Int J Clin Exp Med 2016;9(10):18972-18980
www.ijcem.com /ISSN:1940-5901/IJCEM0038078

Original Article

Comparison of the efficacy of subacromial injection with sodium bicarbonate versus corticosteroid in patients with chronic subacromial bursitis: a prospective, randomized and controlled study

Hua Kang[1*], Hong Jiang[1*], Dongdong Chai[1], Yuan Lin[2], Qifang Li[1]

[1]Department of Anesthesiology, Shanghai Ninth People's Hospital, School of Medicine, Affiliated to Shanghai Jiao Tong University, Shanghai, China; [2]Department of Anatomy, Southern Medical University, Guangzhou, China. [*]Co-first authors.

Received August 17, 2016; Accepted September 1, 2016; Epub October 15, 2016; Published October 30, 2016

Abstract: Objective: Corticosteroid injections have been a widely utilized and well-accepted method of treatment for patients with chronic subacromial bursitis (SAB) who have failed many conservative therapies. As an alternative, we test whether subacromial injection of sodium bicarbonate (SB) can substitute subacromial corticosteroid injection in the treatment for chronic SAB. Methods: 70 patients diagnosed with chronic SAB were divided into two groups randomly. They were treated with SB and triamcinolone (TMC) subacromial injection, respectively. The control (TMC) syringe contained a mixture of 1ml triamcinolone (40 mg), 2 ml of 2% lidocaine and 7 ml of 0.9% saline; and the test (SB) syringe contained a mixture of 2 ml of 2% lidocaine, 6 ml of 5% sodium bicarbonate and 2 ml of 0.9% saline. The visual analog scale (VAS), active range of motion (ROM), and Constant-Murley Score (CMS) of the affected shoulder were respectively completed before and at 1 week, 2 and 4 weeks following the injection. Results: Both groups obtained a significant improvement of VAS, CMS, and active shoulder ROM at 1 week, 2 and 4 weeks follow-up. Pain relief was achieved significantly faster after a steroid injection than after SB injection at 1 week. And there was no significant difference at 2 and 4 weeks following the injection; whereas, no significant difference was found in CMS and active shoulder ROM between the 2 groups at the 4 time points. Conclusion: The efficacy of subacromial SB injection is equivalent to corticosteroid for chronic SAB and may be a potential and useful alternative for the treatment for chronic SAB.

Keywords: Subacromial, bursitis, corticosteroid, sodium bicarbonate

Introduction

Chronic subacromial bursitis (SAB) is a common clinical condition characterized by chronic pain in the anterior and superior part of the shoulder. Patients with chronic SAB usually complain of a dull shoulder pain, restriction of abduction and internal rotation of the shoulder, with tenderness over the deltoid region. Aches usually worsen not only during the night but also when patients are performing overhead activities [1, 2]. The shoulder pain associates with a painful arc of motion. The range of motion (ROM) of the shoulder is limited or may not be limited in a noncapsular pattern. In addition, all resisted movements are painless or equally painful [3]. A history of pain in the lateral shoulder and tenderness to palpation along the acromial border indicate a diagnosis of subacromial bursitis. And it can be confirmed by an infiltration with local anesthetic [3, 4].

The main goal in treating chronic SAB is to reduce pain and improve the range of movement. Although nonoperative treatment options for chronic SAB have included rest, drugs administration, such as NSAIDs, local application of ice, and modifications of the routine physical activity [1, 5, 6]. Corticosteroid injection has been a widely utilized and well-accept-

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1. Shoulder pain duration for more than 3 months	1. Symptoms less than 3 months
2. A visual analog scale (VAS) score for abduction ≥4	2. A surgical or fracture history near the shoulder region
3. The presence of a painful arc of motion or pain at the mid- to terminal range of shoulder abduction or internal rotation	3. Uncontrolled chronic disease, for example, malignant neoplasms, hypocoagulability and local infection
4. Tenderness to palpation anterior/lateral to the acromion	4. Evidence (x-ray) of calcification of the rotator cuff
5. And a reduction in pain after the subacromial injection of 2 mL of 1% lidocaine.	5. Evidence (MRI) or history of rotator cuff tear or tendinopathy
	6. Evidence (Radiographs) or history of shoulder inflammatory arthritis, osteoarthritis, frozen shoulder, subacromial spurs, or deformity of the acromion
	7. The presence of cervical radiculopathy
	8. Previous shoulder injections within the past 3 months
	9. Evidence of shoulder instability

ed method of treatment for patients with chronic SAB who have failed many conservative therapies [1, 3, 7]. It is widely accepted that the pain relief attributes to its anti-inflammatory properties [8, 9]. Unfortunately, the frequency of using corticosteroid injection is limited because of its potentially serious side effects, such as subcutaneous fat atrophy, skin hypopigmentation, tendon rupture, articular cartilage damage and systemic effects like hyperglycemic, HBP, menstrual disorder and osteoporosis [9-13].

