

Original Article

Comparison of Subacromial Ketorolac Injection versus Corticosteroid Injection in the Treatment of Shoulder Impingement Syndrome

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INTRODUCTION

Shoulder pain is a common complaint of patients in all ages. Subacromial impingement syndrome is the most common cause of shoulder pain and restriction in range of motion^[1-3] that leads to debility and decreased quality of life.^[4,5] The pain is commonly resulting from subacromial bursitis and rotator cuff tendonitis.^[6] Nonoperative treatment options for impingement syndrome have included rest, ice, physical therapy, ultrasound, electromagnetic radiation, corticosteroid injections, and systemic nonsteroidal anti-inflammatory drugs (NSAIDs).^[7-10] Corticosteroid

ABSTRACT

Objective: Subacromial impingement syndrome is the most common cause of shoulder pain and restriction in range of motion in the world. The aim of this study was to compare the efficacy of subacromial injection of ketorolac with the injection of corticosteroid for the treatment of subacromial impingement syndrome. **Methods:** A total of forty patients were randomly allocated into two groups. Group A received 40 mg of methylprednisolone and Group B received 60 mg of ketorolac as a subacromial injection along with lidocaine. Each patient was evaluated in terms of visual analog scale (VAS) for evaluating pain and Constant's score for function evaluation (pain, activity level, and range of motion with standard goniometry). The patients were re-examined 1 and 3 months after intervention. All the patients educated for simple home exercise. **Findings:** At 1 and 3 months of follow-up, both treatment arms resulted in an increased range of motion and decreased pain. The difference between the groups was not statistically significant ($P > 0.05$). In ketorolac group, mean pre- and post-treatment (at 12 weeks) VAS scores were 8.6 (range, 3–9) and 4.5 (range 2–4), respectively. In steroid group, mean pre- and post-treatment (at 12 weeks) VAS scores were 8.3 (range, 3–10) and 3.9 (range, 0–7), respectively. The difference was statistically significant within groups at baseline and 1 ($P < 0.001$) and 3 ($P < 0.001$) months after the injection. **Conclusion:** Subacromial injection of ketorolac has an equivalent outcome to subacromial injection of corticosteroid. The use of ketorolac injections can substantially decrease the pain and increase the range of motion of the shoulder and could be a reasonable alternative in case of corticosteroid contraindications.

KEYWORDS: Corticosteroid, external impingement, Ketorolac, nonsteroidal anti-inflammatory drug, subacromial

injections are widely utilized and are a well-accepted method of treatment for patients with subacromial impingement syndrome who have not responded to more conservative therapies. The exact mechanism of corticosteroid injections is not completely understood. It is supposed that the anti-inflammatory effect might reduce the inflammation of bursitis and tendonitis.^[11,12] Unfortunately, the frequency of use of corticosteroid injections is limited because of its potentially serious side effects. Corticosteroids have been associated with

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tendon rupture, subcutaneous atrophy, articular cartilage changes, and systemic effects such as osteoporosis.^[13,14] Rhon *et al.* showed that 1-year outcome of subacromial corticosteroid injection (control) and manual physical therapy (case) are similar in 104 patients with shoulder impingement syndrome.^[15] Since steroids are effective mainly because of their anti-inflammatory properties, there is an argument to use local injections of NSAIDs to decrease inflammation in the subacromial space. There is evidence that subacromial injections of NSAIDs may provide pain relief and restoration of function in shoulder impingement syndrome. Ketorolac is a NSAID that acts by inhibiting the synthesis of prostaglandins which is used for the treatment of moderate-to-severe pain.^[16-19] The objective of this double-blind randomized controlled trial was to compare the efficacy of subacromial injection of methyl prednisolone acetate with the injection of ketorolac. We hypothesize that the efficacy of subacromial injection of ketorolac may be equivalent to the efficacy of methyl prednisolone acetate.

METHODS

A double-blind randomized controlled study was undertaken in a single center from January 2016 to February 2017. Patients were recruited from physical medicine and rehabilitation clinics of Alzahra hospital, a tertiary care medical center, in Isfahan, Iran. The Ethics Committee of Isfahan University of Medical Sciences approved the study. Informed consent was obtained from patients or next of kin, or appropriate surrogate before participation in the study. The study was registered by the Iranian Registry of Clinical Trials (IRCT2017011231906N1).

All patients over the age of 18 years with a clinical diagnosis of subacromial impingement were considered eligible to participate in this study. The inclusion criteria were patients with shoulder pain with passive and/or active abduction, diagnosis of subacromial bursitis based on tenderness to palpation about the acromion, positive Neer's sign, positive Hawkin's sign, pain exacerbated with the shoulder held in internal rotation^[20] and subacromial bursitis or rotator cuff tendinitis detected on magnetic resonance imaging. In addition, all patients had standard radiographs of their affected shoulder to rule out glenohumeral arthritis. Patients were excluded from the study if any of the following criteria were present: evidence of other pathology causing shoulder pain, such as arthritis of the glenohumeral or acromioclavicular joints, adhesive capsulitis, fracture or a major tear of the rotator cuff presenting with weakness and muscle wasting, injection in the same shoulder within the previous 2 months, history of taking regular

systemic NSAIDs or steroids, or whom those drugs were contraindicated for, previous history of gastrointestinal ulcers or bleeding disorders, evidence of local infection, pregnant and breastfeeding mothers, and change in the patient's treatment plan and unable to refer for follow-up visit.

