To cite this article: Solmaz İ. Assessing the efficacy of 5% dextrose prolotherapy in patients with partial anterior cruciate ligament tears. Turk J Clin Lab 2025; 3: 432-438

Research Article

Assessing the efficacy of 5% dextrose prolotherapy in patients with partial anterior cruciate ligament tears

Parsiyel ön çapraz bağ yırtığı olan hastalarda %5 dekstroz proloterapisinin etkinliğinin değerlendirilmesi

İlker Solmaz*

Department of Traditional and Complemantary Medicine, Health Sciences University, Gulhane Training and Research Hospital, Ankara, Turkey.

Abstract

Aim: Prolotherapy is a regenerative injection treatment aimed at promoting the healing of musculoskeletal injuries. This study aimed to evaluate the effectiveness of 5% dextrose prolotherapy on pain levels and functional capacity in patients with partial anterior cruciate ligament (ACL) injuries.

Material and Methods: This retrospective study reviewed medical records of 60 patients with partial ACL tears who were matched 1:1 based on age and sex into two groups: a prolotherapy group (n=30), who had received monthly injections of 5% dextrose solution for six sessions, and a control group (n=30), who had undergone physical therapy alone. Pain intensity was retrospectively assessed using the Visual Analog Scale (VAS), and functional outcomes were evaluated using the Lower Extremity Functional Scale (LEFS) from baseline records and after the 3rd and 6th treatment sessions.

Results: Baseline demographic and clinical characteristics were similar between the two groups. By the third session, the prolotherapy group showed significantly reduced pain compared to the control group (VAS: 5.2 ± 1.1 vs. 7.9 ± 0.9, $p < 0.001$). By the sixth session, further significant pain reduction was observed in the prolotherapy group compared to controls (VAS: 2.8 ± 1.2 vs. 7.3 ± 1.0, $p < 0.001$). Functional capacity significantly improved in the prolotherapy group by the sixth session compared to the control group (LEFS: 68.6 ± 8.5 vs. 52.4 ± 7.3, $p < 0.001$).

Conclusion: Administration 5% dextrose prolotherapy significantly reduced pain and improved functional capacity in patients with ACL tears. Prolotherapy may serve as an effective minimally invasive treatment option for ligamentous injuries of the knee.

Keywords: Dextrose, functional capacity, knee, ligament injury, pain, prolotherapy

Corresponding Author*: İlker Solmaz, Department of Traditional and Complemantary Medicine, Health Sciences University, Gulhane Training and Research Hospital, Ankara, Turkey.
E-mail: i.solmaz@sbu.edu.tr
Orcid: 0000-0002-1959-8159
Doi: 10.18663/tjcl.1710550
Recevied: 31.05.2025 accepted: 21.07.2025

TJCL Volume 16 Number 3 p: 432-438

Öz

Amaç: Proloterapi, kas-iskelet yaralanmalarının iyileşmesini desteklemeyi amaçlayan rejeneratif bir enjeksiyon tedavisidir. Bu çalışma, ön çapraz bağ (ACL) yırtıkları olan hastalarda %5 dekstroz proloterapisinin ağrı seviyeleri ve fonksiyonel kapasite üzerindeki etkinliğini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Bu retrospektif çalışmaya, yaş ve cinsiyete göre 1:1 eşleştirilmiş iki gruba ayrılmış 60 ACL yırtıkları olan hasta dahil edildi. Proloterapi grubu (n=30) altı seans boyunca aylık %5 dekstroz solüsyonu enjeksiyonları alırken, kontrol grubu (n=30) sadece fizik tedavi gördü. Ağrı yoğunluğu Görsel Analog Skala (VAS) kullanılarak değerlendirildi ve fonksiyonel sonuçlar başlangıçta ve 3. ve 6. tedavi seanslarından sonra Alt Ekstremite Fonksiyonel Skalası (LEFS) ile ölçüldü.

