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Original article

Effectiveness of prolotherapy in the treatment of chronic rotator cuff lesions

M.M. Seven [a], O. Ersen [b,*], S. Akpancar [b], H. Ozkan [b], S. Turkkan [b], Y. Yıldız [a], K. Koca [b]

[a] Department of Sports Medicine, Gulhane Military Medicine Academy, Ankara, Turkey
[b] Department of Orthopaedics, Gulhane Military Medicine Academy, Ankara, Turkey

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ABSTRACT

Background: Rotator cuff lesions are one of the major causes of shoulder pain and dysfunction. Numerous non-surgical treatment modalities have been described for chronic rotator cuff lesions, but the debate continues over the optimal procedure. The aim of this report is to present the results of prolotherapy in the treatment of chronic refractory rotator cuff lesions.
Hypothesis: Dextrose prolotherapy will reduce pain and improve shoulder function and patient satisfaction.
Material and methods: We recruited 120 patients with chronic rotator cuff lesions and symptoms that persisted for longer than 6 months. Patients were divided into two groups: one treated with exercise (control group; $n = 60$) and the other treated with prolotherapy injection (prolotherapy group; $n = 60$). In the latter, ultrasound-guided prolotherapy injections were applied under aseptic conditions. In the former, patients received a physiotherapy protocol three sessions weekly for 12 weeks. Both groups were instructed to carry out a home exercise program. Clinical assessment of shoulder function was performed using a visual analog scale (VAS) for pain, Shoulder Pain and Disability Index (SPADI), Western Ontario Rotatory Cuff (WORC) Index, patient satisfaction, and shoulder range of motion. Patients were examined at baseline, weeks 3, 6, and 12, and last follow-up (minimum of one year).
Results: A total of 101 patients (44 controls and 57 in the prolotherapy group) completed all study protocols and were included in the study. Using a within-group comparison, both groups achieved significant improvements over baseline, as measured by the VAS, SPADI, WORC index, and shoulder range of motion ($P < 0.001$). Using a between-group comparison, a significant difference was found in the VAS scores at baseline, weeks 3, 6, and 12, and last follow-up. In addition, significant differences were found in the SPADIs and WORC indices at weeks 6 and 12 and the last follow-up. Significant differences were found in shoulder abduction and flexion at week 12 and last follow-up, and in internal rotation at last follow-up. However, no significant was found in external rotation at any follow-up period. In the prolotherapy group, 53 patients (92.9%) reported excellent or good outcomes; in the control group, 25 patients (56.8%) reported excellent or good outcomes.
Conclusion: Prolotherapy is an easily applicable and satisfying auxiliary method in the treatment of chronic rotatory cuff lesions.
Study type: Randomized prospective comparative trial.
Level of evidence: Level of evidence 1.

1. Introduction

Rotator cuff injuries are very common and one of the major causes of shoulder pain in all age groups [1]. Lesions range widely from acute tendinitis to massive tears involving the supraspinatus, infraspinatus, and subscapularis. Clinical presentation and pathogenesis are different between age groups. In younger individuals, pathologies occur from repetitive overuse injuries or acute traumatic events. However, older individuals usually present without a history of predisposing trauma [2]. Non-operative treatment is the first line treatment option and the traditional methods consist of rest, activity modification, non-steroidal anti-inflammatory medicines, shoulder range of motion exercises or muscle-strengthening exercises, and steroid injections [3,4]. A considerable number of patients can be healed with these traditional conservative methods. However, these may not be effective in some

* Corresponding author.
E-mail address: merschenn@yahoo.com (O. Ersen).

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groups of patients, thus there is a need for new methods that provide tissue renewal and healing in these group of patients.

In recent years, prolotherapy has increased in popularity for the treatment of musculosketal conditions, such as ligamentous laxity, chronic enthesopathy, osteoarthritis and tendinosis [5–7]. The exact mechanism of prolotherapy injections has not been clearly identified. The injections are prepared with hypertonic dextrose in distinct concentrations that can cause the osmotic rupture of local cells [8]. Increased glucose in the extracellular matrix provides local tissue irritation that initiates an acute inflammatory response and improves fibroblast proliferation and subsequent collagen synthesis, which provides healing and tissue renewal [9]. Some studies suggest that hypertonic glucose concentrations lead to an increase in the DNA-encoding growth factors in different

