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Original Research Article

Comparison of Steroid and/or Sodium Hyaluronate Injections in Frozen Shoulder: A Prospective, Double-Blind, Randomized, Placebo-Controlled Trial

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Abstract

Background: Limited research has explored the impacts of concurrent administration of corticosteroid (CS) and hyaluronic acid (HA) for adhesive capsulitis (AC) of the shoulder. This study examines the combined effects of simultaneous intra-articular injections of CS compared to injections of CS or HA alone.

Methodology: A randomized, placebo-controlled trial was conducted with sixty AC patients. They were assigned to one of four groups: saline, CS, HA, and CS with HA. The primary outcome measure was changes in the Shoulder Pain and Disability Index (SPADI) scores after one month. Secondary measures included alterations in pain, range of motion, muscle strength, and overall satisfaction at various intervals up to six months post-injection.

Results: At the one-month mark, SPADI score changes were significantly greater in the CS with HA group (−30.3 ± 11.6) compared to the saline (−4.4 ± 21.1) and HA (−7.8 ± 23.1) groups. The CS with HA group exhibited a larger score change than the CS group (−25.6 ± 11.2). Moreover, regarding pain reduction and range of motion improvement, the CS with HA group demonstrated superior and more rapid effects compared to the saline and HA groups. Additionally, functional scores favored the CS with HA group over the saline and HA groups.

Conclusion: In the management of AC, simultaneous CS and HA injections proved more efficacious in enhancing SPADI scores after one month compared to single CS or HA injections.

Introduction

Adhesive capsulitis of the shoulder presents with spontaneous shoulder pain and a gradual decrease in both active and passive shoulder movement. It affects 2%-5% of the general population and leads to significant pain, disability, and sleep disturbances.[1,2] Although adhesive capsulitis typically resolves within one to three years, a significant portion of patients (20%-50%) continue to experience long-term limitations in shoulder motion even after a decade.[3-5] The progression of adhesive capsulitis is often described in stages of freezing, frozen, and thawing, with overlapping symptoms.[6] Patients can be categorized as either primarily experiencing pain or stiffness. Treatment approaches vary depending on the predominant symptom: physical therapy is typically used for stiffness, while various methods such as analgesics, corticosteroid or hyaluronic acid injections, manipulation under anesthesia, hydrodilatation, and arthroscopic release are employed for pain relief. Intra-articular injections, particularly of corticosteroids or hyaluronic acid, are commonly utilized to alleviate pain and facilitate range of motion exercises, aiming for a swift improvement in function.[7-10]

Both corticosteroid and hyaluronic acid injections have been found effective in reducing inflammation and improving joint function.[11-13] Corticosteroids work by upregulating anti-inflammatory proteins and inhibiting inflammatory gene expression, providing short-term relief but limited long-term benefit for adhesive capsulitis.[14] Hyaluronic acid, on the other hand, has anti-inflammatory properties and aids in cartilage repair and synovial health, with effects lasting up to six months.[15-17]

Combining both medications in treatment is believed to enhance efficacy due to their differing onset and mechanisms of action. However, the evidence supporting these injection therapies for adhesive capsulitis is somewhat lacking, with

variations in study parameters making it challenging to draw definitive conclusions.[2]

Previous research comparing simultaneous corticosteroid and hyaluronic acid injections with corticosteroid are far and few, thus hindering a clear assessment of treatment effectiveness. Our study aims to address this gap by systematically analyzing the effects of simultaneous injections versus single injections of either corticosteroid or hyaluronic acid. We hypothesize that simultaneous administration of corticosteroid and hyaluronic acid will yield better outcomes in terms of improving Shoulder Pain and Disability Index (SPADI) scores one month post-injection compared to either treatment alone.

Methods

Study Design and Eligibility Criteria

A hospital based clinical trial was conducted from 2021 to 2023, focusing on patients aged 25 to 75 with unilateral adhesive capsulitis. AC diagnosis required the presence of shoulder pain and restrictions in both active and passive range of motion (ROM) exceeding 25% in at least two planes: forward flexion (FF), abduction (ABD), external rotation (ER), and internal rotation (IR), in comparison to the opposite shoulder or standard values.[18] Patients within the freezing stage of active capsulitis, with symptom duration under a year, were included. Exclusion criteria encompassed bilateral symptoms, uncontrolled diabetes mellitus, overt thyroid disorders, prior shoulder surgeries or injections, recent shoulder trauma, neurological issues, material allergies, secondary adhesive capsulitis, inflammatory diseases, joint infections, coagulation disorders, rotator cuff tears, severe mental illness, pregnancy, and cerebrovascular incidents.

