A CLINICAL TRIAL COMPARING SUBACROMIAL BURSA INJECTION OF HYALURONIC ACID TO STEROID IN SUBACROMIAL IMPINGEMENT SYNDROME

Abstract

Objective: To evaluate the effects of subacromial bursa injection in subacromial impingement with hyaluronic acid and compare its outcome results with the corticosteroid.

Method: A total of 88 patients with subacromial impingement were randomised to treatment with subacromial bursa injection, 44 patients underwent subacromial bursa injection with hyaluronic acid (Group A) and other 44 patients (Group B) treated with steroid. Patients were followed up for 24 weeks. Primary outcome was pain on Visual analogue scale (VAS) and secondary outcome measured was Constant Murley score.

Result: Both the groups showed statistically significant improvement in VAS, Constant Murley score and shoulder movement range at 3rd week after the injection. However when comparing the extant of improvement of outcome measures at 24 weeks to the baseline in both groups, it was statistically not significant (P>0.05).

Conclusion: The different outcome measures in both hyaluronic acid and steroid injections groups showed similar results, however steroids produces faster pain relieve compared to the hyaluronic acid.

Keywords: Shoulder impingement syndrome, Subacromial bursa injection, hyaluronic acid, steroid
Introduction:

Shoulder pain is very common, it is second most frequent musculoskeletal disorder and shoulder impingement is the leading cause of pain. Initial treatment consist of acetaminophene or low does non-steroidal anti-inflammatory drugs (NSAIDs) in first four to six weeks. When pain relief is insufficient, a subacromial bursa injection of steroid advised for pain control and improvement of shoulder functions. Some guidelines also advocate physiotherapy or manipulative therapy. Crawshaw et al reported that physiotherapy combined with sub-acromial injection give better results than each separately. A few studies have demonstrated improvement in shoulder pain and functions following the injection of hyaluronic acid alone in sub-acromial bursa. The hyaluronic acid is though to work as lubricant and is reported to have an anti-inflammatory effects.

This study aimed to access the efficacy of hyaluronic acid in sub-acromial injection and results were compared with from corticosteroids.

Patients and Methods:

The trial had ethical approval. The study participants, who came to the department of orthopaedics with primary complaint of shoulder pain, were recruited. Thos who met following inclusion criteria were finally considered. (1) All patients, over 18 years of age and had shoulder pain either at rest or at movement. (2) Who had painful arc and positive in Hawkin’s test or Neer impingement sign.

The exclusion criteria were follows. (1) Pain for less than six weeks. (2) Prior injection of steroid or hyaluronate in the same shoulder. (3) Allergy to lidocain, steroid or hyaluronic acid. (4) Pregnancy or suspected pregnancy. (5) Dementia or other psychiatric disorder. (6) Tumor. (7) Previous fractures or surgery on shoulder, upper limb or neck. (8) Flexion at shoulder <100° and external rotation limited by 50% compared with opposite shoulder. (9) Rheumatoid arrhitis, ankylosing spondylitis and polymyalgia. (10) Associated neurological disorder.

A total of 88 patients, who met the inclusion criteria were taken and randomised blindly into two treatment groups with the random block assignment method. All the subjects of both two groups had a sub-acromial injection with either a combination of 2ml lidocain 1% and 2ml hyaluronic acid (Group A) or mixture of 2ml lidocain 1% and 2ml steroid (Methyldapridinosolone acetate) (Group B). Injection were repeated if required at three and six weeks, and no further injection were given.

All the injections were administered via a dorsolateral approach, through the interval just beneath the dorsal acromial edge, with the patient sitting up. Administration of all kind of analgesics or anti-inflammatory drugs was stopped starting one week prior to the trial treatment. Patients were instructed for shoulder exercises after injection. No other associated therapy or drugs treatment were allowed.

Subjects were evaluated, before the first injection, three weeks, six weeks, 12 weeks, 18 weeks and at 24 weeks after the treatment start. Primary outcome measure was pain as measured on visual analogue score (VAS). Secondary outcome measure were the Constant Murley shoulder score and active movement range of the shoulder joint were used to access shoulder function of the patient.

Statistical analysis:

All statistical analyses conducted using SPS software V20.0 for windows with t-test, ANOVA and Fisher exact test. Statistical significance was assumed at P<0.05.

