilage metabolism. In addition, Manganese, Zinc and vitamin D3 have affected the cartilage metabolism, leading to the possibility of being involved in the improvement of the patient's clinic results.

Study limitations: Our study has some limitations. First, the small number of patients might have affected the results. Hence, working with larger patient groups will provide more accurate results. Secondly, the follow-up period was 3 months. Long-term follow-up may affect the results. Thirdly, there is no control group in the study. Further studies with including well-designed randomized controlled trials, can further elucidate the comparative efficacy of these treatments. Also, due to the short follow-up period of our patients, they were not re-evaluated radiologically.

Conclusions

In conclusion, in addition to relieving pain in the treatment of lumbar facet joints, the use of cartilage-preserving or healing agents will be a targeted treatment. Although research on this subject is still ongoing, we believe that combined nutritional support treatments in addition to standard conventional methods such as analgesics, non-steroidal anti-inflammatory drugs, and physical therapy improve pain scores and increase functional capacity in the acute period.

Ethics approval: Yuksek Ihtisas University, Liv Private Hospital, decision number: 2023/006

Conflict of interest: Authors have no competing interest to declare.

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

Authors contributions: A.E and Y.D. conceived this study, designed tool and protocol. Data collection was undertaken by Y.D. Initial analysis and data integration were undertaken by A.E undertook the initial draft of the manuscript, and A.E. and Y.D. contributed substantially to subsequent drafts and revisions.

Availability of data and materials: The data used and/or analyzed during the current study are available from the corresponding author on reasonable request

Acknowledgments: The authors thank to all hospital for their high efforts. The authors also thank Sadiye Dicle Canoruç Emet for her

knowledge on statistical analysis and her contributions to the authors.

References

1. Perolat R, Kastler A, Nicot B, Pellat J-M, Tahon F, Attye A, et al. Facet joint syndrome: from diagnosis to interventional management. Insights into imaging 2018;9(5):773-89.
2. Şenel FBK. Lumbar Facet Syndrome. Turk J Osteoporos 2013:19;90-94
3. Civelek E, Cansever T, Kabatas S, Kircelli A, Yilmaz C, Musluman M, et al. Comparison of effectiveness of facet joint injection and radiofrequency denervation in chronic low back pain. Turkish neurosurgery 2012;22(2);200-206.
4. Proietti L, Schirò G, Sessa S, Scaramuzzo L. The impact of sagittal balance on low back pain in patients treated with zygoapophysial facet joint injection. European Spine Journal 2014;23:628-633.
5. Je G. The lumbosacral articulation. An explanation of many cases of lumbago, sciatica and paraplegia. Boston Med Surg J 1911;164:365-372.
6. Ghormley RK. Low back pain: with special reference to the articular facets, with presentation of an operative procedure. Journal of the American Medical Association 1933;101(23):1773-1777.
7. Han CS, Hancock MJ, Sharma S, Sharma S, Harris IA, Cohen SP, et al. Low back pain of disc, sacroiliac joint, or facet joint origin: A diagnostic accuracy systematic review. Eclinicalmedicine 2023;59;1-13.
8. Du R, Xu G, Bai X, Li Z. Facet joint syndrome: pathophysiology, diagnosis, and treatment. Journal of Pain Research 2022:3689-3710.
9. Kampa N, Kaenkangploo D, Jitpean S, Srithunyarat T, Seesupa S, Hoisang S, et al. Study of the effectiveness of glucosamine and chondroitin sulfate, marine based fatty acid compounds (PCSO-524 and EAB-277), and carprofen for the treatment of dogs with hip osteoarthritis: A prospective, block-randomized, double-blinded, placebo-controlled clinical trial. Frontiers in Veterinary Science 2023;10:60;1-9.
10. Roelofs PD, Deyo RA, Koes BW, Scholten RJ, Van Tulder MW. Nonsteroidal anti-inflammatory drugs for low back pain: an updated Cochrane review. Spine 2008;33(16):1766-1774.
11. Heymans MW, van Tulder MW, Esmail R, Bombardier C, Koes BW. Back schools for nonspecific low back pain: a systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine 2005;30(19):2153-2163.
12. Busanich BM, Verscheure SD. Does McKenzie therapy improve outcomes for back pain? Journal of athletic training 2006;41(1):117-119.
13. Fritz J, Niemeyer T, Clasen S, Wiskirchen J, Tepe G, Kastler B, et al. Management of chronic low back pain: rationales, principles, and targets of imaging-guided spinal injections. Radiographics 2007;27(6):1751-1771.
14. Manchikanti L, Singh V, Vilims BD, Hansen HC, Schultz DM, Kloth DS. Medial branch neurotomy in management of chronic spinal pain: Systematic review of the evidence. Pain Physician 2002;5(4):405-418.
15. Danilov AB, Lila A, Majidova YN, Gromova O, Tkacheva O, Sarvilina I, et al. New pharmaconutraceutical Chondroguard® TRIO for the prevention of musculoskeletal diseases and nutritional support for patients with osteoarthritis and nonspecific back pain: an assessment of clinical options. Resolution of the Multidisciplinary Expert Council. Neurology, Neuropsychiatry, Psychosomatics 2023;15(2):134-146.
16. Vo NX, Le NNH, Chu TDP, Pham HL, Dinh KXA, Che UTT, et al. Effectiveness and Safety of Glucosamine in Osteoarthritis: A Systematic Review. Pharmacy 2023;11(4):117;1-10.
17. Galla R, Ruga S, Aprile S, Ferrari S, Brovero A, Grosa G, et al. New Hyaluronic Acid from Plant Origin to Improve Joint Protection—An In Vitro Study. International Journal of Molecular Sciences 2022;23(15):8114;1-26.
18. Toguchi A, Noguchi N, Kanno T, Yamada A. Methylsulfonylmethane Improves Knee Quality of Life in Participants with Mild Knee Pain: A Randomized, Double-Blind, Placebo-Controlled Trial. Nutrients 2023;15(13):2995;1-14.
19. Jiao Y, Li H, Ren T, Kim IH. Protective effects of methylsulfonylmethane (MSM) on barrier function injury of porcine intestinal epithelial cells (IPEC-J2) induced by

lipopolysaccharide (LPS). Canadian Journal of Animal Science 2023; 103(3): 262-272.
20. Brito R, Costa D, Dias C, Cruz P, Barros P. Chondroitin Sulfate Supplements for Osteoarthritis: A Critical Review. Cureus 2023;15(6);1-8.
21. Hochberg M, Chevalier X, Henrotin Y, Hunter D, Uebelhart D. Symptom and structure modification in osteoarthritis with pharmaceutical-grade chondroitin sulfate: what's the evidence? Current medical research and opinion 2013;29(3):259-267.
22. Messina OD, Vidal Wilman M, Vidal Neira LF. Nutrition, osteoarthritis and cartilage metabolism. Aging clinical and experimental research 2019;31:807-813.
23. Zhu X, Sang L, Wu D, Rong J, Jiang L. Effectiveness and safety of glucosamine and chondroitin for the treatment of osteoarthritis: a meta-analysis of randomized controlled trials. Journal of orthopaedic surgery and research 2018;13(1):1-9.
24. Tant L, Gillard B, Appelboom T. Open-label, randomized, controlled pilot study of the effects of a glucosamine complex on low back pain. Current therapeutic research 2005;66(6):511-521.
25. Sodha R, Sivanadarajah N, Alam M. The use of glucosamine for chronic low back pain: a systematic review of randomised control trials. BMJ open 2013;3(6):e001167 1-10.