Intervention

A single physician administered all injections as outlined earlier in previous studies.[19] To accurately compare the effects of each drug, all medications were injected once at the same dosage. Patients in the saline group received 4 mL of saline along with 4 mL of contrast media (ioxitalamate); those in the CS group received 1 mL of triamcinolone acetonide (40mg/mL), 3 mL of saline, and 4 mL of contrast media; individuals in the HA group were given 2 mL of high-molecular-weight hyaluronic acid with an average molecular weight of 3000 kD, 2 mL of saline, and 4 mL of contrast media; while participants in the CS with HA group received 1 mL of triamcinolone acetonide, 2 mL of hyaluronic acid, 1 mL of saline, and 4 mL of contrast media. Post-injection, three images were captured to confirm the accuracy of the intra-articular injection: a standard shoulder anteroposterior view, a lateral scapular view, and a shoulder axillary view. The precision of the injection was evaluated as previously described.

Outcome Assessment

Follow-up occurred at intervals of 1 day, 1 week, 1 month, 3 months, and 6 months post-injection, utilizing patient-reported questionnaires and performance tests during clinic visits. Based on previous research indicating no discernible differences between treatment groups beyond 6 months, we determined that a 6-month follow-up period was adequate.[10,18,20]

The primary outcome measure was changes in the average Shoulder Pain and Disability Index (SPADI) scores from baseline to 1 month post-treatment. SPADI scores, which decline as pain decreases and patient function improves, are commonly employed in assessing adhesive capsulitis.[21,22]

Secondary outcome measures encompassed alterations in mean pain levels, range of motion (ROM), strength, functional scores, and overall satisfaction from baseline to the follow-up periods. Pain evaluation utilized a visual analog scale (VAS), measuring pain at rest, during motion, at night, and worst pain experienced. ROM was assessed using a goniometer for various shoulder movements, while muscle strength was gauged with a hand-held electronic scale. Patient satisfaction was evaluated through responses to questions regarding intervention willingness, recommendation to others, and return to pre-injury work capacity. Overall shoulder function and satisfaction were also rated using VAS scores.

Following injection, participants were provided with picture leaflets and instructed on a home exercise regimen aimed at improving joint ROM. They were advised to perform exercises twice daily, each session lasting 10 to 15 minutes. Participants were instructed not to seek additional physical therapy or medication. Any adverse effects experienced as a result of the intervention were elicited through open-ended questions during follow-up visits.

Statistical Analysis

The statistician responsible for data analysis remained unaware of the group assignments. Analysis was conducted according to the intention-to-treat principle. Continuous variables were compared using either the Kruskal-Wallis test or analysis of variance, while categorical variables were compared using the Chi-squared test or Fisher's exact test.

The linear mixed-effect model for repeated measures was employed to investigate the therapeutic effects over a short duration in both primary and secondary analyses. This model

incorporated group, time, and group-by-time interaction as fixed factors, with subject variabilities considered as a random factor. In cases where the group-by-time interaction yielded significance, post-hoc tests were conducted to compare group differences at each time point.

Statistical analyses were carried out using SAS 9.4 (SAS Institute, Cary, NC, USA), with the significance level set at a P value of 0.05.

Results

Demographic Profile

Forty patients were randomly assigned and received one of four interventions based on their designated group. Among them, there were 39 female and 21 male patients, with an average age of 52.4 years and an average symptom duration of 8.0 months. Table I presents the demographic and outcome characteristics of the four intervention groups at baseline. Prior to injection, there were no discernible differences in any demographic or outcome variables among the four intervention groups. All groups achieved 100% injection accuracy, with no significant distinctions observed among the four groups. (Table 1).

