COMPARISON OF EFFICACY OF KETOROLAC, TRIAMCINOLONE AND BETAMETHASONE INJECTIONS IN THE TREATMENT OF SHOULDER IMPINGEMENT SYNDROME

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ABSTRACT

BACKGROUND

There is controversial evidence regarding subacromial injections of nonsteroidal anti-inflammatory drugs and corticosteroid providing pain relief and restoration of function in shoulder impingement syndrome. We wanted to assess and compare the efficacy of subacromial ketorolac and steroids injections in treatment of patients with impingement syndrome.

METHODS

This study was a double-blind randomized controlled trial. The intervention groups included: A) Ketorolac; B) Triamcinolone; C) Betamethasone LA. The patients' pain was recorded based on Visual Analogue Scale system, and performance of patients was recorded based on Oxford Shoulder Score in 0, 2, 4, and 6 weeks. One-way ANOVA, chi-square test and repeated measurement were used to compare and analyse obtained results.

RESULTS

One hundred five patients were enrolled in the study. Three groups (each one containing 35 patients) were compatible in age and gender. Performance of patients was significantly improved in all three groups over time ($p<0.001$). The mean pain score of all three groups was significantly decreased over time in the three groups ($p<0.001$). No significant difference was found for pain scores between the groups at different follow-ups.

CONCLUSIONS

The results of present study showed that ketorolac, triamcinolone, and betamethasone are equally effective in improving and reducing patients' performance and pain, respectively, in treatment of impingement syndrome.

KEY WORDS

Shoulder Impingement Syndrome, Ketorolac, Triamcinolone, Betamethasone, Pain

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BACKGROUND

Shoulder pain is the third most common musculoskeletal problem after lumbar and neck pain.[1,2] In the United States, 3 million visits per year are due to the shoulder pain.[3,4] A wide range of potential pathoanatomic problems from a simple sprain to a wide rupture of the rotator cuff can cause shoulder pain.[2] The shoulder has the greatest range of motion in the joints of the body. A heterogeneity in size between the smaller cavity of glenoid and the larger head of the humerus can cause shoulder instability.

The joint stability is maintained by the two static components of the capsule and the labrum and the dynamic component of the rotator cuff muscles. Inappropriate function in each of these two components can lead to pain, weakness and instability.[5]

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Rotator cuff is a muscle tendon complex of four muscles. Supraspinatus muscle causes abduction and infraspinatus and teres minor muscles cause external rotation of the joint. Subscapularis also causes internal rotation of shoulder joint. In addition, the rotator muscles balance the strength of other muscles around the shoulder joint (Most importantly, the deltoid). The contraction of deltoid muscle in the absence of supraspinatus muscle leads to upward deviation of the humeral head and disrupts the joint abduction.[6,7] Periarticular shoulder disorders include a number of different diseases, such as subacromial bursitis and subdeltoid bursitis, rotator cuff diphtheria, calcified tendinitis, and rotator cuff tear with or without adhesive capsulitis that can cause shoulder pain and motion restrictions.[1,8]

Shoulder impingement syndrome is usually treated by resting, use of NSAIDs, subacromial steroids injection, topical anaesthetics, hyaluronate, suprascapular nerve block and physiotherapy.[3,5] Subacromial injection can reduce the side effects of drugs compared with systemic administration. Ketorolac is a nonsteroidal anti-inflammatory drug (NSAID) and is recommended to control short-term moderate to severe pain requiring narcotic drugs.[9] This drug inhibits the production of prostaglandins in the body. It is available as an

eye drop, oral, and intramuscular injection product.[10] In addition, triamcinolone and betamethasone are two drugs of the steroid group (Glucocorticoids), which are highly anti-inflammatory. Triamcinolone is a synthetic analogue of hydrocortisone, which is used for the treatment of inflammatory diseases,[11] and due to its poor water-solubility in tissues, it remains in the region for a long time.[12,13] Betamethasone is a steroid drug used to treat a wide range of inflammatory diseases. This drug has several drug forms. The injectable form of this drug is betamethasone sodium phosphate. Various studies have examined the effect of subacromial injections of different drugs in reducing shoulder pain.[14] There has been little research on the effect of betamethasone LA on shoulder impingement syndrome. The aim of this study was to investigate subacromial ketorolac injection and its comparison with steroids in patients with shoulder impingement syndrome.