Some researches displayed that in some infection or inflammation pathological conditions, the pH around the lesions may reduced, and local tissue acidosis was induced [14, 15]. Extracellular pH change is thought to alter vascular tone [16] and the acidosis in local tissue can evoke pain in animals and humans [17]. It has been demonstrated that in some inflammation pathological conditions that glycolysis accelerated and lactate accumulated, it may result in the abnormal contraction of local vessel, which can disturb the healing of lesion [18, 19]. Therefore, local tissue acidosis has multiple effects on tissues and cellular function, including impaired oxygen delivery, decreased energy generation and impaired glucose metabolism. Clinically, soft tissue inflammation may spontaneously resolve or too often may evolve into a chronic inflammatory condition. It has been widely accepted that sodium bicarbonate is administrated to patients with severe metabolic acidosis in clinical. In consideration of the premises, we propose that the use of subacromial SB injection is to treat chronic SAB instead of corticosteroid injection.

The objective of this prospective, double-blind, randomized and controlled trial was to compare the efficacy of subacromial injection of TMC with SB injection. We hypothesized that the efficacy of subacromial SB injection would be equivalent to the efficacy of corticosteroid injection.

Materials and methods

This was a randomized, prospective, controlled, and double-blind study of sodium bicarbonate versus corticosteroid injection for the treatment of chronic SAB. We recruited ambulatory patients with painful shoulder due to chronic SAB. The procedures followed in this study were evaluated and approved by the local ethics committee. The patients were informed of the study procedures and signed the informed consent form prepared for this study.

The inclusion criteria were as follows: (a) shoulder pain duration for more than 3 months, (b) a visual analog scale (VAS) score for abduction ≥4, (c) tenderness over the subacromial location, (d) the presence of a painful arc of motion or pain at the mid- to terminal range of shoulder abduction or internal rotation, and (e) a reduction in pain after the subacromial injection of 2 mL of 1% lidocaine. The exclusion criteria were as follows: (a) symptoms less than 3 months; (b) a surgical or fracture history near the shoul-