Table 1: Patient characteristics before injection of different regimens (N=40)

Variables	Saline group (n = 10)	CS group (n = 10)	HA group (n = 10)	CS with HA group (n = 10)	*P* value
Mean age	48.2 ± 4.4	54.6 ± 6.5	53.1 ± 8.2	50.3 ± 10.5	0.332
Sex (male : female)	4:6	5:5	7:3	4:6	0.412
Duration (months)	6.3 ± 5.1	6.7 ± 6.8	8.6 ± 5.8	9.9 ± 8.3	0.504
Aggravation (months)	1.2 ± 0.8	1.6 ± 1.0	1.9 ± 1.2	2.4 ± 1.8	0.751
Follow-up (months)	6.3 ± 0.7	6.5 ± 0.9	6.4 ± 0.9	6.4 ± 0.4	0.965
Accuracy (success : fail)	10:0	10:0	10:0	10:0	0.998
HA group, hyaluronic acid group; CS group, corticosteroid group; CS with HA group, combination of corticosteroid and hyaluronic acid group.					

Primary Outcome Assessment

The main outcome assessed, represented by the average change in SPADI scores, is depicted in Table 2. One month post-injection, the CS with HA group demonstrated the most substantial decrease in SPADI scores compared to the other groups. Specifically, there was a mean reduction of -30.3 points in the CS with HA group, significantly surpassing the improvements seen in the saline group (-4.4 points) and the HA group (-7.8 points). Additionally, the CS group exhibited a significantly greater change of -25.6 points compared to the saline group. At one week post-injection, the SPADI scores decreased by -18.7 points in the CS with HA group, outperforming the improvements observed in the saline group (0.6 points) and HA group (3.3 points). Similarly, the CS group demonstrated a significantly greater change of -10.3 points compared to the saline group. While no significant difference was found between the CS with HA group and the CS group, the former exhibited a more pronounced decrease in scores.

No discernible disparity was noted between the groups after three and six months.

Table 2: Mean changes of SPADI after intra-articular injections of different regimens (N=40)

Measurement		Saline group	HA group	CS group	CS with HA	*P* value
SPADI	Preinjection	53.8 ± 25.1	54.3 ± 16.5	54.7 ± 18.9	50.2 ± 11.1	0.004
	1 day	0.2 ± 9.8	2.7 ± 9.4	−6.5 ± 8.8	−10.5 ± 11.6	0.003
	1 week	0.6 ± 11.5	3.3 ± 12.4	−10.3 ± 14.8	−18.7 ± 14.1	<0.001
	1 month	−4.4 ± 21.1	−7.8 ± 23.1	−25.6 ± 11.2	−30.3 ± 11.6	<0.001
	3 months	−16.7 ± 24.3	−25.3 ± 21.2	−33.4 ± 16.4	−33.9 ± 15.3	0.072
	6 months	−28.5 ± 32.8	−42.6 ± 17.9	−38.5 ± 22.9	−38.3 ± 13.5	0.703

Secondary Outcome Assessment

The VAS scores for pain at rest and during the night, as well as the worst and average VAS scores, showed variations between the groups over time. However, there was no distinction in VAS scores for pain during motion among the groups (Table 3).

The CS with HA group exhibited quicker pain relief compared to the saline group in all VAS scores except for those during motion. Conversely, both the CS group and the HA group didn't display any disparity in pain relief compared to the saline group at any stage. One day and one month post-injection, the VAS scores at rest and during the night, along with the worst scores, showed significant enhancements in the CS with HA group, surpassing the improvements seen in the saline and HA groups. Notably, one week after injection, the improvements in the worst VAS scores within the CS with HA group were notably superior to those in the saline group and the HA group. From one day to one month post-injection, enhancements in

VAS scores at rest and during the night, as well as the worst scores, were higher in the CS with HA group compared to the CS group, albeit without reaching statistical significance. The average change in VAS scores in the CS with HA group was notably better than that in the saline group and the CS group after one day, one week, and one month. However, at three and six months post-injection, there were no notable differences between the groups in any pain scores.