METHODS

Locations and Participants

This study was a double-blind randomized clinical trial. Patients who were referred to the orthopaedic clinic during 2016-17 with shoulder pain and have been diagnosed with shoulder impingement syndrome during clinical examination and imaging were enrolled in the study. Patients without diagnosis of shoulder impingement syndrome, or had a history of dislocation or fracture of the shoulder or a systemic disease affecting the joint and soft tissue, or recently received medications for pain were excluded.

Sample Size Calculation

The sample size was estimated as at least 35 patients in each group by a non-inferiority margin of δ=6 that was based on clinical judgement with 80% power, type I error rate of 5%. The mean of the Oxford Shoulder Score (OSS) outcome in the three groups was considered 50, with SD=10.

Randomization

One hundred five patients included in the study and were randomly divided into three groups of intervention by a computer-generated randomization sequence with the opinion of a counsellor. The subjects of the three groups were matched by age and sex.

Interventions

The intervention groups included: A) Ketorolac (2 x 1 cc ampoule with 4 cc lidocaine 2% and 4 cc normal saline in a total of 10 cc); B) Triamcinolone (2 x 1 cc ampoule with 4 cc lidocaine 2% and 4 cc normal saline in a total of 10 cc); C) Betamethasone LA (2 x 1 cc ampoule with 4 cc lidocaine 2% and 4 cc normal saline in a total of 10 cc). All drugs were injected with the posterior approach. The patients and healthcare personnel were blinded to the groups.

Data Collection

The patient's pain was recorded based on the Visual Analogue Scale (VAS) system and the patient's performance based on the OSS system at weeks 0, 2, 4, and 6 of treatments. The severity of the disease was determined based on the pain level assessed by the OSS and VAS methods. The required information was entered into the checklist through observation and interviews with patients. The assessors were blinded to the groups.