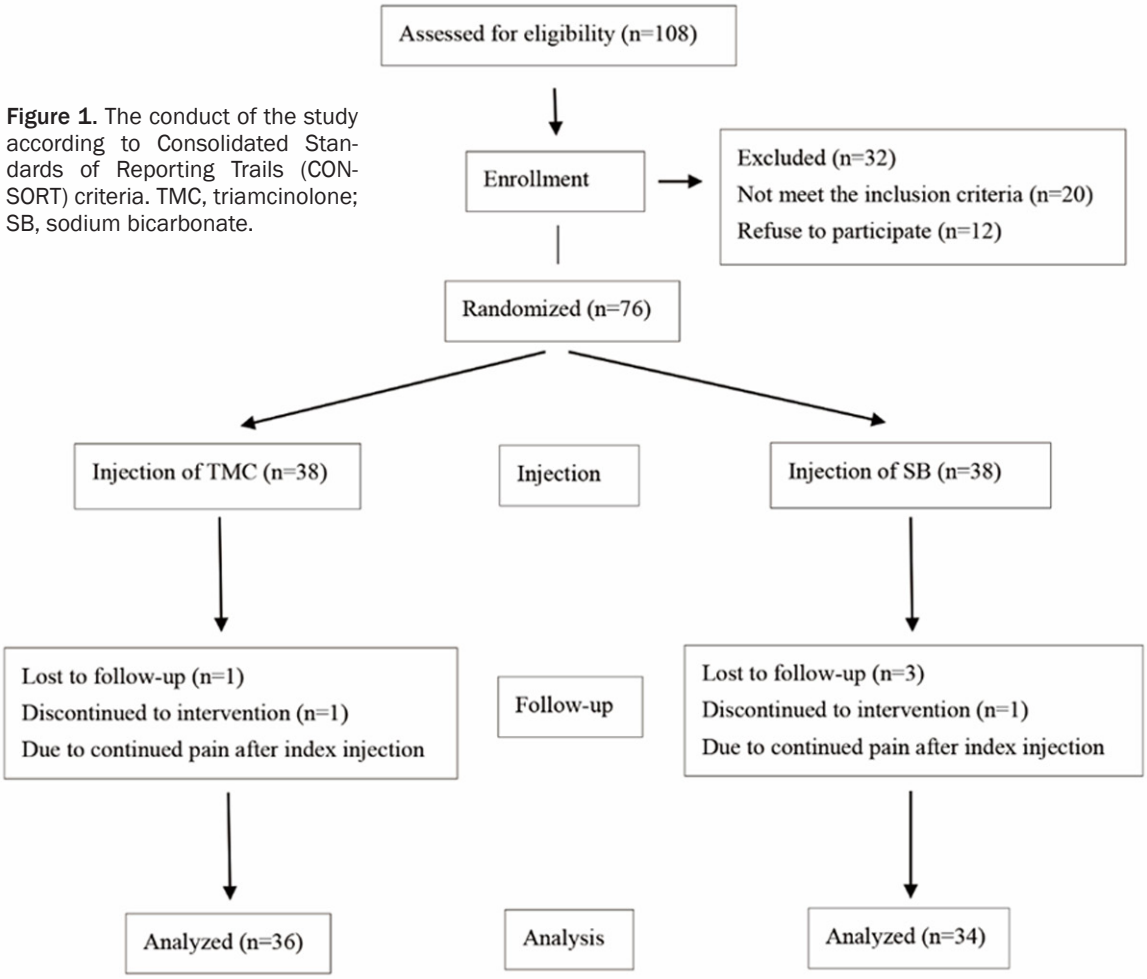

Figure 1. The conduct of the study according to Consolidated Standards of Reporting Trails (CONSORT) criteria. TMC, triamcinolone; SB, sodium bicarbonate.

der region; (c) uncontrolled chronic disease, for example, malignant neoplasms, hypocoagulability and local infection; (d) evidence (x-ray) of calcification of the rotator cuff; (e) evidence (MRI) or history of rotator cuff tear or tendinopathy; (f) evidence (Radiographs) or history of shoulder inflammatory arthritis, osteoarthritis, frozen shoulder, subacromial spurs, or deformity of the acromion; (g) the presence of cervical radiculopathy; (h) evidence of shoulder instability; (i) previous shoulder injections within the past 3 months (**Table 1**).

From February 2014 to March 2016, a total of 108 patients were enrolled in the current study. Among them, 20 patients met the exclusion criteria (9 with calcific tendinitis, 7 with a partial-thickness rotator cuff tear, 3 with a full-thickness rotator cuff tear, 1 with osteoarthritis of the shoulder) and an additional 12 patients did not want to participate in the study. As a result, 38 patients were randomized to the steroid group (TMC group) and 38 patients to the sodium bicarbonate group (SB group). Four patients were lost to follow-up (1 TMC, 3 SB), and 2 patients were later excluded because of a changing treatment method during the study period (1 TMC, 1 SB). Thus, 36 subjects in the TMC group and 34 subjects in the SB group completed the study (**Figure 1**). The injected medication in the two groups was differentiated as follows: The control (TMC) syringe contained a mixture of 1 ml triamcinolone (40 mg), 2 ml of 2% lidocaine and 7 ml of 0.9% saline; and the test (SB) syringe contained a mixture of 2 ml of 2% lidocaine, 6 ml of 5% sodium bicarbonate and 2 ml of 0.9% saline.

In order to ensure a double-blinded evaluation, the following measures were taken: Random numbers for allocating patients of treatment groups were generated by a computer program. And a set of sealed, consecutively numbered envelopes containing the random allocation

Table 2. Demographic data of patients

	TMC group	SB group	*P*
Patients, No	38	38	
Age (mean ± SD) (y)	55.53±10.83 (26-78)	56.87±9.78 (29-80)	0.572†
Sex (M/F)	22/16	21/17	0.817‡
Symptom duration (mean ± SD) (month)	6.21±3.22	6.71±3.63	0.527†
Side (dominant/nondominant)	23/15	21/17	0.642‡
Diabetes mellitus history	4	4	>0.05‡

TMC, triamcinolone; SB, sodium bicarbonate. †Calculated by independent samples t test; ‡Calculated by χ^2 test.

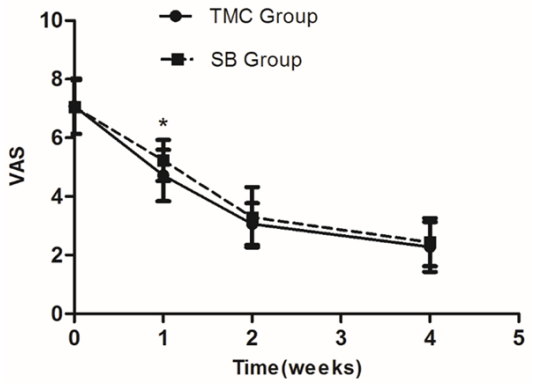

Figure 2. Pain evaluations by using visual analog scale (VAS) improved after patients received a subacromial injection of TMC or SB. There was a significant difference between the two groups at 1 week after injection (*P=0.009). No significant difference was found at 2 and 4 weeks between the two groups (P=0.262, P=0.417).

details for each patient were prepared by an assistant not involved in the study. When a patient was recruited, the nurse not involved in patient assessment was instructed to prepare the syringe containing the appropriate injection according to the individual patient's recruitment number in the envelope. Each syringe was covered in opaque tap, so that the injector, patient, and elevator remained blinded to group assignment.

