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Long-term effect of Prolotherapy on symptomatic rotator cuff tendinopathy

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ABSTRACT

Introduction: The objective of this study was to assess a long-term clinical effect of Prolotherapy on chronic symptomatic rotator cuff tendinopathy.

Methods: We conducted a retrospective, uncontrolled study in the outpatient setting with 12 months follow-up. Adults diagnosed clinically and radiologically with rotator cuff tendinopathy that has been persisting for a minimum of six months were included. Patients received 15% extra-articular and 25% intra-articular hyperosmolar dextrose injections, repeated at weeks 5, 9, 13, 17 and 21. Primary outcome measure was validated Shoulder Pain and Disability Index (SPADI). Secondary outcome measure was validated visual pain analogue scale (VAS 0-10). The third outcome measures were patient's satisfaction with Prolotherapy and adverse reactions after injections.

Results: Twenty-one patients, 14 male and 7 female were treated with 6 sessions of hyperosmolar dextrose Prolotherapy repeated every 4 weeks. Average SPADI before starting the treatment was 73.995 ± 13.6, while 12 months after completed treatment was 20.84 ± 26.03 (P< 0.0001). Average VAS score before starting the treatment was 8.14 ± 1.2, while 12 months after completed treatment was 2.29 ± 2.8 (P<0.0001). Out of 21 patients, 18 (85.71%)would recommend Prolotherapy to other people with the similar condition, and no one participant reported any side effect that was not resolved within one week after the treatment.

Conclusion: Hyperosmolar dextrose Prolotherapy may result in significant reduction of pain and disability index in adult patients with chronic rotator cuff tendinopathy, without eliciting long-lasting side effects. Results of this pilot study need to be validated in prospective controlled randomized trials.

Keywords: rotator cuff tendinopathy; prolotherapy; hyperosmolar dextrose therapy, SPADI, VAS

INTRODUCTION

Rotator cuff tendinopathy presents a spectrum of conditions with multifactorial patho-etiology. The main characteristics are pain, usually localized in the area of rotator cuff tendons, weakness in the arm and limited function. It can be followed by partial or complete tendon tear with the signs of impingement and bursitis. It is one of the most common shoulder conditions affecting people older than 40 years, but also active young people particularly involved in sports activities. Incidence of tear is in direct correlation with increasing age. It is estimated that more than a half of individuals in their 80s

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have a rotator cuff tear (1). Traditional conservative treatments include non-steroidal anti-inflammatory drugs (NSAID), corticosteroid injections and physiotherapy. The meta-analysis study confirmed comparable efficacy of corticosteroid injections to NSAID on short-term, but not on long-term basis (2). Another systematic review of randomized controlled trials of interventions for painful shoulder found little evidence to support the use of any of the common interventions in managing shoulder pain (3). Full width or retracted supraspinatus tears may require a surgical approach. Prolotherapy is an injection based complementary and alternative therapeutic option practiced for decades for chronic musculoskeletal conditions. Term prolo is abbreviation of proliferation what means growth by the rapid multiplication. Hyperosmolar dextrose is commonly used substrate for injections (4). Prolotherapy has been applied in a variety of medical conditions (4). As far as we know there is one case-control study and one randomized control trial assessing the effect of dextrose Prolotherapy on chronic rotator cuff tendinopathy (5,6) and no study was conducted on population living in the Middle East.

We conduced a retrospective, uncontrolled pilot study to test the hypothesis that dextrose Prolotherapy is a safe procedure that improves pain and disability index comparing to baseline values in patients with chronic rotator cuff tendinopathy.

METHODS

This was a retrospective, uncontrolled, case record study conducted on consecutive patients diagnosed with chronic rotator cuff tendinopathy. Medical records were scrutinized for inclusion and exclusion criteria and proceeded to further analysis.