Bulgular: İki grup arasında temel demografik ve klinik özellikler benzerdi. Üçüncü seansta, proloterapi grubu kontrol grubuna kıyasla önemli ölçüde azalmış ağrı gösterdi (VAS: 5,2 ± 1,1'e karşı 7,9 ± 0,9; p < 0,001). Altıncı seansta, proloterapi grubunda kontrol grubuna kıyasla daha da önemli ağrı azalması gözlemlendi (VAS: 2,8 ± 1,2'ye karşı 7,3 ± 1,0; p < 0,001). Proloterapi grubunda fonksiyonel kapasite, kontrol grubuna kıyasla altıncı seansta önemli ölçüde iyileşti (LEFS: 68,6 ± 8,5'e karşı 52,4 ± 7,3; p < 0,001).

Sonuç: %5 dekstroz proloterapisi uygulaması, ACL yırtıkları olan hastalarda ağrıyı önemli ölçüde azalttı ve fonksiyonel kapasiteyi iyileştirdi. Proloterapi, dizdeki bağ yaralanmaları için etkili bir minimal invaziv tedavi seçeneği olarak hizmet edebilir.

Anahtar Kelimeler: Dekstroz, fonksiyonel kapasite, diz, bağ yaralanması, ağrı, proloterapi

Introduction

Ligament injuries can occur in nearly every joint in the body. Among these, ankle sprains are the most common ligament injury, accounting for approximately 30% of all injuries seen in sports medicine clinics and representing the primary musculoskeletal injury encountered in primary care settings (1, 2). Knee pain resulting from ligament injuries is also a frequent complaint, affecting approximately 25% of the general adult population (3, 4). The medial collateral ligament is the most commonly injured ligament in the knee. In many cases, the body heals the injury through a three-stage inflammation and recovery process, resulting in full clinical recovery of joint strength and stability. However, in cases of severe injuries or when multiple injuries occur within a joint, the damage to surrounding ligaments, cartilage, and other joint structures may exceed the body's natural healing capacity. Injuries to the anterior cruciate ligament (ACL) lead to the highest incidence of pathological joint instability (5, 6).

Prolotherapy, a rapidly emerging treatment approach, is based on injecting an irritant solution (e.g., dextrose) into partially torn or degenerative tissues to trigger regeneration mechanisms (7). By inducing controlled inflammation through these injections, prolotherapy aims to support tissue healing, enhance collagen synthesis, and restructure ligament and tendon strength (8). Prolotherapy, particularly in the context of ligament injuries, is a novel and effective adjunct to established treatment norms for osteoarthritis and joint degeneration. Animal studies have demonstrated that ligaments injected with a natural dextrose-based solution trigger cellular proliferation (9, 10). The newly formed tissues closely resemble normal ligament and tendon structures but are thicker, stronger, and contain fibers of varying thicknesses that reflect ongoing collagen formation (11, 12).

Current literature includes limited studies evaluating the effectiveness of prolotherapy in treating ligament injuries. This retrospective study aims to assess the effectiveness of 5% dextrose prolotherapy on pain levels and functional capacity in patients with partial ACL tears.

Material and Methods

This retrospective study was conducted between January 2017 to December 2024 on adult patients treated for partial ACL tears at the SBÜ Gülhane Training and Research Hospital, Traditional and Complementary Medicine (GETAT) Application Center. The study was approved by the SBÜ Gülhane Training and Research Hospital GETAT Clinical Research Ethics Committee (Date: 05.02.2025, Approval No: 2025/2) and was carried out in accordance with the relevant ethical guidelines and the Helsinki Declaration (2013 Brazil revision). The need for informed consent was waived under the approval of the Local Ethics Committee due to the retrospective design.

Patient Selection

During the study period, a total of 175 patients who were treated for partial ACL tears were retrospectively screened for eligibility. The inclusion criteria for this study encompassed

patients aged between 18 and 65 years who had ACL tears confirmed via magnetic resonance imaging (MRI) and clinical findings. Additionally, eligible patients had trauma-related pain and/or instability lasting longer than 3 months, with persistent symptoms despite initial conservative treatment including rest, analgesics, or basic physiotherapy. In addition, clearly documented treatment protocols for prolotherapy, physical therapy, or analgesic regimens, along with questionnaires assessing pain intensity (Visual Analog Scale [VAS]) and functional status (Lower Extremity Functional Scale [LEFS]) scores before and after treatment, were required to be accessible from patients' retrospective medical records.