All patients were assessed with a VAS for evaluating pain and CMS before treatment and at 1 week, 2 and 4 weeks after the treatment. The CMS scoring system consists of subjective assessments of pain, activities of daily living (ADL), range of motion (ROM), as well as the strength of abduction [20]. A hand held goniometer was used to measure the active ROM of the affected shoulder at base line at 1 week, 2 and 4 weeks after the injection. Data regarding clinical evaluations and functional outcomes

Table 3. Pain values measured by visual analog scale (VAS)

Time	TMC group	SB group
Pretreatment	7.08±0.94	7.05±0.92
1 week	4.72±0.88	5.23±0.70‡
2 weeks	3.06±0.71	3.29±1.03
4 weeks	2.28±0.85*	2.44±0.82*

TMC: triamcinolone; SB: sodium bicarbonate; VAS: visual analog scale. Continuous data are presented as the mean ± standard deviation. *Significant difference between pretreatment and post-treatment in both groups (P<0.05). ‡Significant difference at 1 week between two groups (P=0.009).

were collected blindly by an assessor not involved in the study. No patient received physical therapy during the follow-up period.

We injected the subacromial bursa according to Cyriax's method [7]. The patient was asked to relax the affected arm. First we localized the lateral edge of the acromion. And then, using aseptic technique, the 21-gauge needle was inserted medially and in a slightly cranial direction into the bursa at 1-2 cm beneath the middle point of the lateral edge of the acromion. Special attention was paid not to inject the material into the coracoacromial ligament or the capsulotendinous structures. The pharmaceutical material should flow freely into the space without any resistance or significant discomfort for the patients.

The changes in pain and function parameters between and within the groups at 1 week, 2 and 4 weeks after therapy onset were evaluated by a repeated-measures analysis of variance and a multivariate analysis of variance. SPSS 17.0 software (SPSS Inc, Chicago, IL, USA) was used, and all significance levels were set at α=0.05. Demographic comparisons were performed by the independent t-test for age, symp-

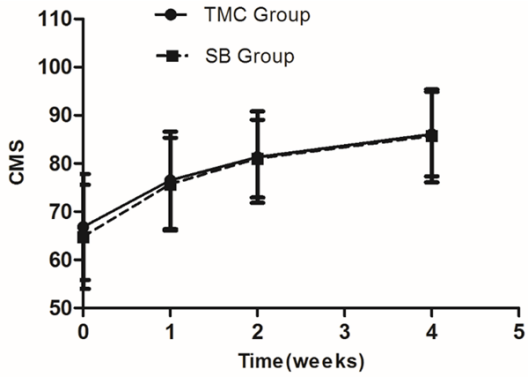

Figure 3. Constant scores improved after patients received a TMC or SB injection in the subacromial space (P<0.05). There were no significant statistical differences between the two groups at final follow-up assessments (P=0.688).

Table 4. Constant-Murley Score (CMS)

Time	TMC group	SB group
Pretreatment	66.83±10.99	64.76±10.80
1 week	76.50±10.11	75.68±9.63
2 weeks	81.33±9.49	81.00±8.05
4 weeks	86.08±8.78*	85.71±9.66*

TMC, triamcinolone; SB, sodium bicarbonate; CMS, Constant-Murley Score. Continuous data are presented as the mean ± standard deviation. *Significant difference between pretreatment and post-treatment in both groups (P<0.05). No significant difference at each time point between the 2 groups (P>0.05).

tom duration and x^2 test for sex distribution, diabetes mellitus history, and dominant shoulder.

A sample size in each group was determined before hand by the use of power and sample size calculation. Power analysis indicated that a sample size of 26 patients in each group would provide a power of 80% to detect a 5% significant difference in Constant-Murley Score (CMS), assuming a mean difference of 8 points and a SD of 13 points [21]. To account for possible loss to 20% of follow-up, we estimated the total number of patients needed to be 32 per group.

Results

The baseline characteristics of these patients are summarized in **Table 2**. Mean age, gender distribution, symptom duration, diabetes mellitus history, and dominant shoulder involvement were similar in the two groups. No significant demographic differences were observed between the two groups. There were no significant differences in pretreatment VAS, ROM, and CMS between the two groups.

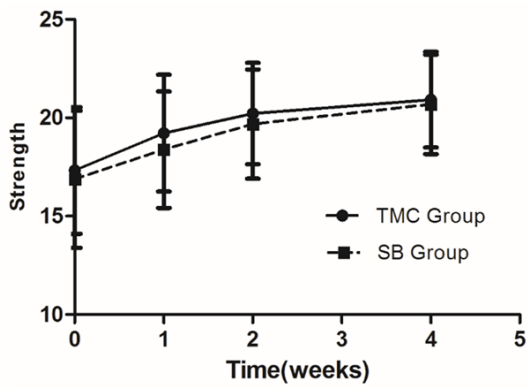

Figure 4. Strength scores in CMS were improved after patients received a TMC or SB injection in the subacromial space (P<0.05).There were no significant statistical differences between the two groups at final follow-up assessments (P=0.441).