Results:

A total of 88 patients were enrolled and randomly assigned into two groups, group A and group B with 44 patients in each groups. Group A patients injected with 2ml lidocain 1% and 2ml Hyaluronic acid combination. Group B patients injected with 2ml lidocain 1% and 2ml steroid (methylprednisolone acetate) mixture.

Mean age of the 44 patients in group A was 44.35±9.40 and in group B it was 43.81±8.34. In group A, 16 were male and 28 were female. Whereas 19 were male and 25 were female in group B, and there was no statistically significant difference (p>0.05) in age, sex, shoulder affected and pre-injection score between the groups (Table 1).

Change in visual analogue scale (VAS):

There was significant improvement in VAS observed at each follow-up intervals after the sub-acromial bursal injection in both groups (P<0.05). Maximum betterment in VAS was observed at six weeks in both groups (Fig 1). However there was a more gain in group A when comparing the degree of improvement at six months to the per-injection in both group, but it was not statistically significant (Table 2)

Change in Constant Murley Score:

For Constant Murley score, there was significant improvement in both
the groups at all stages of observations (P<0.05). Maximum improvement in Constant score was at six weeks after the injection in both groups. Though, there was a larger improvement in group B when comparing intensity of improvement at six months and before sub-acromial injection in both group, but it was not statistically significant (P>0.05) (Table 2, Fig 2).

Change in active range of motion:

A significant recovery in active range of motion of shoulder joint in all planes was observed at all phases of follow up in both group (P<0.05). Maximum gain in the range of flexion, abduction and internal rotation movement of shoulder joint was observed at third week after the injection. External rotation movement showed maximum gain at 12 weeks of follow up. Although, there was a greater improvement in flexion and abduction range of movement in steroid group when comparing the extant of improvement at 24 weeks to the baseline scores in both groups, but it was not statistically significant (P>0.05) (Table 3, Fig 3-6).

Discussion:

Subacromial bursa injection of steroid is often used for pain relief and function improvement in patients with periarticular shoulder disorders, but there are controversy concerning the number of injection and the dose of steroid. As degenerative changes, metabolic and endocrine related adverse effects are of concern in higher dosage, studies are seeking to replace steroid with others like hyaluronic acid or combine it with drugs regimen.

Hyaluronate is glycosaminoglycan, a main component of synovial and it have significant role in joint lubrication. Bursal injection of hyaluronate in osteoarthritis of knee and shoulder joint is being used as one of the treatment method to substitute steroid to relieve joint pain. Hyaluronate also having an anti-inflammatory effects, improving active range of motion of joints, inhibiting the denaturalization of cartilage and normalizing the abnormal joint fluid.

In our trial, when comparing the measurement values at each stages of follow up, both the groups showed significant fast improvement in VAS, Constant Murley score and active range of motion of shoulder joint up to 12 weeks, thereafter it became gradual but progressive (P>0.05).

The steroid injection given better results from start and was slightly better at six to 12 weeks after the injection than hyaluronic acid. Steroids provide faster relieve in pain than hyaluronic acid in the first six weeks. No statistically significant (P>0.05) improvement was observed at 24 weeks of duration after the injection.

Midorika K et al reported on the effectiveness of the hyaluronate and steroid in patients with shoulder disorder, the therapeutic efficacy of
the hyaluronate was equivalent to the steroid group.

Penning et al reported a study of 159 patients with subacromial impingement, treated with subacromial injection using hyaluronic acid, corticosteroid and placebo (NaCl). Patients were followed up to for 26 weeks. They observed no beneficial results from hyaluronic acid injection compared with corticosteroid or placebo injection. Corticosteroid produced a significant reduction in pain in short term (first three to 12 weeks), but in the long term, the placebo injection produced best results.

In this study, we found a beneficial role of corticosteroid injection in short term, but did not find it to be significant different to the hyaluronic acid at mid or long term. During trial, most adverse effects observed were local and mild and concerned increase in pain after injection. There were no infection or allergic reactions to the drugs.

Both hyaluronic acid and steroid injection demonstrate significant pain relief and improvement in shoulder function within three weeks of first dose that sustained for at least 24 weeks. Both the hyaluronic acid and steroid injections showed near equal effects in shoulder functions.