Patients were excluded if they were younger than 18 or older than 65 years (n = 8); had full-thickness ligament tears requiring surgical intervention or a history of previous ligament-related surgery (n = 14); had recent (within the last 6 months) surgery or extensive reconstruction procedures following trauma to the knee or ankle joints (n = 7); had systemic inflammatory diseases or significant comorbidities including rheumatoid arthritis, active joint infections, or severe osteoarthritis (n = 31); had previously undergone prolotherapy treatment or received recent steroid injections (n = 12); were pregnant or lactating (n = 3); or had incomplete medical records (n = 16).

After applying the exclusion criteria, 84 patients remained eligible for further analysis, including 38 patients who received 5% dextrose prolotherapy once monthly for a total of six sessions (prolotherapy group), and 46 patients who underwent physical therapy alone (control group). To address the imbalance in covariates [age, gender, and body mass index (BMI)] between the prolotherapy group and control group, propensity score matching analysis was performed. The analysis involved 1:1 matching with the nearest neighbor matching method, using calipers (0.2) with a width equal to 0.25 of the standard deviation of the logit (13). Individuals who did not have a match were excluded from the statistical analysis. As a result, the analysis included 30 patients who received 5% dextrose prolotherapy once monthly for six sessions and an equal number of patients who underwent physical therapy in the control group.

Study Protocol

Prolotherapy often involves multiple injection sessions; in practice typically 3–6 sessions are used to achieve therapeutic effect. For ACL tears specifically, prolotherapy practitioners have noted that approximately 6–8 treatment sessions may be needed to see significant healing and stability improvements (14). In each session, prolotherapy was performed using a 23-gauge, 0.6×60 mm needle and a syringe containing 5% dextrose solution as the injectate. A 90-degree flexion position was applied to the knee. To inject at the distal insertion of the ACL, the joint was accessed using a lateral intra-articular approach. The needle tip was placed on the tibial plateau and aimed toward the tibial tuberosity. At the bone insertion point of the ACL's distal end, 0.5–1 cc of 5% dextrose was delivered.

All patients were reminded at each appointment during the treatment period to avoid taking non-steroidal anti-inflammatory drugs (NSAIDs) and to limit overuse of the painful joint. Additionally, all patients were prescribed a standard home exercise program consisting of range of motion, stretching, and strengthening exercises for six sessions. The exercise program began three days following the injection. Initially, it included range of motion and stretching exercises. Strengthening exercises were incorporated after two weeks. Patients received instruction regarding the exercise regimen.

Data Collection

Data on demographic and clinical were extracted from patients' electronic records and medical files. Data on pre- and post-treatment pain levels and functional capacity indices for both groups were obtained from patient records. Pain intensity was assessed using the 10-centimeter VAS, a widely accepted method for subjective pain evaluation. Functional capacity was assessed using the LEFS, a validated patient-reported questionnaire consisting of 20 questions designed to evaluate functional limitations in daily activities related to lower limb conditions, where higher scores indicate better functional status (15).

Statistical analysis

All analyses were conducted using IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA) software. The normal distribution of numerical variables was assessed using the Kolmogorov-Smirnov test. Data exhibiting a normal distribution were presented as mean ± standard deviation, and comparisons between groups were made using the Student's T-test. Non-normally distributed data were displayed as median (interquartile range (IQR): 25-75 percentiles) and comparisons between groups were conducted using the Mann-Whitney U test. Value of $P < 0.05$ were considered statistically significant.

Results

The mean age was 35.8 ± 8.5 years in the prolotherapy group and 36.2 ± 7.9 years in the control group (p = 0.84). In terms of gender distribution, the prolotherapy group consisted of 53% females and 47% males, while the control group had an equal gender distribution (50% females and 50% males) (Table 1).

Table 1. Demographic findings of prolotherapy and control group.