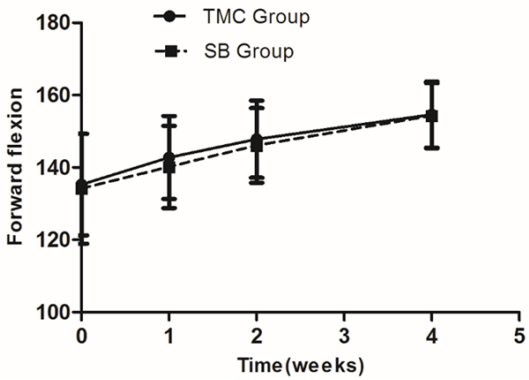

Figure 5. Forward flexion improved regardless of treatment method at final follow-up evaluations. No significant differences were observed between the two groups at final follow-up evaluations (P=0.587).

The VAS score improved significantly throughout the follow-up period in the two groups (**Figure 2**). However, pain relief was achieved significantly faster after a corticosteroid injection than after SB injection, and this difference was maintained for up to 1 week: 4.72±0.88 in TMC group, 5.23±0.70 in SB group (P=0.009). Yet, there were no significant differences in pain VAS at 2 and 4 weeks after injection between the two groups (P=0.262, P=0.417) (**Table 3**).

The CMS improved significantly throughout the follow-up period in the two groups (**Figure 3**). No significant difference in CMS was found

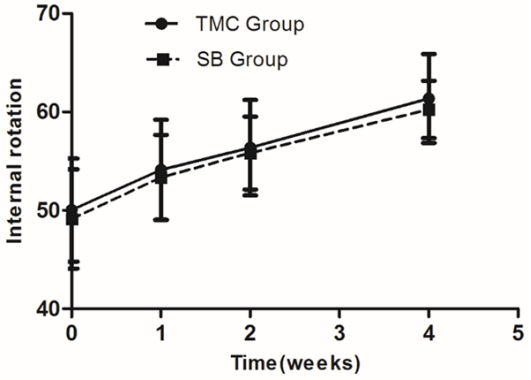

Figure 6. Internal rotation improved regardless of treatment method at final follow-up evaluations. No significant differences were observed between the two groups at final follow-up evaluations (P=0.417).

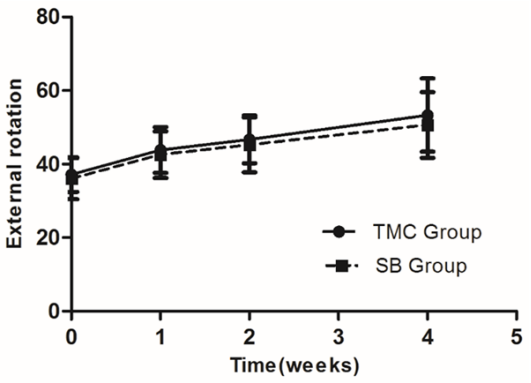

Figure 7. External rotation improved regardless of treatment method at final follow-up evaluations. No significant differences were observed between the two groups at final follow-up evaluations (P=0.293).

between the two groups at final follow-up assessments (P=0.688) (**Table 4**). Strength scores in CMS improved significantly after the treatment in the two groups (**Figure 4**). There were no significant statistical differences between the two groups at final follow-up (P=0.441).

For all active ROM, including forward flexion (**Figure 5**), internal rotation (**Figure 6**), external rotation (**Figure 7**) and abduction (**Figure 8**), increased significantly over time in both groups, and no statistical differences were found between the two groups during serial follow-up assessments (P=0.587, P=0.417, P=0.293, P=0.315) (**Table 5**).

All the patients completed the study. Three complications occurred in the TMC group, including one dizziness which resolved in 3 minutes without intervention, one mild dyspeptic symptom, and one steroid flare reaction. No other adverse events or complications were encountered.

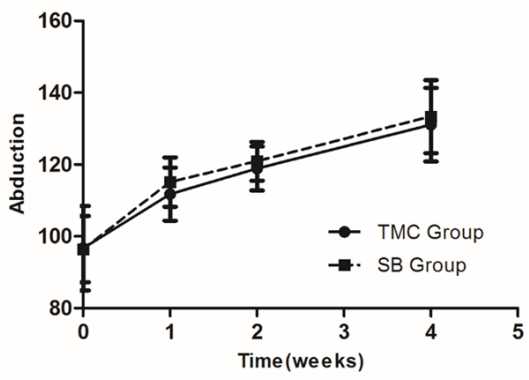

Figure 8. Abduction improved regardless of treatment method at final follow-up evaluations. No significant differences were observed between the two groups at final follow-up evaluations (P=0.315).