Eligibility criteria and recruitment process

Medical records were reviewed for patients aged 20-70 years, treated with dextrose Prolotherapy, from March 2007 through April 2011, for chronic shoulder pain. The diagnosis of rotator cuff tendinopathy was established a minimum of six months before Prolotherapy treatment started. We included consecutively treated patients with shoulder pain VAS>3/10 at the moment of evaluation, abnormal examination findings with either Hawkins, Empty can, Neer test or painful internal and external rotation of the shoulder testing and MRI confirmed rotator cuff tendinopathy without retraction or full-width tear. Inclusion criteria also involved patients with biceps brachii tendinopathy, subacromial/subdeltoid and subcoracoid bursitis as well as mild to moderate acromioclavicular osteoarthritis (arthrosis). All mentioned lesions were found together with rotator cuff tendinopathy. Patients with other shoulder related diagnoses like Bankart and Hill-Sachs lesions, adhesive capsulitis, fractures, severe osteoarthritis were excluded. We also excluded patients with inflammatory and systematic rheumatic disorders and patients who continued the regular use of NSAIDs and painkillers for any condition. The patients were referred from primary health centers in most of the cases by family physicians and from specialty clinics located in two hospitals.

Outcome measures

The primary outcome measure was Shoulder Pain and Disability Index (SPADI) – numerical version. The SPADI was developed to measure current shoulder pain and disability in an outpatient setting. It contains 13 items that assess two domains: a 5-item subscale that measures pain and an 8-item subscale that measures disability (7). The Minimal clinically important difference (MCID) has been reported to be 8 points (8) but if it is used more than one time on the same patient, the minimal detectable change (MDC 95%) is 18 points (9). A higher score indicates greater impairment or disability (10). Secondary outcome included measurement of pain intensity by using Visual analog scale (VAS) 0-10 with meanings 0-"no pain" and 10-"the worst imaginable pain". To the authors' knowledge, the minimal clinically important difference has not been published for VAS related to rotator cuff tendinopathy. The most severe pain experienced in a period between onset of symptoms and first Prolotherapy session was considered as a baseline parameter. The same parameter was used for the calculation in the period between the last Prolotherapy session and evaluation time, 12 months later. Pain reduction was attributed to the therapeutic effect of Prolotherapy. The maximal pain intensity was used as an indicator of the severity of condition, since it usually affects activities of daily living (ADL)

performance. The third measured outcomes were patient's satisfaction with Prolotherapy and side effects of Prolotherapy in the same period after completing the last session. Patient's satisfaction with Prolotherapy was assessed by asking the simple questions: Would you recommend Prolotherapy to other patients with the similar condition to yours (Yes/No)? Regarding side effects, the patients were asked: Did you experience any side effect related to Prolotherapy injections that was not resolved within 1 week after the treatment (Yes/No)?

Intervention

Prolotherapy treatments for all patients were conducted by the same physician in the following way: after palpation to detect potential sources of pain in the shoulder region, the tender points were marked by skin marker and the whole shoulder area was cleaned with Betadine (povidone-Iodine) solution for disinfection. After that, anesthetic skin wheals of 1% Lidocaine were placed to each marked point following by Prolotherapy injections according to the protocol (Table 1). Patients were advised to stop the use of NSAIDs one week before starting the treatment and during the whole treatment of approximately five months. The injections were repeated at weeks 5, 9, 13, 17 and 21.

TABLE 1. Prolotherapy solution and injection points

Injection type and technique	
Intraarticular 25% Dextrose 3 ml 50% Dextrose+ 3 ml 1% Lidocaine	6 ml of 25% dextrose in single injection to the glenohumeral joint using posterior, subacromial approach
Extrarticular 15% Dextrose 3 ml 50% Dextrose 3 ml 1% Lidocaine 4 ml 0.9% Sodium chloride	1 ml solution is injected to the marked insertion of tendons and ligaments, 25 gauge needles were used
Injected points	
Humerus-greater and lesser tuberosity	Tendons: Supraspinatus, infraspinatus, teres minor, subscapularis
Coracoid process	Tendons: Biceps brachii (short), coracobrachialis, pectoralis minor
Acromio clavicular (AC) joint	Ligaments: Coraco-clavicular and Coraco-acromial
Posterior to AC joint - "V part"	Tendon: Long head of biceps brachii

Statistical analysis

The statistical analysis was done by IBM SPSS Statistics 21.0 software (IBM, Chicago, USA). A repeated measures ANOVA with a Greenhouse-Geisser degree of freedom correction was used to determine average SPADI and VAS pain assessment score. Patient satisfaction with treatment was presented in raw data and percentage. The level of statistical significance was determined by the value of $P<0.05$.