Variables	Prolotherapy group n = 30	Control group n = 30	P-value
Age, years	35.8 ± 8.5	36.2 ± 7.9	0.844
Gender, n (%)			
Female	16 (53)	15 (50)	0.817
Male	14 (47)	15 (50)	
BMI, kg/m2	27.6 ± 5.2	26.9 ± 4.8	0.590

Data are mean ± standard deviation or number (%). *p<0.05 indicates statistical significance. Abbreviations: BMI, body mass index.

The mean baseline VAS scores were similar between the prolotherapy and control groups (8.5 ± 0.9 vs. 8.6 ± 0.8, p = 0.75). By the 3rd session, a significant reduction in pain was observed in the prolotherapy group compared to the control group (5.2 ± 1.1 vs. 7.9 ± 0.9, p < 0.001). At the 6th session, the prolotherapy group showed a further decrease in VAS scores (2.8 ± 1.2), while the control group maintained relatively higher pain levels (7.3 ± 1.0), with the difference remaining highly significant (p < 0.001) (Table 2).

Table 2. Change in Visual Analogue Scale (VAS) scores in the prolotherapy and control groups.

Follow-up time	Prolotherapy group n = 30	Control group n = 30	P-value
Baseline	8.5 ± 0.9	8.6 ± 0.8	0.750
3rd Session	5.2 ± 1.1	7.9 ± 0.9	< 0.001*
6th Session	2.8 ± 1.2	7.3 ± 1.0	x

Data are mean ± standard deviation. *p<0.05 indicates statistical significance.

At baseline, the LEFS scores were similar between the prolotherapy and control groups (42.3 ± 7.2 vs. 41.8 ± 6.9, p = 0.820). By the 6th session, the prolotherapy group showed a marked improvement in functional ability, with a mean LEFS score of 68.6 ± 8.5, whereas the control group had a significantly lower mean score of 52.4 ± 7.3. This difference was statistically highly significant (p < 0.001) (Table 3).

Table 3. Change of Lower Extremity Functional Scale (LEFS) scores in prolotherapy and control group.

Follow-up time	Prolotherapy group n = 30	Control group n = 30	P-value
Baseline	42.3 ± 7.2	41.8 ± 6.9	0.820
6th Session	68.6 ± 6.5	52.4 ± 7.3	<0.001*

Data are mean ± standard deviation. *p<0.05 indicates statistical significance.

Discussion

This study indicates that 5% dextrose prolotherapy can significantly improve pain and function in patients with ACL tears. By the third prolotherapy session (approximately 3 months), the prolotherapy group showed marked pain reduction compared to controls, and by the sixth session (~6 months) pain levels had decreased to roughly one-third of baseline. Functional capacity likewise improved dramatically with prolotherapy , as reflected by the LEFS, whereas the control group's functional gains were modest. These findings suggest a clear clinical benefit of dextrose prolotherapy injections over standard physical therapy alone in managing ACL tears.

The number of placebo-controlled RCTs specifically targeting ligament injuries (as opposed to osteoarthritis or tendinopathies) remains limited. Our study helps fill this gap by providing data in a focused population of ACL tears, though we acknowledge it is retrospective. Reeves et al. reported that knees treated with hypertonic dextrose prolotherapy experienced a 44% reduction in pain and 63% reduction in swelling after 6 injections over 12 months (16). Notably, they also observed significant improvements in knee stability and range of motion: buckling episodes decreased by ~85% and flexion range increased by 14°. In knees that had ACL laxity, prolotherapy led to a 57% improvement in anterior translation (laxity) at one year, and 8 of 13 lax knees regained normal stability on instrumented testing (16). A 3-year follow-up of those patients confirmed sustained benefits, with continued pain reduction (approximately 35–45% improvement in pain scores) and durable restoration of stability (17). These improvements in pain, function, and ligamentous stability mirror the trajectory seen in our prolotherapy group, underscoring that prolotherapy can facilitate connective tissue repair and symptomatic relief even in chronic knee injuries.

