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Effects of Subacromial Bursa Injection With Corticosteroid and Hyaluronidase According to Dosage

Won Duck Choi, MD, Dong Hyun Cho, MD, Yong Ho Hong, MD, Jae Hyun Noh, MD, Zee Ihn Lee, MD, Seung Deuk Byun, MD

Department of Rehabilitation Medicine, Daegu Fatima Hospital, Daegu, Korea

Objective To evaluate effects of subacromial bursa injection with steroid according to dosage and to investigate whether hyaluronidase can reduce steroid dosage.

Methods Thirty patients with periarticular shoulder disorder were assigned to receive subacromial bursa injection once a week for two consecutive weeks. Ten patients (group A) underwent subacromial bursa injection with triamcinolone 20 mg; another group of ten patients (group B) with hyaluronidase 1,500 IU and triamcinolone 20 mg; and the other ten patients (group C) with triamcinolone 40 mg. We examined the active range of motion (AROM) of the shoulder joint, visual analogue scale (VAS), and shoulder disability questionnaire (SDQ) at study entry and every week until 1 week after the 2nd injection.

Results All groups showed statistically significant improvements in VAS after 1st and 2nd injections. When comparing the degree of improvement in VAS, there were statistically significant differences between groups C and A or B, but not between groups A and B. SDQ was statistically significantly improved only in groups B and C, as compared to pre-injection. There were statistically significant differences in improvement of SDQ after the 2nd injection between groups C and A or B. Statistically significant improvements in AROM were shown in abduction (groups B and C) and in flexion (group C only).

Conclusion Repeated high-dose (40 mg) steroid injection was more effective in terms of pain relief and functional improvements of shoulder joint than medium-dose (20 mg) steroid injection in periarticular disorder. Hyaluronidase seems to have little additive effect on subacromial bursa injection for reducing the dosage of steroid.

Keywords Shoulder impingement syndrome, Corticosteroid, Dosage

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Corresponding author: Seung Deuk Byun
Department of Rehabilitation Medicine, Daegu Fatima Hospital, 99 Ayang-ro, Dong-gu, Daegu 701-724, Korea
Tel: +82-53-940-7821, Fax: +82-53-940-7417, E-mail: sato1009@hanmail.net

INTRODUCTION

Periarticular shoulder disorder refers to a set of diverse diseases including subacromial and subdeltoid bursitis, rotator cuff tendonitis, calcific tendinitis, and rotator cuff tear. Together with adhesive capsulitis (frozen shoulder), it forms the typical cause of shoulder pain and limited range-of-motion (ROM) [1,2]. As subacromial bursa injection is widely used for pain relief and functional improvements in patients with periarticular shoulder disorder, it is mostly injected corticosteroids with lidocaine [2-5]. According to Yoon et al. [2], it has been shown that high-dose corticosteroids (40 mg) generally makes a significant improvement in pain relief and functional improvement of shoulder, compared to a low dosage (10 mg).

However, the dosage and dosing frequency are often limited due to local or systemic side effects of corticosteroids. There have been recent studies seeking to replace or combine corticosteroids with hyaluronic acid. Seo et al. [6] injected steroids with hyaluronidase into the glenoid cavity in patients with adhesive capsulitis and reported that there was a significant improvement in pain relief and ROM, as compared to patients injected with corticosteroids only. In addition, Byun et al. [7] performed subacromial bursa injection with triamcinolone (40 mg) and hyaluronidase once a week for two consecutive weeks in patients with periarticular shoulder disorder and reported that it improved shoulder joint function as well as active internal rotation.

Varied dosage of injection for periarticular shoulder disorder has been suggested. However, there is no research to clinically compare the efficacy of the usual medium-dose (20 mg) corticosteroids to that of a high-dose (40 mg) in subacromial bursa injection. There is also a lack of comparison between the efficacy of combination therapy (medium-dose corticosteroids with hyaluronidase) and that of monotherapy (high-dose corticosteroids). Therefore, this study aimed to examine the efficacy of medium- (20 mg) and high-dose (40 mg) corticosteroids in subacromial bursa injection and to determine whether hyaluronidase, which the authors have reported on previously, is effective in patients who cannot endure the high-dose corticosteroid treatment while reducing the dosage.