Table 3: Mean changes of pain after intra-articular injections of different regimens (N=40)

Measurement		Saline group	HA group	CS group	CS with HA	*P* value
Pain-rest	Pre injection	3.2 ± 2.4	3.5 ± 2.2	3.8 ± 2.5	2.8 ± 2.2	0.001
	1 day	0.5 ± 1.0	0.2 ± 1.3	−1.3 ± 2.1	−1.5 ± 1.2	<0.001
	1 week	0.3 ± 2.4	−0.5 ± 2.7	−1.5 ± 2.2	−1.5 ± 1.5	0.013
	1 month	−0.7 ± 2.2	−0.9 ± 2.1	−2.7 ± 3.2	−2.5 ± 2.3	0.001
	3 months	−1.8 ± 3.6	−1.5 ± 2.2	−2.7 ± 3.3	−1.9 ± 1.2	0.555
	6 months	−2.7 ± 2.5	−3.2 ± 2.3	−2.7 ± 3.7	−2.2 ± 1.4	0.848
Pain-motion	Pre injection	6.2 ± 2.1	6.2 ± 2.4	6.4 ± 2.3	6.7 ± 2.1	0.174
	1 day	0.0 ± 1.2	−0.2 ± 1.4	−0.8 ± 1.1	−1.9 ± 2.3	
	1 week	0.0 ± 1.2	−0.5 ± 1.3	−1.7 ± 2.1	−2.9 ± 1.9	
	1 month	−0.9 ± 2.2	−1.6 ± 2.2	−2.6 ± 2.8	−4.3 ± 2.9	
	3 months	−2.4 ± 2.3	−3.3 ± 2.2	−3.7 ± 2.2	−4.6 ± 2.8	
	6 months	−3.9 ± 3.3	−4.9 ± 2.2	−4.3 ± 2.8	−5.2 ± 2.7	
Pain-night	Pre injection	5.5 ± 2.6	6.3 ± 2.0	7.0 ± 2.8	5.5 ± 1.5	0.004
	1 day	0.5 ± 1.3	0.0 ± 1.2	-1.3 ± 2.4	-1.8 ± 2.3	0.002
	1 week	-0.5 ± 2.4	-0.4 ± 1.2	-1.8 ± 2.4	-2.9 ± 2.0	0.003
	1 month	-0.5 ± 2.1	-0.6 ± 3.1	-3.2 ± 2.4	-3.5 ± 1.7	<0.001
	3 months	-1.5 ± 2.9	-2.9 ± 2.8	-4.1 ± 2.9	-4.0 ± 2.0	0.066
	6 months	-2.5 ± 3.8	-4.5 ± 2.1	-3.6 ± 3.1	-4.1 ± 1.5	0.145
Pain-average	Pre injection	5.2 ± 2.3	5.4 ± 2.1	5.8 ± 2.3	5.3 ± 1.5	0.021
	1 day	0.5 ± 1.0	0.1 ± 1.2	-1.1 ± 1.8	-1.6 ± 1.7	<0.001
	1 week	0.2 ± 1.7	-0.3 ± 1.5	-1.4 ± 2.0	-2.2 ± 1.3	0.001
	1 month	-0.7 ± 1.8	-0.9 ± 2.4	-2.8 ± 1.9	-3.4 ± 1.6	0.001
	3 months	-1.8 ± 2.1	-2.5 ± 2.1	-3.3 ± 2.3	-3.4 ± 1.6	0.455
	6 months	-3.0 ± 3.0	-4.1 ± 2.0	-3.6 ± 2.5	-3.8 ± 1.4	0.544
Pain-worst	Pre injection	7.7 ± 1.6	7.9 ± 1.7	8.7 ± 1.3	8.2 ± 1.1	0.041
	1 day	0.1 ± 1.2	0.6 ± 1.1	-0.8 ± 2.5	-1.3 ± 2.3	0.003
	1 week	0.1 ± 1.2	0.2 ± 1.6	-1.6 ± 2.3	-2.4 ± 2.0	<0.001
	1 month	-1.1 ± 1.7	-0.2 ± 2.8	-3.0 ± 2.7	-4.0 ± 2.6	<0.001
	3 months	-2.3 ± 2.3	-2.7 ± 2.5	-4.4 ± 2.4	-4.6 ± 2.6	0.067
	6 months	-3.9 ± 3.6	-5.0 ± 2.6	-3.6 ± 2.3	-5.0 ± 2.2	0.542

Range of Motion

The average change in active range of motion (ROM) varied among the groups across different time points (Table 4). Following one month, the average change in active forward flexion (FF) and external rotation (ER) within the CS with HA group was notably higher compared to both the saline and HA groups. Additionally, the average change in active abduction (ABD) within the CS with HA group outperformed that of the saline group. Within the CS group, the average change in active FF and internal rotation (IR) was superior to that observed in the saline group. However, at three and six months post-injection, there were no noteworthy differences between the groups in terms of active FF, ABD, or ER. One and three months following injection, the average change in active IR in the CS with HA group was superior to that in both the saline and HA groups. Nevertheless, at six months post-injection, there were no significant differences between the groups in terms of active IR.