Discussion

To our knowledge, this study is the first research to show that subacromial injection of sodium bicarbonate can be beneficial for chronic SAB. Our study suggests that SB injection has similar clinical outcomes compared to corticosteroid injections, as measured by improvement in the VAS, ROM and CMS for 4 weeks. Furthermore, the best available evidence doesn't limit the use of subacromial injection of SB and the side effects of corticosteroid could be avoided. Thus, subacromial injection of SB may provide an alternative to corticosteroid, especially for the diabetic patients or someone else with chronic SAB who rejects the injection of steroid.

The histological and molecular changes of chronic SAB implied chronic nonspecific inflammation, elevated presence of the inflammatory cytokines, increased abnormal vascularity, associated with abnormal metabolism of local tissues, and local metabolic acidosis in the bursa, which may cause pain and bursa impingement during active or passive ROM of the shoulder. Steen et al. found that direct infusion of isotonic acidic solutions into human skin caused sustained pain [22]. Issberner et al. demonstrated a significant correlation between pain intensity and pH change in the human muscle pain induced by acid [23]. The painful inflammatory and ischemic condition

Table 5. Active range of motion measurements

Time	Range of motion	TMC group	SB group
Pretreatment	Abduction	96.69±11.73	96.44±9.24
	Flexion	135.28±14.04	134.15±15.15
	Internal rotation	50.03±5.23	49.12±5.04
	External rotation	37.14±4.71	36.03±5.58
1 Week	Abduction	111.78±7.39	115.12±6.86
	Flexion	142.75±11.46	140.15±11.35
	Internal rotation	54.11±5.11	53.35±4.31
	External rotation	43.83±6.21	42.56±6.36
2 Weeks	Abduction	118.89±6.14	120.91±5.40
	Flexion	147.83±10.69	146.12±10.32
	Internal rotation	56.36±4.86	55.82±3.70
	External rotation	46.72±6.50	45.21±7.46
4 Weeks	Abduction	131.11±10.29*	133.35±10.18*
	Flexion	154.64±9.13*	154.29±8.98*
	Internal rotation	61.36±4.52*	60.24±2.91*
	External rotation	53.33±9.95*	50.65±8.94*

TMC: triamcinolone; SB: sodium bicarbonate; ROM: range of motion. Continuous data are presented as the mean ± standard deviation. *Significant difference between pretreatment and post-treatment in both groups ($P<0.05$). No significant difference at each time point between the two groups ($P>0.05$).

were accompanied by local tissue acidosis [15]. Therefore, we are supposed one of the causes of pain in patient with SAB is that the tissue acidosis and inflammation evoking the local tissue. Low pH in tissue is an important factor in hyperalgesia [17]. And several researches found that tissue acidosis in muscles related to ischemia and inflammation had a profound effect on the initiation and development of chronic muscle pain [23, 24]. Acidosis is the process leading to an abnormally high concentration of hydrogen ions. Then extracellular protons provoke the pain by opening excitatory cation channels in nociceptors [15]. In this study we obtained almost complete pain relief with a subacromial injection of SB (**Table 3**). Therefore, the hydrogen ions dissociated from the acids may be buffered by bicarbonate in the extracellular compartment. Meanwhile, hyperalgesia is reduced, and the inflammation cascades may be interdicted partly.

Many researches proved that the external pH regulated vascular tone [25-28]. Wilson and Woodward had ever demonstrated that the coronary circulation of the rat constricts in response to acidosis by perfusing rat hearts with langendorff model [16]. Local tissue acidosis resulted in the abnormal contraction and diastole function of local vascular. Furthermore, abnormal proliferation of endothelial cells were found in the vascular channels along with subacromial bursa [29]. Therefore, this may worsen tissue perfusion and aggravate acidosis as well as oxygen deficit. SB can not only buffer the H^+ around the bursa but also improve the abnormal vascular contraction diastole. One of the causes of effective treatment for local tissue acidosis is cessation of acid production via improvement of tissue oxygenation.

In the early part of the twentieth century, researches suggested that lactic acid accumulation was a predominant cause of skeletal muscle fatigue, which occurred most rapidly under anaerobic conditions and during rapid contractions. It was reported that orally ingested sodium bicarbonate ($NaHCO_3$) improved running performance [30]. Recent researches also found that the supplementation of sodium bicarbonate could increase performance or delay fatigue in intermittent high-intensity exercise by decreasing intramuscular [H^+] [30, 31]. In our study, the strength scores in CMS were significantly improved after the treatment in SB group at final follow-up, which was probably due to the effectiveness of SB to improve the skeletal muscle fatigue in some degree.