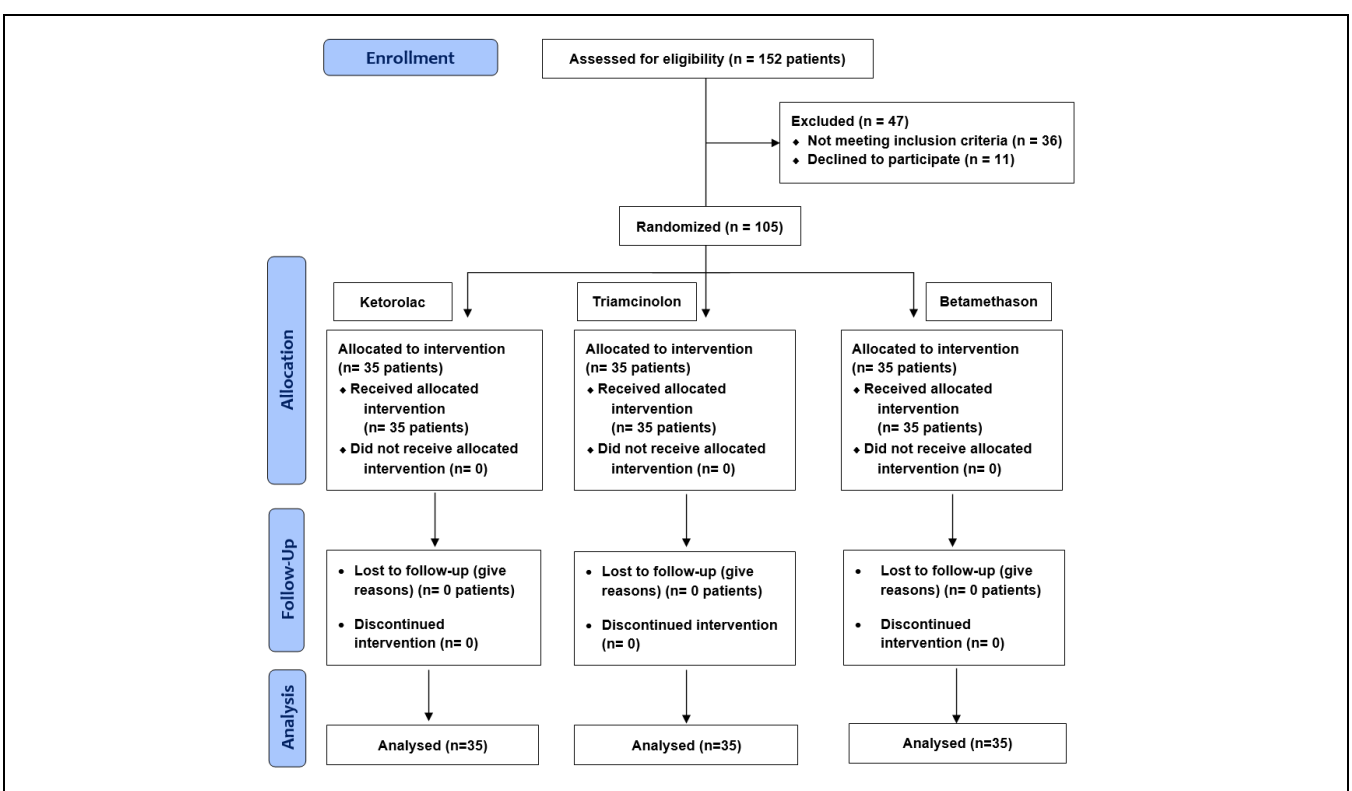

Figure 1. Consort Flow Diagram

Variables	Group A	Group B	Group C	p-Value
Sex				
Man	16 (45.7)	17 (48.6)	15 (42.9)	0.96
Women	19 (54.3)	18 (51.4)	20 (57.1)	
Age Group				
<40 years old	23 (65.7)	18 (51.4)	19 (54.3)	0.45
≥40 years old	12 (34.3)	17 (48.6)	16 (45.7)	

Table 1. Basic and Clinical Data of Patients Studied in Three Groups

	Beginning of the Study	Second Week	Fourth Week	Sixth Week	p-Value*
Group A (Ketorolac)	35.94±5.25	41.14±5.62	44.40±5.50	45.37±4.95	<0.001
Group B (Triamcinolone)	34.66±6.56	38.26±7.11	42.37±6.49	44.20±5.34	<0.001
Group C (Betamethasone)	35.5±14.00	39.4±26.79	43.4±34.22	46.2±23.98	<0.001
P-value**	0.06	0.12	0.30	0.17	

Table 2. The Mean Score of Patients' Performance on The Basis of Oxford Shoulder Score Scale in Three Groups in Four Time Intervals

* Using Repeated Measurement at various time intervals
** Using One Way ANOVA at any time interval

	Beginning of the Study	Second Week	Fourth Week	Sixth Week	P-Value*
Group A (ketorolac)	6.37±1.30	3.43±1.39	1.62±1.69	1.11±1.54	<0.001
Group B (triamcinolone)	6.40±1.45	3.31±2.48	1.89±2.22	1.46±2.11	<0.001
Group C (betamethasone)	6.1±1.19	3.1±1.53	2.11.57±	1.01±1.25	<0.001
P value**	0.67	0.32	0.21	0.26	

Table 3. The Mean Score of Patients' Pain Based on Visual Analogue Scale in Three Groups in Four Time Intervals

*Using Repeated Measurement at various time intervals
** Using One Way ANOVA at any time interval