The average change in passive range of motion (ROM) also exhibited variations among the groups across different time intervals. Following one month, the average changes in all passive ROM within the CS with HA group were notably higher compared to both the saline and HA groups. Specifically, for passive abduction (ABD), the CS with HA group surpassed the CS group. Moreover, the average change in passive forward flexion (FF) and internal rotation (IR) within the CS group outperformed those of the saline and HA groups after one month. At the three-month mark post-injection, the average change in passive ABD within the CS with HA group was superior to that observed in the HA group. However, at six months post-injection, there were no significant differences between the groups in any passive ROM.

Table 4: Mean changes of active and passive range of motion after intra-articular injections of different regimens (N=40)

Measurement		Saline group	HA group	CS group	CS with HA	*P* value
Active FF	Pre injection	115.5 ± 23.0	114.1 ± 16.5	110.8 ± 27.5	121.5 ± 26.3	<0.001
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.655
	1 week	-5.5 ± 19.5	4.1 ± 18.1	13.8 ± 24.8	11.0 ± 15.2	0.033
	1 month	8.5 ± 17.6	13.8 ± 16.7	31.5 ± 20.3†	30.8 ± 26.5	<0.001
	3 months	28.8 ± 28.2	26.8 ± 21.3	36.8 ± 28.2	37.1 ± 21.5	0.145
	6 months	43.5 ± 35.1	49.1 ± 23.2	41.1 ± 40.5	46.1 ± 23.0	0.545
Active AB	Pre injection	86.5 ± 15.6	93.1 ± 17.6	92.8 ± 26.8	90.5 ± 29.0	0.003
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.642
	1 week	4.8 ± 15.8	-0.9 ± 6.5	11.5 ± 15.8	12.5 ± 18.6	0.005
	1 month	9.5 ± 25.7	21.5 ± 19.4	26.1 ± 21.6	44.5 ± 32.9	0.002
	3 months	35.1 ± 37.0	31.5 ± 24.3	42.5 ± 30.5	59.1 ± 33.6	0.044
	6 months	63.1 ± 40.1	61.5 ± 30.6	55.8 ± 46.7	74.8 ± 34.0	0.345
Active ER	Pre injection	23.5 ± 12.8	21.1 ± 6.1	24.5 ± 11.6	24.5 ± 15.7	0.001
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.633
	1 week	-1.0 ± 12.8	1.5 ± 3.0	3.8 ± 8.1	2.8 ± 8.0	0.211
	1 month	2.5 ± 13.8	4.5 ± 12.5	10.8 ± 15.5	19.1 ± 8.4	<0.001
	3 months	10.8 ± 21.8	6.8 ± 15.0	14.1 ± 14.1	18.5 ± 13.7	0.058
	6 months	23.8 ± 24.8	20.5 ± 17.5	15.1 ± 15.3	21.8 ± 21.5	0.754
Active IR	Pre injection	2.5 ± 1.8	2.2 ± 1.8	2.5 ± 1.9	2.8 ± 1.7	<0.001
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.843
	1 week	0.3 ± 1.6	0.0 ± 2.9	2.0 ± 2.0	1.7 ± 1.3	<0.001
	1 month	1.2 ± 1.3	1.5 ± 2.0	3.5 ± 2.2	5.5 ± 2.5	<0.001
	3 months	3.2 ± 3.3	2.9 ± 3.1	5.2 ± 2.1	5.2 ± 2.5	0.001
	6 months	6.0 ± 3.7	6.2 ± 3.0	5.5 ± 3.3	6.6 ± 2.1	0.233
Passive FF	Pre injection	121.5 ± 20.8	120.1 ± 17.1	117.5 ± 28.2	128.1 ± 25.6	0.002
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.886
	1 week	1.1 ± 15.6	5.5 ± 19.0	12.8 ± 22.7	8.8 ± 14.8	0.132
	1 month	11.1 ± 14.9	13.1 ± 16.9	30.8 ± 21.1	30.8 ± 22.9	<0.001
	3 months	29.1 ± 25.3	27.5 ± 23.1	35.5 ± 25.0	35.8 ± 21.9	0.122
	6 months	41.1 ± 31.2	45.5 ± 25.3	37.8 ± 39.2	43.8 ± 24.9	0.331
Passive AB	Preinjection	91.5 ± 18.1	99.8 ± 19.3	97.1 ± 25.3	95.1 ± 26.4	0.001
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.542
	1 week	7.5 ± 16.7	-3.2 ± 8.2	15.0 ± 17.9	11.7 ± 19.9	0.003
	1 month	15.5 ± 25.8	18.1 ± 23.7	27.8 ± 18.5	53.1 ± 28.0	<0.001
	3 months	37.1 ± 34.5	24.3 ± 37.1	43.5 ± 29.2	59.8 ± 32.2	0.027
	6 months	61.8 ± 37.4	58.1 ± 34.1	54.5 ± 44.2	73.8 ± 27.3	0.233
Passive ER	Pre injection	28.5 ± 12.5	24.8 ± 7.8	26.8 ± 10.6	28.8 ± 18.4	0.003
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.673
	1 week	-1.0 ± 13.2	0.5 ± 1.6	4.5 ± 8.6	2.1 ± 8.2	0.156
	1 month	1.1 ± 12.7	3.1 ± 12.0	13.8 ± 14.9	19.5 ± 13.6	<0.001
	3 months	8.1 ± 21.7	8.8 ± 15.0	18.5 ± 15.3	20.1 ± 19.0	0.033
	6 months	23.1 ± 25.0	20.1 ± 18.7	18.1 ± 17.7	23.5 ± 28.0	0.543
Passive IR	Pre injection	3.1 ± 2.1	3.1 ± 2.9	3.2 ± 2.0	3.7 ± 2.1	<0.001
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.678
	1 week	0.3 ± 1.8	-0.4 ± 2.9	1.8 ± 2.0	1.4 ± 1.3	0.001
	1 month	1.0 ± 1.6	0.6 ± 1.3	3.8 ± 2.1	5.0 ± 2.3	<0.001
	3 months	3.3 ± 3.4	3.0 ± 3.5	5.3 ± 2.1	5.3 ± 2.5	0.013
	6 months	6.0 ± 3.8	6.2 ± 3.1	5.5 ± 3.4	6.6 ± 2.2	0.346