Although the exact biological mechanisms remain under investigation, prolotherapy is generally thought to promote ligament healing by injecting an irritant solution—most commonly hypertonic dextrose—which initiates a controlled inflammatory process. This inflammatory response triggers the release of growth factors, stimulates neovascularization, and enhances collagen deposition, thereby improving ligament stability (18, 19). Thus, the significant LEFS functional gains and pain reductions in our prolotherapy group likely stem from actual improvements in ligament integrity and joint stability, which in turn allow patients to resume activities with less pain. Animal and clinical studies support this, indicating that thicker collagen bundles formed after prolotherapy contribute to increased joint stability and pain reduction (12, 20-22). Our study employed an isotonic 5% dextrose solution, whereas traditional protocols typically use higher concentrations (10–25%) to induce marked inflammation (23). Our positive results suggest that lower-concentration

prolotherapy can effectively stimulate ligament repair through regenerative mechanisms that may not involve pronounced inflammation. Indeed, clinical evidence from perineural injection therapy indicates that 5% dextrose can reduce chronic pain and modulate neurogenic inflammation (11, 24, 25). Although higher concentrations may offer greater connective tissue proliferation—such as the superior outcomes observed with 15% versus 5% dextrose in tendinopathy—our findings confirm that low-dose prolotherapy is a clinically viable option, potentially reducing injection-site discomfort while maintaining efficacy (26). Also, in our clinical experience, 5% dextrose injections were associated with mild injection-site pain but no significant complications, which is consistent with the literature's characterization of prolotherapy as a low-risk intervention (7, 27).

Our findings also align with several previous reports highlighting the potential benefits of dextrose-based prolotherapy for musculoskeletal injuries, lower limb and sports-related tendinopathies (28-30). In a study on hallux valgus, a common foot deformity that causes significant pain and functional impairment, prolotherapy was shown to be more effective than dry needling in reducing pain severity and improving foot function (31). A 2016 comprehensive review by Hauser et al. concluded that dextrose prolotherapy is a supported therapy for various chronic musculoskeletal conditions, including pain due to ligament dysfunction (7). On the other hand, a more recent meta-analysis by Chung et al., focused on high-quality randomized trials, found mixed results: overall, prolotherapy did not always outperform placebo for chronic tendon/ligament injuries in pooled analyses, aside from some short-term pain and activity improvements (32). The authors deemed the evidence still insufficient and called for more rigorous studies. This discrepancy likely reflects differences in patient populations and study design. However, several studies have demonstrated the efficacy of prolotherapy in the treatment of ankle ligament injuries. A recent study by Kazempour Mofrad et al. evaluated dextrose prolotherapy in patients with chronic ankle sprains and instability. After 6 months, patients showed a dramatic increase in ankle stability scores [Cumberland ankle instability tool (CAIT) from ~2 at baseline to ~22] and a corresponding drop in pain (VAS reduced from 6.1 to 1.2) (25). The authors concluded that prolotherapy effectively decreased pain and functional instability in chronic ankle ligament injury (25). On the other hand, a randomized controlled trial protocol has been published to test dextrose prolotherapy versus saline injections in patients with chronic ankle instability (33). The results of such trials will further clarify prolotherapy's efficacy and may solidify its role as a primary non-surgical treatment for ligament injuries.

This study has several limitations. First, it had a single-center, retrospective design. Second, the relatively small sample size limits the statistical power to detect subtle differences, and it may restrict the generalizability of findings to broader patient populations. Third, the follow-up period was limited to six months, restricting our ability to assess longer-term effectiveness and durability of the prolotherapy treatment outcomes. Additionally, this study relied exclusively on subjective patient-reported outcomes (VAS and LEFS scores), lacking objective evaluation methods such as imaging or biomechanical stability testing, which could provide deeper insights into actual ligamentous healing and structural improvement. Finally, although patients were matched by age and sex, other potential confounding factors such as activity levels or adherence to therapy protocols were not fully controlled. Future studies should adopt a prospective randomized controlled trial design, include larger and more diverse patient cohorts, incorporate objective ligament stability assessments, and extend follow-up periods to better evaluate the sustained efficacy of prolotherapy.