RESULTS

There was a total of 21 patients, 14 (67%) male and 7 (33%) female, with an average age of 48.7 years. They were diagnosed with rotator cuff tendinopathy lasting from 6 months to 7 years, in average the period of 38.28 months, before starting with Prolotherapy (Table 2). The causal factors for all injuries were overuse and repetitive activities. Most of the patients were treated conservatively with at least one of the following modalities: NSAID, physiotherapy, corticosteroid injections, ozone therapy, and acupuncture. Average SPADI score before the Prolotherapy treatment was 73.995 ± 13.6, while 12 months after completed treatment it was 20.84 ± 26.03, which was a significant reduction ($P<0.0001$) (Table 3). Average VAS score before the Prolotherapy treatment was 8.14 ± 1.2, while 12 months after the treatment it was 2.29 ± 2.8, which was a significant reduction of pain intensity ($P<0.0001$) (Table 4).

Nineteen patients (90.48%) reported improvement from baseline in pain intensity measured by VAS and shoulder function measured by SPADI. This exceeds MCID for SPADI, which is 8 points reduction (8). Eighteen patients (85.71%) would recommend dextrose Prolotherapy to other patients with a similar condition (Figure 1) and no one patient reported significant side effects, which were not resolved within one week.

DISCUSSION

This uncontrolled pilot study on patients diagnosed with chronic rotator cuff overuse injury confirmed substantial pain reduction and functional improvement 12 months after the Prolotherapy treatment. Almost all the patients (90.48%) reported

TABLE 2. Patients with rotator cuff tendinopathy treated with dextrose Prolotherapy

Patient	Gender	Age (years)	MRI Diagnosis	Duration of symptoms (months)
1	F	61	(L) Partial supraspinatus tear	7
2	F	66	(R) Partial supraspinatus tear subacromial bursitis AC joint osteoarthritis	30
3	M	42	(R) Supraspinatus and infraspinatus tendinosis AC joint osteoarthritis	42
4	M	45	(R) Bicipitis tendinosis supraspinatus tendinosis subacromial/subdeltoid bursitis	72
5	M	41	(R) Supraspinatus partial tear	10
6	F	36	(L) Supraspinatus partial tear	8
7	M	55	(L) AC osteoarthritis bicipitas tendinosis supraspinatus and infraspinatus tendinosis subcoracoid bursitis	60
8	M	48	(R) Supraspinatus and bicipitis tendinosis	72
9	F	39	(R) Supraspinatus partial tear	6
10	M	49	(R) AC osteoarthritis supraspinatus tendinosis subacromial/subdeltoid bursitis	54
11	M	56	AC osteoarthritis supraspinatus and bicipitis tendinosis	84
12	M	68	AC osteoarthritis supraspinatus partial thickness tear	66
13	M	43	(R) AC joint osteoarthritis partial thickness supraspinatus tear	36
14	M	52	(R) AC hypertrophic degenerative changes supraspinatus and infraspinatus tendinosis subacromial bursitis	18
15	F.	67	(R) AC hypertrophic osteoarthritis partial supraspinatus and biceps tendon tear subacromial bursitis	72
16	M	45	(L) AC osteoarthritis subacromial bursitis partial supraspinatus tear	48
17	F	64	(R) AC joint osteoarthritis partial thickness tear supraspinatus subacromial bursitis infraspinatus and subscapularis tendinosis	84
18	M	26	(R) Partial tear supraspinatus tendon	6
19	M	44	(R) Shoulder supraspinatus and biceps tendinosis	8
20	F	28	(R) Biceps and infraspinatus tendinosis	12
21	M	47	(L) Supraspinatus partial tear	9

M: Male, F: Female, R: Right, L: Left, AC: Acromioclavicular

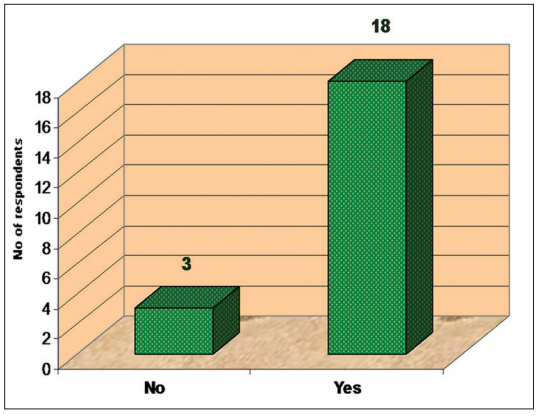

FIGURE 1. Patients' satisfaction. Answer to question „Would you recommend Prolotherapy to other patients with similar condition?"