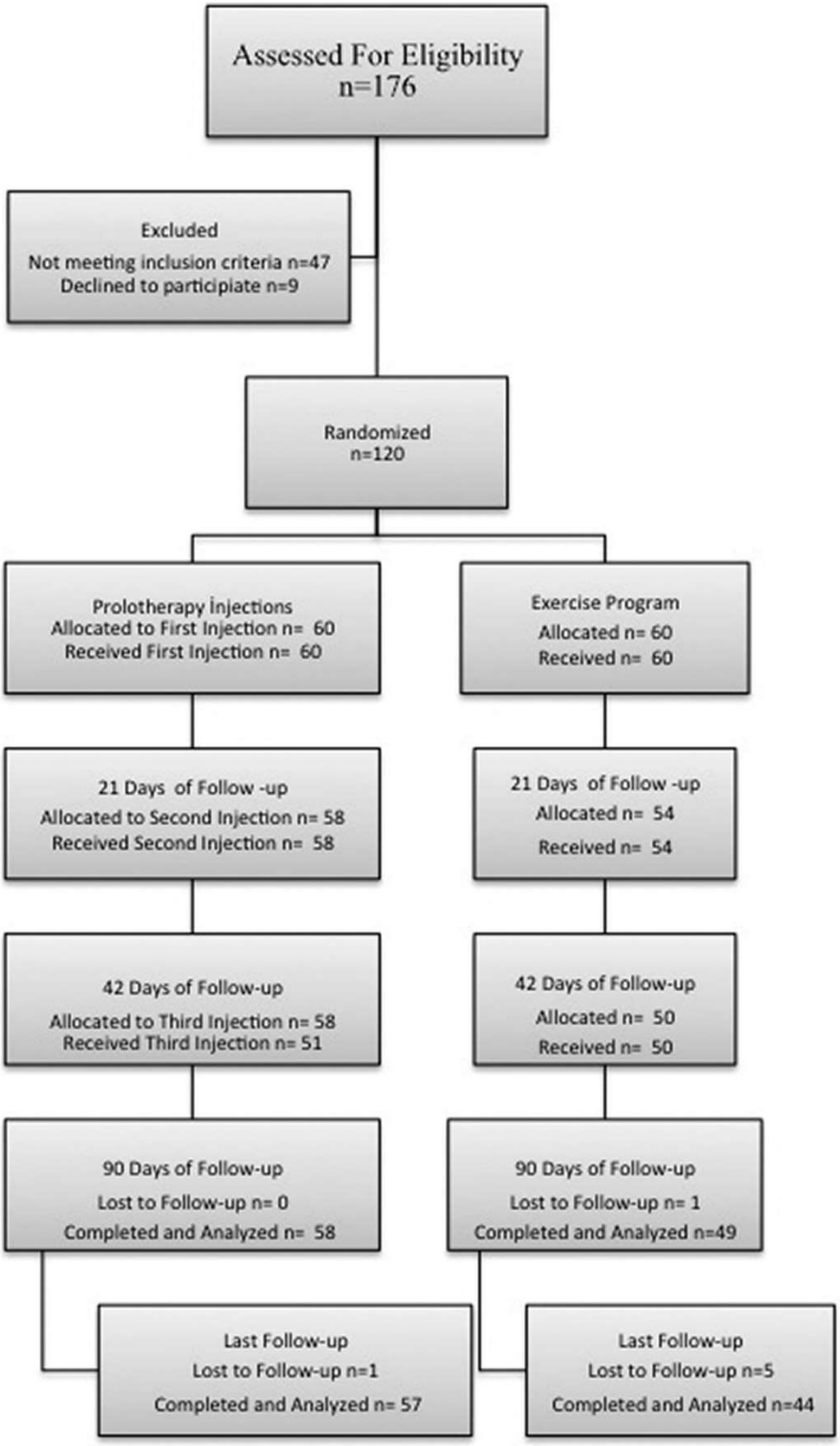

Fig. 1. Flowchart of subjects in the study.

types of human cells and subsequent healing [10–12]. Jensen at al. [13,14] reported increased inflammatory agents at the injection sites after prolotherapy in rat models, and showed significant enlargement in the ligament or the cartilage structures. The effect of hypertonic glucose was also investigated in human studies. Di Paolo et al. [10] showed that high levels of glucose induce the activation of platelet-derived growth factor (PDGF), which stimulates TGF-beta gene expression in human mesangial cells and induces DNA synthesis. High glucose levels act as a stimulus for the expression of connective tissue growth factor and other genes in human mesangial cells [11]. Rabago at al. showed that cartilage volume stability was enhanced by prolotherapy injections, as assessed by magnetic resonance imaging [15].

We hypothesized that dextrose prolotherapy would reduce pain, improve shoulder function, and patient satisfaction. The aim of this report was to present the results of prolotherapy for the treatment of chronic refractory rotator cuff lesions.

2. Materials and methods

Each patient enrolled in this study signed an informed consent. The local institutional ethics committee approved this study.

2.1. Participants

Between May 2014 and April 2016, this prospective randomized controlled study recruited 120 patients with chronic rotator cuff injury, who had symptoms for more than 6 months. The patients were randomly assigned to receive either prolotherapy or rehabilitation protocol with the use of a computer-generated random list. Patients were asked to return for control examination 3, 6 and 12 weeks after the first treatment, as well as a final follow-up examination (minimum of one year) (Fig. 1).