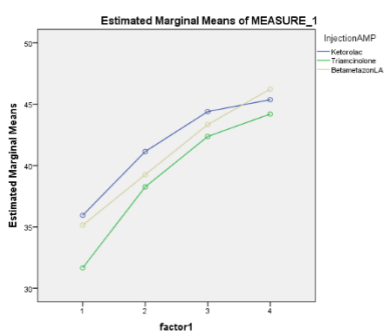

Figure 2. The Mean Scores of Patients' Performance Based on The Injected Drugs

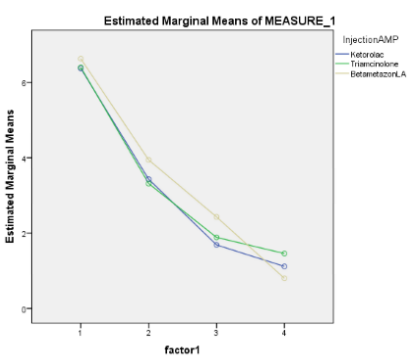

Figure 3. The Mean Scores of Patients' Pain Scores Based on Injected Drugs

Statistical Analysis

The collected data were analysed using SPSS V.22 software. Chi-square, one-way ANOVA and Repeated measurement tests were used. P-value less than 0.05 was considered significant.

Ethical issues

The study was confirmed by the Research Council and the Ethics Committee of Babol University of Medical Sciences (code: MUBABOL.HRI.REC.1395.112). The trial was also registered in Iranian Registry of Clinical Trials website with code IRCT2017042927797N2. All patients were aware of the study process and the potential risks of injection process were explained for them. Informed consent was taken from all subjects.

RESULTS

In this study, 105 patients were selected initially. Group A (n=35) was injected by using ketorolac, group B (n=35) triamcinolone and group C (n=35) betamethasone LA. The mean age of the patients was 37.38 ± 9.45 years with a range of 20-53 years old. Figure 1 indicates CONSORT flow diagram. The basic and clinical data for patients in the three groups were presented in Table 1.

Patients' performance scores based on the OSS were evaluated in three groups at different time intervals and shown in Table 2. As observed, there were significant differences in the patient performance between different follow-ups for each group, that is, the performance was significantly improved over time in all groups (p<0.001) (Figure 2). On the other hand, no significant difference was seen in the patient performance between the three groups at different follow-ups.

Table 3 shows the mean score of patients' pain based on VAS in three groups in four time intervals. The mean score of pain in all three groups decreased significantly over time (p<0.001) (Figure 3), while there was no difference between the groups at different times (Table 3).

The mean score of patients' performances in 0, 2, 4, and 6 weeks between three groups and based on age groups were also investigated. There was no significant difference between groups in all four-time intervals in patients under 40 years of age. In patients older than 40 years old, there was a significant difference between the groups at the second week (p=0.05) and the sixth week (p=0.03). There were no significant differences between the groups in men and women at any follow-ups.

In patients less than 40 years old, it was found that the mean score of pain was significantly different at the second week (p<0.001) and fourth week (p=0.001) between the three groups. In patients more than 40 years old, it was also observed that patients with injection of betamethasone significantly had a higher mean pain score in the second week compared with other groups (p=0.006). The significant higher score was still seen in the sixth week (p=0.04). On the other hand, the mean pain score in men in the fourth week was significantly lower in betamethasone group compared with other treatments (p=0.03).

DISCUSSION

According to the obtained results, patients' performance improved on the basis of OSS scores in all three groups

during follow-up. In different weeks, there were no significant differences between the three groups in the performance. The pain score of patients also decreased with the administration of various drugs over time, although there was no difference between drugs in this case.