MATERIALS AND METHODS

Subjects

Patients who came to the Department of Rehabilitation Medicine with the primary complaints of shoulder pain from January 2011 to June 2012 were selected. Those who met the following inclusion criteria were finally considered: 1) who had a clinical sign of a painful arc and positive in Hawkins test or Neer impingement sign; 2) who had a precise rotation cuff injury including partial or full rotation cuff tears, or subacromial bursitis under ultrasonography; and 3) who showed limited active ROM and stiffness to the extent not to be included in the exclusion criteria of adhesive capsulitis. The exclusion criteria were as follows: 1) who was diagnosed with adhesive capsulitis—normal findings on X-ray; <100° of active or passive elevation of arm, when raising the arm above the head to a maximum; and passive external rotation of glenohumeral joint being 50% less than the unaffected side when measured with the examiner holding the wrist of the subject and bending his/her elbow to 90°; 2) who underwent shoulder surgery; 3) who had corticosteroids or hyaluronic acid injection into the shoulder due to same etiology; 4) who had hemiplegic shoulder pain; and 5) who showed any suspected fracture on X-ray. Eligible subjects were randomized into three groups A, B and C. The participants were assigned into the groups with the random block assignment method, and patients were lined up to be assigned. Six patient-blocks were further subdivided into groups A, B and C. For every sixth participant, one method was randomly selected and assigned to that individual.

Subacromial bursa injection

We performed physical examination and evaluation of shoulder pain and function and used ultrasonography to confirm the lesion. Then, the subject made his/her arms to internal rotation and hypertension and put the forearms close to the back. The target area was disinfected, and ultrasound-guided subacromial bursa injection was carried out. All subjects of the three groups had an injection once a week for two consecutive weeks with different dosage: group A, triamcinolone acetonide 20 mg (0.5 mL) and 0.5% lidocaine 5.5 mL, total 6 mL; group B, triamcinolone acetonide 20 mg (0.5 mL), H-lase (Kuhnil Pharm., Seoul, Korea) 1,500 IU (1 mL) and 0.5% lidocaine 4.5 mL,

total 6 mL; and group C, triamcinolone acetonide 40 mg (1 mL) and 0.5% lidocaine 5 mL, total 6 mL. They were asked to discontinue any medication including painkiller and anti-inflammatory drug 1 week before the injection. The patients were educated on perishoulder stabilization and stretching exercises to be performed at home. At each visit, the patients were also educated and recommended to perform other self-exercises including the scapular stabilization exercise. There was no additional physiotherapy or medication.

Efficacy evaluation

Subjects were evaluated three times: before the 1st injection, 1 week after the 1st injection, and 1 week after the 2nd injection. The examinations were conducted by one examiner, who had evaluated the subjects before the 1st injection. The examiner asked the subjects to rate the average degree of pain for 24 hours before the evaluation, on the visual analogue scale (VAS, 0 to 10).

The examiner then measured active ROM of the shoulder but did not limit its movement. To measure shoulder flexion and abduction, the examiner measured the range-of-movement of the arms in sagittal and coronal planes while the subject was asked to sit and extend the elbow joint. For external and internal rotation, the subject was sat and externally rotated the shoulder to 90°. The normal range of shoulder flexion and abduction was defined as 180°, while that of external and internal rotation was 90°. We adapted the shoulder disability questionnaire (SDQ) to evaluate the shoulder function of subjects. SDQ is a tool whose reliability and validity have been verified for evaluating the degree of shoulder disability that a patient feels. It is composed of 22 self-reported questions (0, no disability; up to 22, maximum disability) [8].

Statistical analysis

SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA) for Windows was used for all analyses. All values were measured for the groups before 1st injection, 1 week after 1st injection, and 1 week after 2nd injection. Differences in sex, age, and shoulder-affected as well as pre-injection scores between groups A, B, and C were analyzed using Kruskal-Wallis test with Mann-Whitney U test. Differences in VAS, SDQ, and ROM between groups A and B and between groups A and C were analyzed using Mann-Whitney U test. The degree of VAS, SDQ, and ROM before and after injection in each group was analyzed by using Wilcoxon signed-rank test. Statistical significance was assumed at $p<0.05$.

RESULTS

Subject characteristics and ultrasonic findings

Thirty subjects were randomly assigned to groups A, B,

Table 1. General characteristics of subjects

	Group A (n=10)	Group B (n=10)	Group C (n=10)
Sex (male:female)	6:4	4:6	5:5
Age (yr)	56.3±6.8	55.7±8.0	56.2±7.9
Shoulder affected			
Dominant	6 (60)	7 (70)	7 (70)
Non-dominant	4 (40)	3 (30)	3 (30)
Visual analogue scale	5.4±1.2	5.0±1.7	4.9±0.9
Shoulder disability questionnaire	7.5±3.9	7.0±3.4	8.7±3.1
Range of motion (°)			
Flexion	173.0±8.2	166.5±16.0	167.0±11.6
Abduction	168.0±13.9	156.5±25.8	162.0±16.2
Internal rotation	88.0±6.3	82.0±10.3	83.0±9.5
External rotation	81.0±8.7	80.0±10.2	77.0±10.6

Values are presented as mean±standard deviation or number (%).
Group A, patients injected with 0.5% lidocaine 5.5 mL+triamcinolone 20 mg; group B, patients injected with 0.5% lidocaine 4.5 mL+triamcinolone 20 mg+hyaluronidase 1 mL (1,500 IU); group C, patients injected with 0.5% lidocaine 5 mL+triamcinolone 40 mg.
$p<0.05$ between groups A, B, and C.

and C (10 subjects in each group). There was no significant difference in sex, age, and shoulder-affected as well as in pre-injection scores between the groups (Table 1).