The source population consisted of patients referred to the orthopedics and sports medicine departments for treatment of chronic shoulder pain. A total of 120 patients met enrollment criteria and were enrolled in the study. Patients were divided into two groups including exercise (control group, $n = 60$) and prolotherapy injection (prolotherapy group, $n = 60$). A total of 101 patients out of 120 were included in the results. Demographics and baseline characteristics of the groups were similar (Table 1).

Patients from 30 to 60 years old with long-lasting symptoms of at least 6 months, refractory to at least 3 months of conservative methods, and rotator cuff lesions in the form oftendinosis, partial tear [if the soft tissue (the muscle fibers) will not be completely disrupted in MRI], as determined on MRI, were included. Diagnosis was confirmed clinically by physical examination and ultrasonography.

Patients with rheumatic disease or other systemic inflammatory disease, diabetes mellitus, osteomyelitis, active infection or history of chronic infection in the treatment area, previous operation on the shoulder, local corticosteroid injection within previous 12 weeks, bleeding tendency (hereditary or acquired), evidence of infection (systemic or local to shoulder), and pregnancy were excluded from the study.

3. Methods

In the prolotherapy group, the injections were performed while the patient was sitting in an upright position and the arms were positioned behind their backs with internal rotation and hyperextension of shoulder and the elbow bent for longitudinal supraspinatus view. Ultrasonography was used to identify the location and the depth of injection points. The type of rotator cuff lesion (tendinosis partial thickness) was also recorded. Prolotherapy injections were applied under aseptic conditions using a 27G needle as follows: 4 mL of prolotherapy solution (a mixture containing 3.6 mL of 25% dextrose and 0.4 mL lidocaine) was injected to the subacromial bursa using an injection site that is in posterolateral aspect of the acromion, and a maximum of 20 mL dextrose solution (a mixture containing 18 mL of 15% dextrose and 2 mL lidocaine) to supraspinatus, infraspinatus, teres minor insertions (tuberculum majus), pectoralis minor, coracobrachialis and biceps brachii insertions (coracoid process) with the shoulder in neutral rotation. The biceps long head, subscapularis, and inferior glenohumeral ligament insertions (supraglenoid tubercle, tuberculum minus) were injected with the shoulder in external rotation and abduction/adduction. Origins of the teres minor, teres major, and the posterior inferior glenohumeral ligament were injected posteriorly (Fig. 2). In order to provide safer and more efficient injection sessions, prolotherapy was combined with ultrasound guidance [16] (Fig. 3). Sterile transducer covers were used throughout the injection procedures. After the injections, patients were instructed to rest the injected shoulder for 3 days, refrain from any heavy

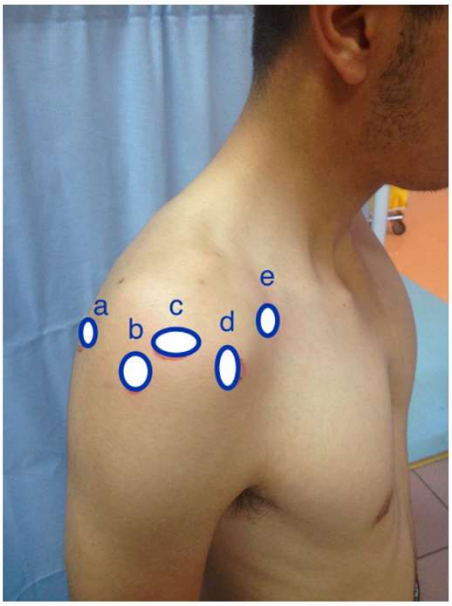

Fig. 2. The injection points; a: subacromial bursa; b: infraspinatus, teres minor insertion (tuberculum majus); c: supraspinatus insertion (tuberculum majus); d: subscapularis (tuberculum minus); e: coracoid process.

Table 1
Demographics and baseline characteristics of the patients.

	Prolotherapy group (mean ± SD)	Control group (mean ± SD)	P^a
n	57	44	
Age	50.19 ± 12.13	46.31 ± 10.6	0.096
Gender	19 female, 23 male	16 female, 19 male	0.718
Time of symptoms	19.22 ± 12.6 months	19.75 ± 12.12 months	0.834
Side (right/left)	36/21	25/19	0.697
Follow-up	17.08 ± 5.42 months	16.95 ± 3.82 months	0.890
Rotator cuff pathology as determined on USG	29 tendinosis, 28 partial tear	24 tendinosis, 20 partial tear	

[a] Inter-group analyze (student *t*-test).