Random numbers for allocating patients to treatment groups were generated using a computer program. The patients were randomized to have either a single injection of 60 mg ketorolac mixed with 1 ml 2% lidocaine, or 40 mg methylprednisolone mixed with 1 ml 2% lidocaine. Throughout the preparation and follow-up, all patients, and treating consultants were blinded to the medication used.

The researcher gave the injection, using a 21-gauge needle with the covered syringe, into the patient's subacromial bursa via the anterolateral approach applying an aseptic technique. A reduction in pain of at least 50% with full active abduction 10 min after the injection (Neer's impingement test) confirmed accurate placement of the injection in the subacromial bursa. All the patients educated for simple home exercise such as pendulum, stretching of posterior capsule, and strengthening of peri-scapular stabilizer exercises. Patients were advised to take simple analgesia if required, but to avoid any preparation containing NSAIDs.

Visual analog scale (100 mm VAS) for pain intensity^[21] and Constant's score for function evaluation (pain, activity level, and range of motion with standard goniometry)^[22] were evaluated and recorded at baseline, 1 month, and 3 months after the treatment.

SPSS for Windows version 20.0 software program (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continuous variables were expressed as mean \pm standard deviation (SD) and categorical variables as frequencies and proportions. Chi-square test was used to compare the proportions. For normally distributed data, the Student's *t*-test, multivariate analysis of variance (MANOVA), and *post hoc* (Bonferroni) tests were applied. Otherwise, the Mann-Whitney U-test was used as a nonparametric test. Deviation from a Gaussian distribution was tested by the Kolmogorov-Smirnov test. All analyses were exploratory and utilized $P = 0.05$ (two tailed) for significance.

RESULTS

Forty-eight patients met the inclusion and exclusion criteria and were enrolled in the study: 20 patients in the steroid group (mean \pm SD of age 47.53 ± 6.92 years) and 20 patients in the NSAID group (mean \pm SD of age 49.76 ± 4.83 years) ($P: 0.24$). There were 8 males and 12 females in the ketorolac group, whereas 9 males and

Table 1: Changes in visual analog scale and Constant's scores in ketorolac and steroid groups

Parameters	Baseline	Follow-up period	
		4 weeks	12 weeks
VAS scale			
Ketorolac	8.6±1.46	4.45±1.96	4.55±1.96
Steroid	8.3±1.13	3.75±1.71	3.9±1.74
<i>P</i> *	0.5	0.23	0.3
Constant's score			
Ketorolac	54.9±22.34	36.9±19.42	37.55±20.09
Steroid	52.1±16.07	29.1±17.70	30.3±16.67
<i>P</i> *	0.65	0.2	0.2

*A two-tailed Student's *t*-test was used to compare the outcome measures of two treatment groups. Data presented as mean±SD. SD=Standard deviation, VAS=Visual analog scale

11 females in the corticosteroid group (*P*: 0.74). Two groups were comparable in baseline characteristics.

In ketorolac group, mean pre- and post-treatment (at 12 weeks) VAS scores were 8.6 (range, 3–9) and 4.5 (range 2–4), respectively. In steroid group, mean pre- and post-treatment (at 12 weeks) VAS scores were 8.3 (range, 3–10) and 3.9 (range, 0–7), respectively. The median improvement in the Constant's score at 12 weeks was 30.3 for patients in the steroid group and 37.5 for patients in the ketorolac group [Table 1]. This difference was found to be not statistically significant (MANOVA, *P* = 0.22).

Both subacromial steroid and subacromial ketorolac injections could significantly improve VAS and Constant's scores at all-time points of follow-up (*P* < 0.001). The improvement in Constant's score was slightly higher in the steroid group but difference between the two groups was not statistically significant. No adverse events or complications, either locally or systemically, were encountered in both groups.

DISCUSSION

In this study, we used an injectable NSAID to provide a localized area of anti-inflammatory action. Our study suggests that, at 12 weeks, NSAID injection has equivalent efficacy compared to corticosteroid injection, as measured by improvement in the VAS and Constant's score.