Strength

The strength of the supraspinatus, infraspinatus, and subscapularis muscles demonstrated an increase over time across all groups. However, there were no notable differences in strength observed between the groups. (Table 5)

Table 5: Mean changes of power of rotator cuff muscle after intra-articular injections of different regimens (N=40)

Measurement		Saline group	HA group	CS group	CS with HA	*P* value
Power-SST	Pre injection	5.2 ± 4.3	6.5 ± 2.7	5.3 ± 2.6	5.2 ± 4.3	0.056
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
	1 week	0.3 ± 2.5	1.1 ± 2.1	1.8 ± 2.4	2.5 ± 3.3	
	1 month	2.1 ± 2.5	2.4 ± 3.1	2.9 ± 1.8	4.8 ± 4.1	
	3 months	3.4 ± 3.3	4.4 ± 4.0	4.1 ± 2.9	4.2 ± 6.1	
	6 months	4.2 ± 4.4	6.9 ± 3.9	4.2 ± 3.1	5.8 ± 4.0	
Power-IST	Pre injection	5.2 ± 3.8	6.1 ± 3.4	4.9 ± 2.2	6.6 ± 3.6	0.255
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
	1 week	0.4 ± 2.3	0.7 ± 2.5	2.0 ± 2.1	0.6 ± 3.4	
	1 month	2.7 ± 2.6	1.3 ± 2.5	2.2 ± 2.9	1.9 ± 3.1	
	3 months	3.3 ± 3.6	2.1 ± 2.9	3.2 ± 3.1	2.7 ± 2.5	
	6 months	2.4 ± 5.5	2.3 ± 2.7	2.5 ± 3.5	2.5 ± 3.2	
Power-SB	Pre injection	8.3 ± 4.0	11.2 ± 3.8	7.4 ± 4.6	9.9 ± 5.8	0.022
	1 day	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.224
	1 week	0.9 ± 3.0	1.0 ± 3.4	2.3 ± 3.8	1.6 ± 4.8	0.647
	1 month	3.1 ± 3.6	1.1 ± 3.1	3.7 ± 3.8	5.1 ± 4.6	0.056
	3 months	3.4 ± 5.3	2.3 ± 3.0	4.5 ± 5.0	4.8 ± 6.3	0.926
	6 months	4.4 ± 5.9	2.3 ± 3.2	5.8 ± 6.2	6.6 ± 6.1	0.161