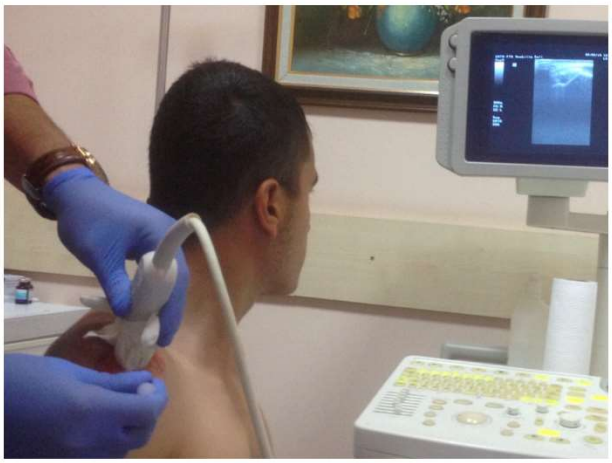

Fig. 3. Ultrasound-guided injections.

lifting activity, and to apply hot water bags for 20 to 30 minutes every 2 or 3 hours, and not to use anti-inflammatory drugs other than acetaminophen (if pain the became unbearable, the patient was instructed to take 500 mg of acetaminophen up to 4 times per day). Patients were also enrolled in a home exercise program described by Kibler [17], which was 3 times a day after 3 days of injections. Injection was dropped if the pain score reduced at least to quarter compared with pre-injection levels, patients received the maximum 6 rounds of injections, or wanted to draw away from the treatment.

In the control group, patients received a physiotherapy protocol described by Kibler [17], which consisted of 3 sessions (an average of 30 minutes per season) per week for 12 weeks at a sports medicine department. Limited glenohumeral internal rotation and tightness of muscles originating from the coracoid process were rehabilitated with open stretching in the supine position, while patients one arm extended out into a keep their palm facing down and arm at 90° to their body. Other arm is by their other shoulder. They slowly roll the other side of their body off the floor, and rotation–stretching exercises; while the patients lay on their back with their shoulder abducted to 90° and elbow flexed to 90°, the physiotherapist externally rotates the shoulder. Scapula control was provided by exercises of the trapezius and serratus anterior muscles with the arm below 90° of abduction. RC activation exercises were then given, including horizontal and vertical closed-chain, horizontal open-chain, and diagonal closed-chain exercises. In closed-chain exercises, patient's hands remain in a fixed position while their body moves. They keep their hand stationary stabilizes the supporting muscles of their shoulder without putting unwanted stress on the joint and its supporting connective tissue. In open-chain exercises, patient's body remains in place and the limb performing the action moves and overcome the resistance. The final stage open-chain plyometric exercises were given. Patients were instructed to refrain from any heavy lifting activity. The patients were also advised to perform a home exercise program with same exercises on their own three times a day for the other days. If the pain became unbearable, patients were allowed to take 500 mg of acetaminophen up to 4 times per day. The home exercise program was also recommended for patients after the 12 weeks of the rehabilitation program.

3.1. Assessment methods

Pain was investigated using a visual analog scale, with 0 for no pain and 10 for severe pain. The clinical outcomes were presented as excellent, good, fair, or poor. Feeling no pain during the daily activities including sports, work was defined as 'excellent'; feeling less than 50% of the pain was defined as 'good'; feeling 50% to 75% of the pain was defined as 'fair'; feeling 75% or more of the pain was defined as 'poor'. The Western Ontario Rotator Cuff Index (WORC), which is a valid and reliable disease-specific, quality of life self-assessment score for rotator cuff disease, consists of 21 questions, including physical symptoms, sports and recreation, work, social and emotional well-being. Each question is scored on a 100-mm scale and summed to a total score ranging from 0 to 2100, with a higher score indicating worse function [18]. The total score can be converted to a percentage score, where a score of 100% is the best possible score. The Shoulder Pain and Disability Index (SPADI) was also used, which was developed to measure current shoulder pain and disability in an outpatient setting. The SPADI contains 13 parameters that assess two domains: 5 parameters that measure pain and 8 parameters that measure disability [19]. The range of motion of the shoulder was evaluated using goniometry (flexion, abduction, internal rotation, and external rotation). Baseline characteristics were collected from all participants. Follow-up examinations were performed on all of the patients independently by one of the coauthors, who was blinded to patient treatment status at baseline, 3, 6, and 12 weeks after the first the treatment, and the final follow-up examination (minimum of 1 year). Patients were requested to report any adverse effects at each visit.

3.2. Statistical analysis

A power analysis was performed on the primary outcome of the study [20]. The VAS score was used because the study focused on the effects of prolotherapy on rotator cuff tendinopathy starting with three homogeneous groups determined by the mean value of VAS at baseline [21]. When we established a type I error of 0.5 and type II error of 0.01, the calculated mean improvement of VAS scores were 2.9 ± 0.6 in the prolotherapy group and 1.8 ± 0.7in the control group. The minimum number of subjects per group was calculated as 12.

The Statistical Package for Social Sciences software version 22.0 for Windows was used for statistical analysis. The clinical data were presented as number, percent, and mean ± SD. Congruity of continuous variables to normal distribution was evaluated with the Kolmogorov–Smirnov test. Chi^2 (χ^2) test was used for assessment of the relationship between two categorical variables. Student's *t*-test was used for the continuous variables. ANOVA in the repeated measurements was used for intra-group analyses. The Bonferroni adjustment test was used for post-hoc analysis. A $P < 0.05$ was considered to indicate a statistically significant difference.