Conclusion

This retrospective analysis indicates that monthly administration of 5% dextrose prolotherapy significantly improves pain relief and functional outcomes in patients with ACL tears compared to physical therapy alone. These findings reinforce existing evidence suggesting prolotherapy as a beneficial, minimally invasive treatment for ACL injuries, providing a meaningful alternative to conventional conservative approaches.

Ethics Committee Approval

The study was performed in accordance with the Declaration of Helsinki, and was approved by the Health Sciences University, SBU Gulhane Training and Research Hospital GETAT Clinical Research Ethics Committee (Date: 05.02.2025, Decision No: 2025/2).

Informed Consent

The need for informed consent was waived under the approval of the Local Ethics Committee due to the retrospective design.

Conflicts of Interest

The authors declare they have no conflicts of interest.

Financial Disclosure

The authors declared that this study has received no financial support.

Conflict of Interest/ Funding

The study received no financial support from any individual or organization, and the authors declare no conflict of interest.

References

1. MacAuley D. Ankle injuries: same joint, different sports. Med Sci Sports Exerc. 1999;31(7 Suppl):S409-11.
2. Jung HJ, Fisher MB, and Woo SL. Role of biomechanics in the understanding of normal, injured, and healing ligaments and tendons. Sports Med Arthrosc Rehabil Ther Technol. 2009;1(1):9.
3. Bunt CW, Jonas CE, and Chang JG. Knee Pain in Adults and Adolescents: The Initial Evaluation. Am Fam Physician. 2018;98(9):576-85.
4. Nguyen US, Zhang Y, Zhu Y, Niu J, Zhang B, and Felson DT. Increasing prevalence of knee pain and symptomatic knee osteoarthritis: survey and cohort data. Ann Intern Med. 2011;155(11):725-32.
5. Wheaton MT and Jensen N. The Ligament Injury-Osteoarthritis Connection: The Role of Prolotherapy in Ligament Repair. Journal of prolotherapy. 2011;3(4):790-812.
6. Torgutalp ŞŞ, Dönmez G, and Korkusuz F. Incidence rates of injuries associated with anterior cruciate ligament tear diagnosed by magnetic resonance imaging: A retrospective cohort study. Spor Hekimliği Dergisi. 2021;56(1):033-37.
7. Hauser RA, Lackner JB, Steilen-Matias D, and Harris DK. A Systematic Review of Dextrose Prolotherapy for Chronic Musculoskeletal Pain. Clin Med Insights Arthritis Musculoskelet Disord. 2016;9:139-59.
8. Rabago D, Slattengren A, and Zgierska A. Prolotherapy in primary care practice. Prim Care. 2010;37(1):65-80.
9. Zhou L, Liang H, Chen Y, Hu K, and Liu X. Dextrose prolotherapy at varying concentrations ameliorates tendon injury via IGF-2R: an integrated study of Mendelian randomization and an animal model. J Orthop Surg Res. 2025;20(1):556.
10. Oh S, Ettema AM, Zhao C, et al. Dextrose-induced subsynovial connective tissue fibrosis in the rabbit carpal tunnel: A potential model to study carpal tunnel syndrome? Hand (N Y). 2008;3(1):34-40.
11. Dagenais S, Yelland MJ, Del Mar C, and Schoene ML. Prolotherapy injections for chronic low-back pain. Cochrane Database Syst Rev. 2007;2007(2):CD004059.
12. Jensen KT, Rabago DP, Best TM, Patterson JJ, and Vanderby R, Jr. Response of knee ligaments to prolotherapy in a rat injury model. Am J Sports Med. 2008;36(7):1347-57.
13. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat. 2011;10(2):150-61.
14. Van Pelt RS. Prolotherapy Technique on Injecting the Anterior Cruciate Ligament. Journal of Prolotherapy. 2009;1(1):36-38.
15. Binkley JM, Stratford PW, Lott SA, and Riddle DL. The Lower Extremity Functional Scale (LEFS): scale development, measurement properties, and clinical application. North American Orthopaedic Rehabilitation Research Network. Phys Ther. 1999;79(4):371-83.
16. Reeves KD and Hassanein K. Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. Altern Ther Health Med. 2000;6(2):68-74, 77-80.
17. Reeves KD and Hassanein KM. Long-term effects of dextrose prolotherapy for anterior cruciate ligament laxity. Altern Ther Health Med. 2003;9(3):58-62.
18. Reeves KD, Sit RW, and Rabago DP. Dextrose Prolotherapy: A Narrative Review of Basic Science, Clinical Research, and Best Treatment Recommendations. Phys Med Rehabil Clin N Am. 2016;27(4):783-823.
19. Hauser R, Blakemore P, Wang J, and Steilen D. Structural basis of joint instability as cause for chronic musculoskeletal pain and its successful treatment with regenerative injection therapy (prolotherapy). The Open Pain Journal. 2014;7:9-22.
20. Freeman JW, Empson YM, Ekwueme EC, Paynter DM, and Brolinson PG. Effect of prolotherapy on cellular proliferation and collagen deposition in MC3T3-E1 and patellar tendon fibroblast populations. Transl Res. 2011;158(3):132-9.
21. Jensen KT, Rabago DP, Best TM, Patterson JJ, and Vanderby R, Jr. Early inflammatory response of knee ligaments to prolotherapy in a rat model. J Orthop Res. 2008;26(6):816-23.
22. Martins CA, Bertuzzi RT, Tisot RA, et al. Dextrose prolotherapy and corticosteroid injection into rat Achilles tendon. Knee Surg Sports Traumatol Arthrosc. 2012;20(10):1895-900.
23. Köroğlu Ö, Örsçelik A, Karasimav Ö, Demir Y, and Solmaz İ. Is 5% dextrose prolotherapy effective for radicular low back pain? Gülhane Tip Dergisi. 2019;61(3):123-27.
24. Rabago D and Nourani B. Prolotherapy for Osteoarthritis and Tendinopathy: a Descriptive Review. Curr Rheumatol Rep. 2017;19(6):34.