Overall Satisfaction

The VAS scores for overall shoulder function and overall satisfaction showed improvement over time across all groups. However, there were no significant differences observed between the groups in terms of these improvements. (Table 6)

Table 6: Mean changes of overall shoulder function (VAS) after intra-articular injection and values of overall satisfaction (VAS) after intra-articular injections of different regimens (N=40)

	Measurement	Saline group	HA group	CS group	CS with HA	*P* value
Overall Shoulder Function (VAS)	Pre injection	4.5 ± 2.0	4.1 ± 1.7	3.8 ± 1.8	3.2 ± 1.8	0.233
	1 day	-0.6 ± 2.1	0.4 ± 2.3	0.6 ± 3.3	2.5 ± 2.8	
	1 week	-0.4 ± 1.7	0.4 ± 2.3	1.2 ± 2.4	2.6 ± 3.1	
	1 month	0.4 ± 3.3	1.2 ± 2.7	2.7 ± 2.1	3.6 ± 2.8	
	3 months	1.7 ± 3.2	2.2 ± 2.0	3.1 ± 2.3	3.9 ± 2.5	
	6 months	2.8 ± 3.0	3.6 ± 2.0	3.4 ± 2.3	4.2 ± 2.3	
Overall Satisfaction (VAS)	1 day	5.3 ± 2.0	5.0 ± 2.0	5.2 ± 2.2	6.6 ± 2.4	0.98
	1 week	6.4 ± 1.8	5.2 ± 2.3	6.5 ± 2.2	8.2 ± 1.6	
	1 month	7.0 ± 2.3	5.5 ± 2.1	7.0 ± 1.5	8.6 ± 1.9	
	3 months	6.8 ± 2.2	6.2 ± 2.3	7.2 ± 2.1	7.8 ± 2.0	
	6 months	7.6 ± 2.4	7.7 ± 2.0	6.8 ± 2.4	8.2 ± 1.0	

Discussion

The primary findings of this study indicate that within one month, the group receiving simultaneous injections of corticosteroids (CS) with hyaluronic acid (HA) demonstrated notably better improvements in SPADI scores, active and passive range of motion (ROM) compared to both the saline and HA groups. While there wasn't a significant disparity between the CS group and the CS with HA group, the latter exhibited greater improvements. Moreover, in terms of pain relief at rest and during the night, as well as worst and average pain scores over the course of one month post-injection, the CS with HA group outperformed both the saline and HA groups, with no substantial difference observed between the CS and HA groups compared to saline. Conversely, there were no significant distinctions between the HA group and the saline group in any outcome measure among patients with adhesive capsulitis (AC). Therefore, the study suggests that for the treatment of AC, combining CS with HA injections may offer a swifter and more effective means of alleviating pain and enhancing functionality compared to administering either CS or HA alone.

Our study employed saline as a positive control, ensured a uniform patient group with symptom duration less than one year, and administered a single standardized dose to each group. This approach allowed for a comprehensive assessment of each treatment's efficacy compared to saline, as well as a comparison between simultaneous CS and

HA injections versus single CS or HA injections. Our findings demonstrated that all treatment groups exhibited improvements in pain and function, with no significant differences observed between groups at 3 and 6 months. This variance from the prior study's results could be attributed to the monthly injections over 6 months in the previous study versus our single injection approach. Additionally, our study commenced the comparison with saline injections immediately after administration, enabling an early evaluation of each treatment's objective effects. Most prior studies evaluated CS or HA injections one month or later post-injection.[18,20,23] Our study revealed that the mean changes in SPADI scores and active FF and active IR were superior in the CS and CS with HA groups compared to the saline group. Moreover, the CS with HA group exhibited significantly better SPADI scores and passive IRthan the saline group one week post-injection, with greater changes compared to the CS group.