4. Results

Among the 120 patients, three cases were excluded from the results in the prolotherapy group: one case due to incomplete evaluation (lost at last follow-up examination), 1 case had hypotension and 1 case had extreme pain after the first injection, thus refused to participate in further study protocols. Sixteen cases were excluded from control group: four were dissatisfied with the protocol and 12 patients were excluded due to incomplete data. Therefore, 101patients (prolotherapy group: $n = 57$, control group: $n = 44$) were included in the study [22] (Fig. 1).

Using within-group comparison, the prolotherapy group achieved a significant improvement in the VAS, SPADI, and WORC scores, and shoulder of motion at 3 weeks of treatment when compared to pre-injection values, and this significant improvement continued after the repeated injections ($P < 0.001$) (Tables 2 and 3). Fifty-three patients (92.9%) reported excellent or good outcomes (excellent: $n = 25$, good: $n = 28$), 4 patients (7.1%) reported fair or

Table 2
Clinical outcomes of baseline, 3, 6, and 12 weeks after the first treatment, and the final follow-up examination (minimum of 1 year).

SCORE	ProloMean ± SD	ControlMean ± SD	P[a]
VAS (baseline)	7.85 ± 1.29	7.36 ± 1.38	0.072
VAS (3 weeks)	5.47 ± 1.58	6.63 ± 1.30	< 0.001
VAS (6 weeks)	3.35 ± 1.67	4.39 ± 1.92	0.04
VAS (12 weeks)	2.35 ± 1.98	4.00 ± 2.11	< 0.001
VAS (min a year)	0.89 ± 1.64	3.77 ± 2.15	< 0.001
P[b]	< 0.001	< 0.001	
WORC (baseline)	32.21 ± 17.49	37.77 ± 16.03	0.154
WORC (3 weeks)	52.25 ± 16.43	46.59 ± 15.28	0.08
WORC (6 weeks)	72.07 ± 14.48	59.98 ± 16.03	< 0.001
WORC (12 weeks)	84.98 ± 12.13	66.14 ± 17.11	< 0.001
WORC (min a year)	90.37 ± 10.12	69.08 ± 16.70	< 0.001
P[b]	< 0.001	< 0.001	
SPADI (baseline)	74.76 ± 18.54	68.62 ± 20.4	0.118
SPADI (3 weeks)	53.17 ± 16.44	58.70 ± 18.49	0.116
SPADI (6 weeks)	31.30 ± 14.19	41.97 ± 16.42	0.01
SPADI (12 weeks)	16.12 ± 12.82	37.25 ± 20.32	< 0.001
SPADI (min a year)	7.66 ± 10.64	34.94 ± 19.14	< 0.001
P[b]	< 0.001	< 0.001	

[a] Inter-group analyze (student *t*-test).
[b] Intra-group analyze (ANOVA in the repeated measurements).

poor outcomes (fair: $n = 2$, poor: $n = 2$). Two patients with poor results decided to go to surgery.

The control group achieved a significant improvement in the VAS, SPADI, and WORC scores, and shoulder of motion at 3 weeks of treatment when compared to pre-injection values, and this significant improvement continued after the repeated injections ($P < 0.001$) (Tables 2 and 3). Twenty-five patients (56.8%) reported excellent or good outcomes (excellent: $n = 3$, good: $n = 22$), and 19 patients (33.2%) reported fair or poor outcomes (fair: $n = 14$, poor: $n = 5$). Five patients with poor results and one patient with fair result decided to go to surgery. Surgery rate of control group found higher.

Using between-group comparison, significant differences were determined in the VAS scores between the two groups at 3, 6 and 12 weeks, and at the final follow-up after treatment ($P < 0.001$). There was no significant difference between prolotherapy and control groups in the WORC and SPADI scores at 3 weeks when compared to baseline ($P = 0.15$ and $P = 0.47$). However, significant differences were determined between groups 6 and 12 weeks after treatment ($P < 0.001$). There was a significant difference in shoulder abduction and flexion at 12 weeks and at last follow-up, and in internal rotation at last follow-up. However, there was no significant difference in shoulder external rotation at any follow-up periods. None of the patients in the groups experienced any serious complications (e.g., bleeding, infection, cellulitis, septic joint). Only 3 patients had extreme pain one or two days after injections in the prolotherapy group that was reduced after 2 days of rest and local application of heat therapy, 2 patients had grade 2 skin burns after first injection because of improper use of hot water bags and local anesthetic effect of the injections, and 1 patient had hypotension. There is no difference between the groups according to pain killer need. Six patients in the prolotheraphy group and seven patients in the control group need medications only in the first week of the treatment.

Table 3
Ranges of shoulder of motion at baseline, 3, 6, and 12 weeks after the first the treatment, and the final follow-up examination (minimum of 1 year).