25. Kazempour Mofrad M, Rezasoltani Z, Dadarkhah A, Hamidi Panah S, Tabatabaee SM, and Azarakhsh A. Neurofascial Dextrose Prolotherapy for Managing Chronic Ankle Ligament Injury. Anesth Pain Med. 2022;12(1):e118317.
26. Ciftci YGD, Tuncay F, Kocak FA, and Okcu M. Is Low-Dose Dextrose Prolotherapy as Effective as High-Dose Dextrose Prolotherapy in the Treatment of Lateral Epicondylitis? A Double-Blind, Ultrasound Guided, Randomized Controlled Study. Arch Phys Med Rehabil. 2023;104(2):179-87.
27. Nair LS. Prolotherapy for tissue repair. Transl Res. 2011;158(3):129-31.
28. Rabago D, Best TM, Beamsley M, and Patterson J. A systematic review of prolotherapy for chronic musculoskeletal pain. Clin J Sport Med. 2005;15(5):376-80.
29. Capotosto S, Nazemi AK, Komatsu DE, and Penna J. Prolotherapy in the Treatment of Sports-Related Tendinopathies: A Systematic Review of Randomized Controlled Trials. Orthop J Sports Med. 2024;12(11):23259671241275087.
30. Sanderson LM and Bryant A. Effectiveness and safety of prolotherapy injections for management of lower limb tendinopathy and fasciopathy: a systematic review. J Foot Ankle Res. 2015;8:57.
31. Sağlam S, Aydın M, Yüzügüldü U, Erşen Ö, and Uludağ V. The Effect of Prolotherapy and Dry Needling on Pain and Foot Functions in Hallux Valgus. Duzce Medical Journal. 2024;26(2):118-21.
32. Chung MW, Hsu CY, Chung WK, and Lin YN. Effects of dextrose prolotherapy on tendinopathy, fasciopathy, and ligament injuries, fact or myth?: A systematic review and meta-analysis. Medicine (Baltimore). 2020;99(46):e23201.
33. Sit RWS, Wu RWK, Ling SKK, et al. A protocol for a randomized clinical trial assessing the efficacy of hypertonic dextrose injection (prolotherapy) in chronic ankle instability. Trials. 2022;23(1):1063.