improvement from baseline in pain intensity measured by VAS 0-10 and shoulder function measured by SPADI. This exceeds MCID for SPADI, which is 8 points reduction (8). Patient's satisfaction with dextrose Prolotherapy was very high, considering that 85.7 % of patients would recommend this treatment to other people with the similar condition. It is very important to notify that in this study no one patient reported any side effect that was not resolved within seven days after the treatment. Most of the complaints were related to temporarily increased pain, tenderness in the area of injections and small bruises. Overall VAS and SPADI data suggest that Prolotherapy might improve the condition in a majority of patients suffering chronic rotator cuff tendinopathies. These results are consistent with two previous studies (5,6) in which authors also reported significant improvement of tested parameters after Prolotherapy injections. However, direct comparison with these studies is limited because of different

TABLE 3. SPADI score before and 12 months after Prolotherapy treatment

Patient	Before treatment	12 months after the treatment
1	76.9	6.1
2	68.3	3.7
3	51.5	58.5
4	93.1	2.3
5	80.0	7.7
6	84.6	70.0
7	77.7	81.5
8	82.3	8.5
9	43.8	21.5
10	53.8	16.9
11	69.2	13.5
12	53.1	3.1
13	92.3	24.6
14	79.2	73.1
15	80.0	0
16	70.0	10.0
17	86.1	0
18	69.2	3.1
19	86.9	12.3
20	79.8	2.1
21	76.1	19.2

Before treatment: Average 73.995±13.6, after the treatment: Average 20.84±26.03; P<0.0001

TABLE 4. VAS (0-10) score before and 12 months after the treatment with Prolotherapy

Patient	Before treatment	12 months after the treatment
1	8	0
2	7	0
3	7	7
4	10	0
5	9	0
6	10	8
7	8	7
8	9	2
9	6	3
10	7	3
11	7	1
12	7	0
13	10	2
14	8	8
15	7	0
16	8	2
17	9	0
18	8	1
19	10	2
20	8	1
21	8	1

Before treatment: Average 8.14±1.2; after the treatment: Average 2.29±2.8; P<0.0001

study designs and treatment protocols. Dextrose Prolotherapy confirmed to be efficient in a variety of chronic musculoskeletal conditions in humans, such as Achilles tendinosis (11), anterior cruciate ligament laxity (12), coccygodynia (13), knee osteoarthritis (14), cervical spine instability (15), plantar fasciitis (16) and tennis elbow (17). Treatment of chronic low back pain with Prolotherapy provided conflicting results (18). Mechanism of action of dextrose Prolotherapy remains unclear. Three possible effects were described: natural elevation of growth factors, stimulation healing cascade by promoting inflammatory reaction and needling effect (19). It was found that elevation of glucose from 0.1% (normal extracellular level) to 0.45% (level in diabetics) results in the production of as many as 15 different proteins including key growth factors for soft tissue; IE connective tissue growth factor (CTFG) and transforming growth beta factor (TGFβ). These effects occur within 20 minutes of cellular exposure to 0.45% dextrose (20). These growth factors involved in a complex process known as a healing cascade will contribute to remodeling of fibrous collagen structure. It will eventually thicken and strengthen injured tendons and ligaments. The recent animal study confirmed the presence of fibrous tissue in the carpal tunnel after injection of hyperosmolar dextrose (21).

This is a retrospective pilot study conducted on a small sample of participants. The lack of a control group excludes the possibility to compare dextrose injections with placebo, or with other known therapeutic alternatives. That is why this study can be used for the formulation of hypothesis rather than for conclusions about the effect of dextrose Prolotherapy on chronic rotator cuff tendinopathies. A collection of information about patients' satisfaction with Prolotherapy although conducted by the physiotherapist who did not participate in evaluation and treatment of patients might be biased to some extent. This is the first study on Prolotherapy conducted on the population of Middle East. This treatment is quite

unknown in this part of the world and just recently gained more popularity. There was no drop out among the patients who were selected as participants. Consistency in positive effect even 12 months after the treatment can increase the likelihood of success in further controlled randomized trials.

CONCLUSIONS

Clinical studies related to the effect of dextrose Prolotherapy on chronic rotator cuff tendinopathies are very rare. In the first pilot study conducted in the Middle East, we suggest that Prolotherapy might be efficient and safe therapeutic option. Since the sample was small, these preliminary results need future verification in controlled randomized trials with larger samples.

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