ROM	ProloMean ± SD	ControlMean ± SD	P[a]
Flexion (baseline)	126.89 ± 40.89	133.75 ± 34.84	0.376
Flexion (3 weeks)	149.91 ± 29.13	147.61 ± 29.93	0.698
Flexion (6 weeks)	167.19 ± 20.93	161.59 ± 21.66	0.192
Flexion (12 weeks)	173.50 ± 14.57	165.00 ± 18.26	0.011
Flexion (min a year)	176.57 ± 9.50	166.36 ± 16.95	< 0.001
P[b]	< 0.001	< 0.001	
Abduction (baseline)	125.96 ± 35.98	128.52 ± 34.54	0.719
Abduction (3 weeks)	141.84 ± 30.94	142.38 ± 30.66	0.930
Abduction (6 weeks)	163.77 ± 24.66	158.29 ± 22.54	0.254
Abduction (12 weeks)	170.78 ± 19.38	162.38 ± 20.55	0.038
Abduction (min a year)	175.26 ± 12.15	164.65 ± 17.92	0.001
P[b]	< 0.001	< 0.001	
Int. rot. (baseline)	59.73 ± 26.03	56.47 ± 15.64	0.465
Int. rot. (3 weeks)	61.92 ± 11.86	62.27 ± 10.36	0.879
Int. rot. (6 weeks)	65.78 ± 8.59	65.00 ± 7.92	0.637
Int. rot. (12 weeks)	67.63 ± 5.98	65.56 ± 7.40	0.125
Int. rot. (min a year)	68.77 ± 4.25	66.02 ± 7.11	0.018
P[b]	< 0.001	< 0.001	
Ext. rot. (baseline)	77.19 ± 17.9	79.31 ± 17.30	0.55
Ext. rot. (3 weeks)	81.49 ± 15.29	83.75 ± 11.86	0.42
Ext. rot. (6 weeks)	84.47 ± 11.20	85.34 ± 10.42	0.692
Ext. rot. (12 weeks)	87.71 ± 5.98	86.59 ± 9.69	0.473
Ext. rot. (min a year)	88.94 ± 4.09	86.59 ± 9.69	0.101
P[b]	< 0.001	< 0.001	

[a] Inter-group analyze (student *t*-test).
[b] Intra-group analyze (variance analyze in the repeated measurements).

5. Discussion

Rotator cuff tendinopathy is the leading cause of shoulder pain in all age groups [1]. Numerous non-surgical treatment modalities have been described but an optimal procedure continues to be debated [3].

Recently, injection-based complementary procedures have been studied for musculoskeletal conditions and rotator cuff tendinopathy, including plasma rich platelet injection, steroid injection, and sodium hyaluronate. All of these methods are controversial and have not received general acceptance by many authors [23–26]. Platelet-rich plasma (PRP) injection is a popular method in the treatment of musculosketal problems. Many studies have been conducted for the effectiveness of PRP on rotator cuff repair and have given contradictory results. Some studies have had better results, but most have had poor outcomes after using PRP injections [23,24]. Subacromial injections of sodium hyaluronate is another method for the management of rotator cuff tendinopathy, with beneficial results declared in short-term periods, but not long-term periods [25]. Corticosteroid injections are the most used conventional method in the treatment of rotator cuff tendinitis [26]. Most studies reported pain relief and functional improvement in the treatment of rotator cuff tendinopathy, but steroid injections do not improve healing and have side effects, such as focal inflammation, necrosis, fragmentation of collagen bundles in the subacromial space, tendon/ligament weakening or rupture, and worsening osteoarthritic changes [26–28].

Prolotherapy injections have shown beneficial effects in the treatment of lateral epicondylitis, achillestendinopathy, plantar fasciitis, and hip adductor tendinopathy [29–31]. Easy application, treatment success, and shortening the rehabilitation process are reasons for the preference of prolotherapy in the treatment of these conditions. Prolotherapy injections also improve healing by stimulating extracellular matrix, which enhances the stability of the joints by tightening and strengthening the ligaments, tendons, and joint stabilizing structures, which improves durability and functionality of these structures [10,11,12,32]. Moreover, no serious side effects or adverse events were reported for prolotherapy when used for previously reported indications [33].

The effectiveness of prolotherapy injections in patients with chronic RC tendinopathy was also reported in the literature [21,34,35]. It was first investigated by Doo-Hyung at al. [35] in their non-randomized retrospective case-control study. They used prolotherapy for patients with non-traumatic refractory rotator cuff disease who had 3 months of complaints. They performed 3 to 8 sessions of injections with an interval of 2 to 4 weeks, with an improvement in pain, disability, isometric strength, and

shoulder motion. Then, Helene at al. [21] used prolotherapy in the treatment of rotator cuff tendinopathy in their randomized controlled study and showed that prolotherapy provided long-term pain improvement and patient satisfaction, but there was no difference in shoulder healing when compared to control groups, which were subjected to saline injections.