Blair's study [32] looked at the effect of 1% lidocaine alone vs 1% lidocaine and triamcinolone in patients with impingement. At a mean follow-up of 33 weeks suggests a moderate efficacy of pure local anaesthetic and patients who received a corticosteroid injection had a significantly lower mean pain scores, and large increased in mean forward elevation and external rotation. But Plafki's study [33] showed no positive effect in only 0.5% bupivacaine group and 4 patients complained of pain aggravation. In our study, the VAS score for pain was significantly improved after the treatment in the 2 groups at final follow-up. Although immediate pain relief and increased ROM could be explained by the potency of lidocaine, the potency disappear in a few hours. The effec-

tiveness of SB injection group at 1 week, 2 weeks and 1 month after injection was mostly due to the effect of SB. And there were no statistical differences in pain VAS at 2 and 4 weeks after injection between the two groups. Nevertheless, local anaesthetic injection is considered to be a worthwhile tool to differentiate subacromial pathology from a painful intraarticular condition or an affection of the acromioclavicular joint.

The study has several limitations. Firstly, a subacromial SB injection has never been used to treat SAB before, and it is not fully known how it affects pain relief and function recovery, despite the good clinical results obtained. Secondly, the limitation is the small numbers of patients in the groups to draw a strong conclusion. Further studies with large study populations and long-term follow-up are needed to prove our hypothesis. Furthermore, for ethical and practical reasons, we did not include a control group receiving a placebo injection to eliminate the possibility that a placebo effect was responsible for the improvements. However, because the patients we recruited had experienced shoulder pain for longer than 3 months without signs of spontaneous improvement, we believed spontaneous self-healing in a month was impossible. Finally, although we used the immediate improvement in active shoulder abduction as an indicator of accurate placement when infiltrating the subacromial space, there was a high incidence of non-bursal infiltration. And the advanced imaging technology like ultrasound guidance would have been a more accurate method of injection.

Conclusions

We find that the efficacy of subacromial SB injection is equivalent to corticosteroid for chronic SAB and it may be a potential and useful alternative for the treatment of chronic SAB, especially for the diabetic patients or someone else with chronic SAB who rejects the injection of steroid.

Disclosure of conflict of interest

None.

Address correspondences to: Dr. Qifang Li, Department of Anesthesiology, Shanghai Ninth People's Hospital, School of Medicine, Affiliated to Shanghai Jiao Tong University, 639 Zhizaoju Road, Shanghai 200011, China. Tel: 86-21-23271699; Fax: 86-21-53591385 ; E-mail: drliqifang@163.com

References

[1] Gasparre G, Fusaro I, Galletti S, Volini S and Benedetti MG. Effectiveness of ultrasound-guided injections combined with shoulder exercises in the treatment of subacromial adhesive bursitis. Musculoskelet Surg 2012; 96 Suppl 1: S57-61.

[2] Silvestri E. Subacromial-Subdeltoid Bursa Injections. In: Sconfienza LM, Serafini G, Silvestri E, editors. ultrasound-guided musculoskeletal Procedures. Milan: Springer-Verlag; 2012. pp. 25-28.

[3] Hsieh LF, Hsu WC, Lin YJ, Wu SH, Chang KC and Chang HL. Is ultrasound-guided injection more effective in chronic subacromial bursitis? Med Sci Sports Exerc 2013; 45: 2205-2213.

[4] Tallia AF and Cardone DA. Diagnostic and therapeutic injection of the shoulder region. Am Fam Physician 2003; 67: 1271-1278.

[5] Chen MJ, Lew HL, Hsu TC, Tsai WC, Lin WC, Tang SF, Lee YC, Hsu RC and Chen CP. Ultrasound-guided shoulder injections in the treatment of subacromial bursitis. Am J Phys Med Rehabil 2006; 85: 31-35.

[6] Baldwin AL, Fullmer K and Schwartz GE. Comparison of physical therapy with energy healing for improving range of motion in subjects with restricted shoulder mobility. Evid Based Complement Alternat Med 2013; 2013: 329731.

[7] Ombregt L, Bisschop P, J ter Veer H. A System of Orthopaedic Medicine. London: Churchill Livingstone; 2003. pp. 333-335.

[8] Cole BJ and Schumacher HR Jr. Injectable corticosteroids in modern practice. J Am Acad Orthop Surg 2005; 13: 37-46.

[9] Min KS, St Pierre P, Ryan PM, Marchant BG, Wilson CJ and Arrington ED. A double-blind randomized controlled trial comparing the effects of subacromial injection with corticosteroid versus NSAID in patients with shoulder impingement syndrome. J Shoulder Elbow Surg 2013; 22: 595-601.

[10] Dahl J and Hammert WC. Overview of injectable corticosteroids. J Hand Surg Am 2012; 37: 1715-1717.

[11] Ford LT and DeBender J. Tendon rupture after local steroid injection. South Med J 1979; 72: 827-830.

[12] Melmed EP. Spontaneous bilateral ruptureOF the calcaneal tendon during steroid therapy. J Bone Joint Surg Br 1965; 47: 104-105.