These novel findings suggest that simultaneous CS and HA injections may elicit a more rapid effect as early as one week post-injection, which is earlier than previously reported. A previous in vivo study suggested that the combination of CS and HA accelerated the CS concentration increase.[24] We speculate that the swift effect observed in our study could be attributed to this synergistic phenomenon. In summary, simultaneous CS and HA injections appear to be the quickest and most effective method for the functional recovery of AC patients, while CS injections alone also exhibit efficacy but with a slower and less potent effect compared to the combined approach.

Patients with AC often experience heightened nighttime pain, leading to discomfort when sleeping on the affected side. Previous research has highlighted the early pain-relieving benefits of CS injections.[8,18,20,23] In our investigation, significant pain improvement, except for pain during motion, was observed from one day to one month post-injection only in the group receiving simultaneous CS and HA injections compared to the saline group, indicating swift pain alleviation. While CS injections alone did not exhibit statistically significant effects compared to saline, they demonstrated a trend towards rapid pain reduction from the first day post-injection. Conversely, night pain increased one day after injection in the saline and HA groups compared to pre-injection levels. At 3 and 6 months post-injection, pain relief was observed in all groups, with faster onset of relief noted in the CS and CS with HA groups. Additionally, average pain scores in the CS with HA group surpassed those in the CS group at 1 day, 1 week, and 1 month post-injection. These findings indicate that intraarticular CS injections effectively improve sleep quality, ROM, and function by swiftly alleviating pain in AC patients. Furthermore, simultaneous injection with HA appears to enhance this effect synergistically.

In comparison to the other groups, including the saline group, the administration of HA alone did not yield significant differences in any outcome measures across any follow-up period and did not lead to rapid pain alleviation. Conversely, up to the 3-month follow-up, the injection of CS alone demonstrated superiority over HA alone in terms of swift pain relief and enhancement in ROM, suggesting that the efficacy of HA alone may be suboptimal. Previous studies have reported positive effects of HA for painful shoulder conditions at the three-month mark.[9,25,26] However, due to the patient experiencing multiple painful events, HA injection is perceived to be less effective compared to CS injection. Additionally, considering previous studies that have shown improvements in pain and function with any treatment after six weeks, evaluating the effects of injection at three months may not be appropriate.

One reason for recommending HA injection was the concern regarding systemic side effects associated with CS. However, given the shoulder joint's less vascularized synovial surface and the presence of pathological changes such as fibrosis and adhesion that hinder systemic steroid absorption, the systemic dissemination of CS is minimal.

Numerous studies have explored the simultaneous injection of CS and HA for treating knee osteoarthritis.[27-30] According to these studies, CS works by depolymerizing the superoxide anion produced by inflammatory cells, while HA shields joints from CS's detrimental effects when administered together. This combined approach demonstrates synergistic effects and yields excellent clinical outcomes. Additionally, simultaneous injection of CS and HA offers the advantage of rapidly increasing CS concentration while maintaining a sustainable level for a longer duration.

In the context of treating adhesive capsulitis (AC), effective execution of range of motion (ROM) exercises hinges on rapid pain relief. Consequently, the simultaneous intra-articular injection of CS and HA, which provides swift pain alleviation and functional enhancement, is suggested to be a more efficacious treatment option compared to HA alone, which typically entails three injections and exhibits delayed onset of action. This study faced several limitations. Firstly, being a single-center study, the number of subjects was relatively small. Despite determining the sample size through power analysis, the small sample size may have impacted the outcome measures, leading to a lack of significant differences between groups despite

notable variances in mean changes. Additionally, while the standard regimen typically involves three weekly injections of HA for intra-articular administration, only a single HA injection was administered in this study to assess the efficacy of the singular drug.

Conclusion

In the treatment of adhesive capsulitis (AC), the concurrent administration of corticosteroid (CS) and hyaluronic acid (HA) proved to be more efficacious in improving SPADI scores one month post-injection compared to HA alone, and it was not found to be inferior to CS alone. These findings suggest that the simultaneous injection of CS and HA can be considered as a recommended approach for the effective and safe treatment of AC.

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