In the recent study, two major shoulder functional scores (WORC and SPADI) were investigated in the treatment of chronic RC tendinopathy, with significant improvement with prolotherapy injections at 6 and 12 weeks after treatment. Pain scores were also significantly decreased when compared to the control group. Physiotherapy was selected as the comparison because its effectiveness was proven in the management of shoulder tendinopathy and was also recommended by the recent European guidelines (2008) [36]. A standard and proper physiotherapy program was found to be effective in providing flexibility, strength and mobility of RC, and reduced the risk of re-injury [17]. In the intra-group analysis, shoulder VAS, WORC, SPADI scores, and shoulder range of motion were significantly enhanced with a physiotherapy program. However, VAS, WORC and SPADI scores were significantly improved with repeated prolotherapy injections when compared to physiotherapy. The range of shoulder motion was increased with prolotherapy injections but there was no significant difference between the groups.

When considering the complications of traditional treatments, such as corticosteroid injections (tendon-ligament weakening or rupture, post-injection pain flare, soft tissue or subcutaneous fat atrophy, and skin hypopigmentation), prolotherapy is a safe and effective method [37]. A small number of minor complications including light-headedness, allergic reaction, infection, or nerve damage were reported in the literature [37]. In this study, we did not observe any complications. Moreover, ultrasound guidance improved the safety and the accuracy of needle placement.

Prolotherapy is an invasive treatment method requiring three injection sessions, which may seem to be excessive and costly. At least three injection sessions were performed in previous studies that investigated the efficacy of prolotherapy in the treatment of various musculosketal conditions. Moreover, some studies declared that the most effective benefits could be gained with repeated injections [6,7,29,34]. In this study, we performed 2 to 6 injection sessions (a mean of 5.23 sessions) of prolotherapy, which provided maximum pain relief and improved function to patients with chronic rotator cuff lessons. Improved patient satisfaction, pain and shoulder function scores were significantly increased after each injection periods.

The most significant limitations of this study were its small sample size, lack of placebo control, and relative short follow-up. Therefore, larger studies with longer follow-up times are needed.

We had successful results using prolotherapy in patients with chronic rotator cuff lesions. Shoulder function, pain level, and patient satisfaction were substantially improved. We consider that it will be a successful non-operative treatment option.