Among all shoulder injuries, shoulder impingement syndrome is more common and is considered as the most common cause of pain and motion restriction in the shoulder region. In United States, 13.5% of the population aged 18-38 suffers from shoulder joint injury, that is, shoulder disorders are the third leading cause of referral to the treatment centers after shoulder and neck pain.[15] In this study performance of patients with shoulder impingement syndrome was improved by using injections of drugs such as ketorolac, triamcinolone and betamethasone. Since the shoulder joint is the most movable joint in the body and both groups of inactive components (Bony structures and ligaments) and the active components (Muscles) are involved in its stability,[16] the treatment gives the patient satisfaction and returns them to the daily activity. In a clinical trial study by Min et al.[17] on 32 patients with diagnosis of shoulder impingement syndrome, patients were injected with triamcinolone and ketorolac. After one month of follow-up, in both groups, the range of motion increased, and the pain of the patients decreased significantly. By performing intergroup analysis, it was found that ketorolac injection had a better recovery than triamcinolone.[17]

In the present study, it has been shown that the use of ketorolac, as a NSAID, does not differ with corticosteroids, such as triamcinolone and betamethasone. In 2003, Buchbinder et al. systematically reviewed the effect of NSAIDs and corticosteroids and found that corticosteroid injections had no superiority to NSAIDs. Major research on the treatment of shoulder impingement syndrome is based on physiotherapy and various exercises. Therefore, a few studies have been conducted to compare different drugs in the treatment of this disorder. According to the results of the present study (Showing no significant difference in the efficacy between ketorolac and other two corticosteroids), and also due to less side effects of the NSAID drug, it can be recommended to use NSAIDs in improving the performance of patients.

In addition, Aksakal et al.[18] investigated the effect of betamethasone injection and lornoxicam in performance of patients with shoulder impingement syndrome. They reported that a single dose of subacromial lornoxicam injection had a better improvement in comparison with betamethasone at the second week. In addition, lornoxicam injection improved performance of patients faster.[18] In the above studies, it has been argued that NSAIDs respond better than corticosteroids. In contrast, in a study by Onat et al, they found that the kinesiotaping group and the corticosteroid group had a better range of motion than the NSAID group.[19] This study showed that injection of drugs such as ketorolac, triamcinolone or betamethasone can reduce pain in the patients. In this disease, pain occurs due to entrapment of bursa.[20] In another study, Yegane et al.[21] investigated the effect of local corticosteroid injection and physiotherapy on the severity of pain, range of motion and muscle strength in patients with shoulder impingement syndrome. They indicated a significant improvement in pain intensity and the range of motion in the two groups. They also found that local corticosteroid injection is effective in short-term, while physiotherapy has better results in long-term.[22]

Due to easy use, high variation in exercise movements and home-based exercises in the treatment of this disease have been widely considered. Therefore, there are few studies in the field of pharmacotherapy. In 2002, Yamakado et al. conducted a study on 53 patients with symptoms of shoulder impingement syndrome. They injected a combination of betamethasone and radiographic contrast and lidocaine in a group. They found that patients who had injection, their shoulder pain significantly was reduced.[22] Frequent complaints of shoulder impingement syndrome include pain, weakness, crypto and stiffness, which may reduce activity and lead to sleep disturbance.[23] In a study by Say et al.[24] the single-dose corticosteroid and PRP were compared. In the follow-up of 6 weeks and 6 months, they found that pain in patients with both steroids at both time intervals was lower than the PRP group.[25] Also, Radnovich et al. investigated the effect of corticosteroid injections and patches of lidocaine/tetracaine on the treatment of shoulder impingement syndrome. They concluded that the short-term and non-invasive therapeutic effect of lidocaine/tetracaine patch is quite similar to that of corticosteroids in treating the pain caused by this syndrome.[25] It should be noted that in recent years, the use of resistance exercises, especially in the rehabilitation, has been very much taken into account, with the advantages of low cost, low volume and safety.

Lack of examination of the range of motion of shoulder joints in patients with shoulder impingement syndrome and lack of long-term patient follow-up and evaluating the effect of drugs over a long period of time are among the limitations of this study. It is suggested that a study should be performed to compare each of these drugs used in this study with resistance training to identify an effective method for treating the disease.

CONCLUSIONS

Taken together, the results of this study showed that the injection of ketorolac, triamcinolone and betamethasone are equally effective in increasing the performance and reducing pain in patients with shoulder impingement syndrome.

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