Table 2. Ultrasonographic diagnosis before injection

Finding	Group A (n=10)	Group B (n=10)	Group C (n=10)
RC partial-tear	4	3	4
RC full-thickness tear	2	3	3
SA-SD bursitis	4	4	3

RC, rotator cuff; SA-SD, subacromial-subdeltoid.

No significant difference was observed in pre-injection ultrasonic findings between the groups (Table 2).

Changes in VAS

All groups showed statistically significant improvement after 1st injection in VAS, compared to pre-injection. The significant improvement was also observed after 2nd injection, compared to 1st injection (Table 3). When comparing the degree of improvement after 2nd injection to that before injection, there was statistically significant difference between groups C and A or B, but not between groups A and B (Table 4).

Table 3. Summary of treatment effects in groups A, B, and C

Group	Pre-injection	1 wk after 1st injection	1 wk after 2nd injection
Visual analogue scale			
A	5.4±1.2	3.3±1.3[a)]	1.6±1.8[b,c)]
B	5.0±1.7	2.9±1.6[a)]	1.6±1.4[b,c)]
C	4.9±0.9	2.9±1.4[a)]	1.6±0.7[b,c)]
Shoulder disability questionnaire			
A	7.5±3.9	4.9±5.7	1.5±3.8[b)]
B	7.0±3.4	5.6±3.5[a)]	1.9±2.2[b,c)]
C	8.7±3.1	6.3±3.8	2.0±1.8[b,c)]
Range of motion (°)			
Flexion			
A	173.0±8.2	177.0±4.8	180.0±0.0[c)]
B	166.5±16.0	171.0±9.9	176.0±5.2[b,c)]
C	167.0±11.6	176.0±7.0[a)]	178.0±6.3[c)]
Abduction			
A	168.0±13.9	174.0±8.4	179.0±3.2[c)]
B	156.5±25.8	170.0±14.1[a)]	175.0±7.0[c)]
C	162.0±16.2	173.0±15.7[a)]	177.0±9.5[c)]
Internal rotation			
A	88.0±6.3	88.0±4.2	90.0±0.0
B	82.0±10.3	84.0±8.4	85.0±7.1
C	83.0±9.5	86.0±6.9	88.0±4.2
External rotation			
A	81.0±8.7	86.0±6.9	87.0±4.8
B	80.0±10.2	83.0±6.7	88.0±3.5[b,c)]
C	77.0±10.6	85.0±8.5	87.0±4.8[c)]

Values are presented as mean±standard deviation.
Group A, patients injected with 0.5% lidocaine 5.5 mL+triamcinolone 20 mg; group B, patients injected with 0.5% lidocaine 4.5 mL+triamcinolone 20 mg+hyaluronidase 1 mL (1,500 IU); group C, patients injected with 0.5% lidocaine 5 mL+triamcinolone 40 mg.
[a)]p<0.05, pre-injection vs. 1 weekk after 1st injection.
[b)]p<0.05, 1 week after 1st injection vs. 1 week after 2nd injection.
[c)]p<0.05, pre-injection vs. 1 week after 2nd injection.

Table 4. Changes in measurement values of groups A, B, and C after 2nd injection

	Group A	Group B	Group C
Visual analogue scale	3.8±1.4	3.4±1.2	7.2±1.6[a,b]
Shoulder disability questionnaire	6.6±3.4	5.2±2.2	11.8±4.3[a,b]
Range of motion (°)			
Flexion	7.0±8.2	9.5±14.2	16.5±16.3
Abduction	11.0±11.9	18.5±20.6	29.5±25.6
Internal rotation	2.0±6.3	3.0±4.8	5.0±9.7
External rotation	6.0±8.4	8.0±9.2	14.0±12.6

Values are presented as mean±standard deviation.
Group A, patients injected with 0.5% lidocaine 5.5 mL+triamcinolone 20 mg; group B, patients injected with 0.5% lidocaine 4.5 mL+triamcinolone 20 mg+hyaluronidase 1 mL (1,500 IU); group C, patients injected with 0.5% lidocaine 5 mL+triamcinolone 40 mg.
[a]$p<0.05$ group A vs. group C.
[b]$p<0.05$ group B vs. group C.