In conclusion, prolotherapy is an easily applicable and satisfying auxiliary method in the treatment of partial rotatory cuff lesions. The results confirmed our hypothesis; as it has reduced pain, improved shoulder function, and patient satisfaction.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Shoulder impingement and rotator cuff lesions.Baker CL, editor. The Hughston Clinic Sports Medicine Book. Baltimore, MD: Lippincott Williams and Wilkins; 1995. p. 272–9.
[2] Patte D. Classification of rotator cuff lesions. Clin Orthop Relat Res 1990;254:81–6.
[3] Bishay V, Gallo RA. The evaluation and treatment of rotator cuff pathology. Prim Care 2013;40:889–910.
[4] Wilson JJ, Best TM. Common overuse tendon problems: a review and recommendations for treatment. Am Fam Phys 2005;72:811–8.
[5] Distel LM, Best TM, Prolotherapy:. A clinical review of its role in treating chronic musculoskeletal pain. PMR 2011;3(Suppl. 1):78–81.
[6] Ekinci S, Tatar O, Akpancar S, Turgut H, Seven MM. A new treatment option in osteoarthritis: prolotherapy injections. J Arthritis 2016;5:197–8.
[7] Seven MM, Koca K, Akpancar S, Turkkan S, Uysal B, Yildiz Y, et al. Prolotherapy injections in the treatment of overuse injuries. BMMR Online First 2016 [in press].
[8] Rabago D, Slattengren A, Zgierska A. Prolotherapy in primary care practice. Prim Care 2010;37(1):65–80.
[9] Reeves KD, Topol GA, Fullerton BD. Evidence-based regenerative injection therapy (prolotherapy) in sports medicine. In: Seidelberg PH, Beutler PL, editors. The sports medicine resource manual. Philadelphia: Saunders; 2008. p. 611–9.
[10] Di Paolo S, Gesualdo L, Ranieri E, Grandaliano G, Schena FP. High glucose concentration induces the overexpression of transforming growth factor-beta through the activation of a platelet-derived growth factor loop in human mesangial cells. Am J Pathol 1996;149(6):2095–106.
[11] Murphy M, Godson C, Cannon S, Kato S, Mackenzie HS, Martin F, et al. Suppression subtractive hybridization identifies high glucose levels as a stimulus for expression of connective tissue growth factor and other genes in human mesangial cells. J Biol Chem 1999;274(9):5830–4.
[12] Krump E, Nikitas K, Grinstein S. Induction of tyrosine phosphorylation and Na^+/H^+ exchanger activation during shrinkage of human neutrophils. J Biol Chem 1997;272(28):17303–11.
[13] Jensen K, Rabago D, Best TM, et al. Early inflammatory response of knee ligaments to prolotherapy in a rat model. J Orthop Res 2008;26:816–23.
[14] Jensen KT, Rabago D, Best TM, et al. Longer term response of knee ligaments to prolotherapy in a rat injury model. Am J Sports Med 2008;36:1347–57.
[15] Rabago D, Kijowski R, Woods M, Patterson JJ, Mundt M, Zgierska A, et al. Association between disease-specific quality of life and magnetic resonance imaging outcomes in a clinical trial of prolotherapy for knee osteoarthritis. Arch Phys Med Rehabil 2013;94(11):2075–82.
[16] Louis LJ. Musculoskeletal ultrasound intervention: principles and advances. Radiol Clin North Am 2008;46:515–33.
[17] Kibler WB. Rehabilitation of rotator cuff tendinopathy. Clin Sports Med 2003;22:837–47.
[18] Kirkley A, Alvarez C, Griffin S. The development and evaluation of a disease-specific quality-of-life questionnaire for disorders of the rotator cuff: the Western Ontario Rotator Cuff Index. Clin J Sport Med 2003;13:84–92.
[19] Roach KE, Budiman-Mak E, Songsiridej N, Lertratanakul Y. Development of a shoulder pain and disability index. Arthritis Care Res 1991;4:143–9.
[20] DSS Research. Sample Size Measurament; 2016. Available at: http://www.dssresearch.com/KnowledgeCenter/toolkitcalculators/samplesizecalculators [Accessed: April 28, 2016].
[21] Bertrand H, Reeves KD, Bennett CJ, Bicknell S, Cheng AL. Dextrose prolotherapy versus control injections in painful rotator cuff tendinopathy. Arch Phys Med Rehab 2015;97(1):17–25.
[22] Kesikburun S, Tan AK, Yılmaz B, Yaşar E, Yazıcıoğlu K. Platelet-rich plasma injections in the treatment of chronic rotator cuff tendinopathy. A randomized controlled trial with 1-year follow-up. Am J Sports Med 2013;41(11):2609–16.
[23] Bergeson AG, Tashjian RZ, Greis PE, Crim J, Stoddard GJ, Burks RT. Effects of platelet-rich fibrin matrix on repair integrity of at-risk rotator cuff tears. Am J Sports Med 2012;40(2):286–93.
[24] Merolla G, Bianchi P, Porcellini G. Ultrasound-guided subacromial injections of sodium hyaluronate for the management of rotator cuff tendinopathy: a prospective comparative study with rehabilitation therapy. Musculoskelet Surg 2013;97(Suppl. 1):49–56.
[25] Tillander B, Franzén LE, Karlsson MH, Norlin R. Effect of steroid injections on the rotator cuff: an experimental study in rats. J Shoulder Elbow Surg 1999;8:271–4.
[26] Tempfer H, Gehwolf R, Lehner C, et al. Effects of crystalline glucocorticoid triamcinolone acetonide on cultered human supraspinatus tendon cells. Acta Orthop 2009;80:357–62.
[27] Stannard JP, Bucknell AL. Rupture of the triceps tendon associated with steroid injections. Am J Sports Med 1993;21:482–5.
[28] Scarpone M, Rabago DP, Zgierska A, Arbogast G, Snell E. The efficacy of prolotherapy for lateral epicondylosis: a pilot study. Clin J Sport Med 2008;18:248–54.
[29] Yelland MJ, Sweeting KR, Lyftogt JA, Ng SK, Scuffham PA, Evans KA. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. Br J Sports Med 2011;45:421–8.
[30] Ryan MB, Wong A, Gillies J, Wong J, Taunton J. Sonographically guided intratendinous injections of hyperosmolar dextrose/lidocaine: a pilot study for the treatment of chronic plantar fasciitis. Br J Sports Med 2009;43:303–6.
[31] Rabago D, Patterson J, Mundt M, Kijowski R, Grettie J, Segal N. Dextrose prolotherapy for knee osteoarthritis: a randomized controlled trial. Ann Fam Med 2013;11:229–37.
[32] Sanderson LM, 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.

[33] Seven MM, Koca K, Akpancar S, Turkkan S, Uysal B, Yildiz Y, et al. A promising results of prolotherapy in an elderly male with bilateral partial rotator cuff lesions. BMMR Online First 2016 [in press].
[34] Lee DH, Kwack KS, Rah UW, Yoon SH, Prolotherapy for refractory rotator cuff disease: retrospective case-control study of 1-year follow-up. Arch Phys Med Rehab. 2015;96(11):2027–32.
[35] Littlewood C, Ashton J, Chance-Larsen K, May S, Sturrock B. Exercises for rotator cuff tendinopathy: a systematic review. Physiotherapy 2012;98(2):101–9.
[36] Nichols AW. Complications associated with the use of corticosteroids in the treatment of athletic injuries. Clin J Sport Med 2005;15(5):370–5.
[37] Dorman TA. Prolotherapy: a survey. J Orthop Med 1993;15:49–50.