[13] Rostron PK and Calver RF. Subcutaneous atrophy following methylprednisolone injection in

Osgood-Schlatter epiphysitis. J Bone Joint Surg Am 1979; 61: 627-628.
[14] Chen X, Peng LH, Shan YH, Li N, Wei W, Yu L, Li QM, Liang WQ and Gao JQ. Astragaloside IV-loaded nanoparticle-enriched hydrogel induces wound healing and anti-scar activity through topical delivery. Int J Pharm 2013; 447: 171-181.
[15] Ugawa S, Ueda T and Shimada S. Acid-sensing ion channels and pain: therapeutic potential? Expert Rev Neurother 2003; 3: 609-617.
[16] Wilson DA and Woodward B. Acidosis-induced coronary constriction in the rat heart: evidence for the activation of L-type calcium channels. Heart Vessels 1999; 14: 59-66.
[17] Sluka KA, Winter OC and Wemmie JA. Acid-sensing ion channels: a new target for pain and CNS diseases. Curr Opin Drug Discov Devel 2009; 12: 693-704.
[18] Sawyer RG, Spengler MD, Adams RB and Pruett TL. The peritoneal environment during infection. The effect of monomicrobial and polymicrobial bacteria on pO2 and pH. Ann Surg 1991; 213: 253-260.
[19] Stassen WN, McCullough AJ, Bacon BR, Gutnik SH, Wadiwala IM, McLaren C, Kalhan SC and Tavill AS. Immediate diagnostic criteria for bacterial infection of ascitic fluid. Evaluation of ascitic fluid polymorphonuclear leukocyte count, pH, and lactate concentration, alone and in combination. Gastroenterology 1986; 90: 1247-1254.
[20] Constant CR and Murley AH. A clinical method of functional assessment of the shoulder. Clin Orthop Relat Res 1987; 160-164.
[21] Holmgren T, Oberg B, Adolfsson L, Bjornsson Hallgren H and Johansson K. Minimal important changes in the Constant-Murley score in patients with subacromial pain. J Shoulder Elbow Surg 2014; 23: 1083-1090.
[22] Steen KH and Reeh PW. Sustained graded pain and hyperalgesia from harmless experimental tissue acidosis in human skin. Neurosci Lett 1993; 154: 113-116.
[23] Issberner U, Reeh PW and Steen KH. Pain due to tissue acidosis: a mechanism for inflammatory and ischemic myalgia? Neurosci Lett 1996; 208: 191-194.
[24] Frey Law LA, Sluka KA, McMullen T, Lee J, Arendt-Nielsen L and Graven-Nielsen T. Acidic buffer induced muscle pain evokes referred pain and mechanical hyperalgesia in humans. Pain 2008; 140: 254-264.
[25] Aoyama Y, Ueda K, Setogawa A and Kawai Y. Effects of pH on contraction and Ca2+ mobilization in vascular smooth muscles of the rabbit basilar artery. Jpn J Physiol 1999; 49: 55-62.
[26] Kim YC, Lee SJ and Kim KW. Effects of pH on vascular tone in rabbit basilar arteries. J Korean Med Sci 2004; 19: 42-50.
[27] Koltsova SV, Luneva OG, Lavoie JL, Tremblay J, Maksimov GV, Hamet P and Orlov SN. HCO3-dependent impact of Na+,K+,2Cl- cotransport in vascular smooth muscle excitation-contraction coupling. Cell Physiol Biochem 2009; 23: 407-414.
[28] Nakanishi T, Gu H and Momma K. Effect of acidosis on contraction, intracellular pH and calcium in the rabbit mesenteric small artery. J Mol Cell Cardiol 1996; 28: 1715-1726.
[29] Sarkar K and Uhthoff HK. Ultrastructure of the subacromial bursa in painful shoulder syndromes. Virchows Arch A Pathol Anat Histopathol 1983; 400: 107-117.
[30] Higgins MF, Tallis J, Price MJ and James RS. The effects of elevated levels of sodium bicarbonate (NaHCO(3)) on the acute power output and time to fatigue of maximally stimulated mouse soleus and EDL muscles. Eur J Appl Physiol 2013; 113: 1331-1341.
[31] Wu CL, Shih MC, Yang CC, Huang MH and Chang CK. Sodium bicarbonate supplementation prevents skilled tennis performance decline after a simulated match. J Int Soc Sports Nutr 2010; 7: 33.
[32] Blair B, Rokito AS, Cuomo F, Jarolem K and Zuckerman JD. Efficacy of injections of corticosteroids for subacromial impingement syndrome. J Bone Joint Surg Am 1996; 78: 1685-1689.
[33] Plafki C, Steffen R, Willburger RE and Wittenberg RH. Local anaesthetic injection with and without corticosteroids for subacromial impingement syndrome. Int Orthop 2000; 24: 40-42.