Changes in SDQ

In group B, SDQ was significantly improved after 1st injection, compared to pre-injection. SDQ was statistically significantly improved after 2nd injection in all groups, compared to 1st injection, but when compared to pre-injection, only in groups B and C (Table 3). There was statistically significant difference in improvement after 2nd injection between groups C and A or B, compared to pre-injection, but not between groups A and B (Table 4).

Changes in active ROM

When comparing the 1st injection results to pre-injection, there were statistically significant improvements in abduction (groups B and C) and flexion (group C only). In comparison of the 2nd injection results to 1st injection, statistically significant improvements in abduction and external rotation were observed in group B only. When comparing the 2nd injection results to pre-injection, flexion and abduction were statistically significantly improved in all groups and additionally external rotation in groups B and C (Table 3). In regard to the degree of improvement after 2nd injection, compared to pre-injection, there was no statistically significant difference between the groups (Table 4).

DISCUSSION

Subacromial bursa injection with steroid is widely used for pain relief and functional improvement in patients with periarticular shoulder disorder. Recent research has studied the proper number and interval of injection and steroid dosage [9-11]. As degenerative change or metabolic and endocrine-related side effects are of concern in higher steroid dosage [2,12], studies are seeking to replace steroids or combine it with hyaluronic acid [8,13,14]. Hyaluronidase is a mammalian water-soluble enzyme secreted by the testis or the intestinal canal. It hydrolyzes the glucosamic bond between hyaluronic acid and connective tissues to remove the interstitial barrier, thereby modifying the permeability of connective tissues and reducing the viscosity of intercellular interaction [15]. It is subcutaneously injected into tissues with edema as an absorption enhancer, thereby relieving swelling and edema. It can also be injected together with local anesthesia or steroids to increase permeability. Hyaluronidase is thereby widely used in ophthalmology, gynecology, and anesthesiology [16,17].

Byun et al. [7] performed subacromial bursa injection with triamcinolone (40 mg) and hyaluronidase in patients with periarticular shoulder disorder, and compared it to steroid monotherapy. The study reported that additional improvement was observed in shoulder joint function and active internal rotation. A recommendation for observance following 2nd injection was made in the study, as there was no difference in the efficacy between 2nd injection and 3rd injection at 1-week interval. In this study, hyaluronidase, which is known to be effective in combination therapy with steroids in spine nerve root injection or adhesive capsulitis [6,18], was injected with corticosteroids, once a week for 2 consecutive weeks into

subacromial bursa of patients with periarticular shoulder disorder. The treatment was compared to corticosteroid monotherapy. This study has aimed to determine whether hyaluronidase is effective as an adjuvant while reducing the dose of corticosteroids and to examine the efficacy of medium- (20 mg) and high-dose (40 mg) steroid injection [6,18].

To compare the degree of improvement after 2nd injection to pre-injection, we used VAS and SDQ. Statistically significant improvement was observed in group C than in A or B, suggesting that hyaluronidase combination therapy did not reduce steroid dosage. As shown in statistically significantly improved SDQ in group B when comparing the 1st injection results to SDQ pre-injection, 20 mg steroids and hyaluronidase combination therapy once may be effective in improving shoulder function of patients with uncontrollable diabetes or for those who cannot endure high-dose steroids.

In addition, this study compared the 1st injection results of active ROM to pre-injection; and improvements in flexion and abduction were observed in group C only. In comparing the 2nd injection results to pre-injection, all groups showed improvement in flexion and abduction, and additionally, external rotation in groups B and C. There was no significant difference in improvement of active ROM between the groups.

This study excluded patients with adhesive capsulitis in order to exclude patients with capsular pattern. However, as the symptoms of early adhesive capsulitis is similar to that of shoulder impingement syndrome, this study is limited to not completely exclude patients with early adhesive capsulitis. The study has included patients with stiffness and precise lesion under ultrasonography, so that the patients with early adhesive capsulitis may be excluded to some degree.

With a small sample size and short-term follow-up, this study is limited in understanding the long-term effects of corticosteroid and hyaluronidase combination therapy. A further long-term study with more patients is required. We think that the results of this study may be helpful in determining the proper dosage of corticosteroids. It may also aid in finding an effective adjunctive material while reducing corticosteroid side effects in patients with periarticular shoulder disorder.

In conclusion, repeated high-dose (40 mg) steroid injection was more effective in terms of pain relief and functional improvements of shoulder joint than medium-dose (20 mg) steroid injection at subacromial bursa in patients with periarticular disorder. Hyaluronidase has little additive effect in subacromial bursa injection for reducing the dosage of steroid.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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