Although a majority of studies mention the beneficial effects of subacromial corticosteroid injections, various questions exist on the detrimental effect of steroids such as effects on cartilage structure, infection, drug allergy, bone fracture, hyperglycemia in diabetic patients, tendon/ligament weakening or rupture, postinjection pain flare, soft-tissue/subcutaneous fat atrophy, and skin hypopigmentation.^[23,24] Besides, steroids should be used with caution in patients with diabetes mellitus and

hypertension. Hill *et al.* reported most of the common complications of corticosteroid injection in orthopedic treatment including subcutaneous fat atrophy (64%), skin depigmentation (54%), and tendon rupture (39%).^[25]

Various modes of anti-inflammatory therapy have been implemented including local corticosteroid injections and systemic NSAID therapy. NSAIDs have analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandin, prostacyclin, and thromboxane.^[26]

A few clinical studies have directly compared the local injection of steroid with systemic NSAIDs, but the current literature does not conclusively provide evidence to support that one treatment is better than the other. Min *et al.* compared the efficacy of a single subacromial injection of ketorolac with a single injection of methylprednisolone in 32 patients with impingement syndrome. They found that ketorolac was equally effective in the treatment of shoulder impingement with better improvement in the University of California at Los Angeles (UCLA) shoulder scores during 4-week follow-up.^[27] Min *et al.* performed the same study on 48 patients and showed that, at 4 weeks, a ketorolac injection had better efficacy than triamcinolone injections, as proved by the improvements of the UCLA Shoulder Assessment Score, forward flexion strength, and patient satisfaction.^[28] Karthikeyan *et al.*^[29] compared the efficacy of a single subacromial injection of tenoxicam, with a single injection of methylprednisolone in patients with impingement syndrome. Although tenoxicam injection exerted positive effects, they found significantly greater improvements in the methylprednisolone group. Their results were different from our study and this could be due to low potency of analgesic effect of tenoxicam compared to methylprednisolone or ketorolac. Aksakal *et al.* compared the efficacy of single-dose subacromial injections of betamethasone and lornoxicam for the treatment of subacromial impingement syndrome and reported that patients in the steroid group showed a significant improvement at 2-, 4-, and 6-week follow-ups compared to pretreatment (*P* < 0.001) and previous follow-ups (*P* < 0.05) at all times. Patients in the lornoxicam group showed a significant functional improvement in week 2 (*P* < 0.001), which was not evident in the following weeks (*P* > 0.05). They concluded that, although a single subacromial lornoxicam injection provides rapid functional recovery, which partially extends into the intermediate term, its results are inferior to betamethasone and it may be an alternative only in patients where corticosteroids are contraindicated.^[30]

In addition, Karthikeyan *et al.*^[29] found that a single methylprednisolone injection was significantly more

effective than tenoxicam injection, although tenoxicam injection had positive effects. Their results were different from our study and this could be due to the low potency of analgesic effect of tenoxicam compared with methylprednisolone or ketorolac. In accordance to our results, Çift *et al.* showed that both tenoxicam and methylprednisolone injections could be successfully used in the treatment of subacromial impingement, and tenoxicam could be preferred in patients with corticosteroid injection contraindication.^[19]

A systematic review conducted by the Cochrane Collaboration concluded that, although there is evidence in support of corticosteroid injections, the effect may not be better than systemic NSAIDs.^[31] Johansson *et al.*^[32] reported short-term efficacy of subacromial corticosteroid injection in their systematic review about the interventions of subacromial pain and concluded that both subacromial corticosteroid and tenoxicam injections could be successful after 1 year in patients with impingement syndrome.

Assuming that both NSAIDs and corticosteroids function by locally decreasing inflammation, this study provides evidence of equivalent if not superior results of injectable ketorolac. We believe that the improvement in function and satisfaction are directly associated with the patient's ability to strengthen the rotator cuff. While there is no evidence that NSAIDs reverse the pathophysiology of subacromial impingement, decreased pain may allow the patient to strengthen the rotator cuff and decrease the impingement between the supraspinatus and acromion.^[2]

Long-term follow-up of patients and close monitoring of patients for not using oral NSAIDs and homogeneity of both groups in baseline characteristic are some of the strengths of our study. On the other hand, lack of a physical therapy protocol is a limitation in our study. Differing levels of physical therapy and additive treatment measures may have skewed the results. Moreover, no radiological and pathological findings were evaluated to correlate with the Constant's and VAS scores and examined the efficacy of ketorolac on tendon structure. Furthermore, there is a high incidence of nonbursal injections of the shoulder; advanced imaging technology such as ultrasound guidance would have been a more accurate method of injection. Hence, these limitations should be considered in the future studies to clarify the complete effect of NSAID injections for shoulder pain. Our follow-up was limited to 12 weeks, with only a single injection. Our short-term results do not address the long-term effects of either treatment group. Most practitioners will perform multiple subacromial injections which should be addressed in the future studies.

In this study, a single injection of 60 mg ketorolac resulted in equivalent improvements in outcome compared to a single injection of 40 mg methylprednisolone for the treatment of subacromial impingement when assessed at 12 weeks. While both methylprednisolone and ketorolac are effective in the treatment of isolated subacromial impingement, ketorolac appears to have equivalent if not superior efficacy and also may decrease the patient exposure to the potential side effects of corticosteroids. Immediately following the injection, both groups increased their active abduction, indicating accurate injection. Practitioners may utilize this as a possible short-term alternative for nonoperatively treating subacromial impingement syndrome.

AUTHORS' CONTRIBUTION

Parisa Taheri and Farnaz Dehghan designed the study, and analyzed the data. Sahar Mousavi collected, interpreted the data and drafted the manuscript and Reza Solouki revised the manuscript.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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