Hence we conclude that injection hyaluronic acid is safe and effective drug in treatment of subacromial impingement of shoulder and might be useful where steroid related adverse effects needs to be avoided.

| Table 1. Baseline characteristics of subjects |
|---------------------------------------------|
|                                            |
| **Group A** (Hyaluronic acid) | **Group B** (Corticosteroid) | (P – value) |
|---------------------------------|------------------------------|-------------|
| **Male : Female** | 16 : 28 | 19 : 24 | 0.7763 |
| **Mean (SD) age (yrs)** | 44.35 (9.40) | 43.81 (8.34) | |
| **Shoulder affected** | | | |
| Dominant (n,%) | 40 (90.91) | 41 ((3.18) | |
| Non-dominant (n,%) | 4 (9.09) | 3 (6.82) | |
| **Duration of complaint** | | | 0.5689 |
| < 6 weeks | 21 (47.73) | 18 (40.91) | |
| 6 – 12 weeks | 18 (40.91) | 23 (52.27) | |
| >12 weeks | 5 (11.36) | 3 (6.82) | |
| **Mean outcome measures** | | | |
| Visual Analogue Score | 7.89 (0.99) | 7.86 (0.86) | 0.8797 |
| Constant Murley Score | 47.07 (5.29) | 47.21 (4.27) | 0.8917 |
| **Mean (SD) range of movement (°)** | | | |
| Flexion | 103.83 (2.22) | 103.77 (2.32) | 0.9016 |
| Abduction | 91.74 (2.65) | 92.00 (2.73) | 0.6500 |
| External rotation | 31.78 (2.74) | 32.19 (2.86) | 0.4942 |
| Internal rotation | 2.93 (1.06) | 2.93 (0.91) | 0.9999 |

| Table 2. Summary of outcome measures in patients with subacromial impingement and difference in groups by treatment at different times of follow-up |
|---------------------------------------------------------------|
|                                                              |
| **Hyaluronic acid (A)** | **Corticosteroid (B)** | **P - value** |
| Visual Analogue Score | 7.89 (0.99) | 7.86 (0.86) | 0.8797 |
| Week 3 | 5.98 (1.11) | 5.88 (1.10) | 0.6723 |
| Week 6 | 3.61 (1.08) | 3.23 (1.17) | 0.1171 |
| Week 12 | 2.04 (0.94) | 2.23 (0.90) | 0.3365 |
| Week 18 | 1.02 (0.95) | 0.91 (0.65) | 0.5281 |
| Week 24 | 0.13 (0.40) | 0.26 (0.49) | 0.1765 |
| **P - value** | <0.0001 | <0.0001 |
| Constant Murley Score | 47.07 (5.29) | 47.21 (4.27) | 0.8917 |
| Week 3 | 61.59 (5.00) | 62.14 (5.31) | 0.6182 |
| Week 6 | 84.65 (5.60) | 84.44 (5.66) | 0.8615 |
| Week 12 | 90.72 (3.07) | 91.14 (2.96) | 0.5153 |
| Week 18 | 94.26 (2.51) | 94.35 (2.46) | 0.8655 |
| Week 24 | 98.65 (1.16) | 98.70 (1.21) | 0.8436 |
| **P - value** | <0.0001 | <0.0001 |

Values are mean (standard deviation), Fisher exact test applied.
### Table 3. Shoulder movement range (°) and differences by treatment at different time interval.

| Movement range of motion (°) | Hyaluronic acid (A) | Corticosteroid (B) | P - value |
|-----------------------------|---------------------|-------------------|-----------|
| **Flexion**                 |                     |                   |           |
| Baseline                    | 103.83 (2.22)       | 103.77 (2.32)     | 0.9016    |
| Week 3                      | 122.96 (4.17)       | 120.93 (5.44)     | 0.0529    |
| Week 6                      | 134.26 (6.28)       | 134.70 (5.24)     | 0.7221    |
| Week 12                     | 151.00 (5.33)       | 151.40 (5.93)     | 0.7401    |
| Week 18                     | 159.48 (2.55)       | 159.77 (2.01)     | 0.5552    |
| Week 24                     | 160.22 (2.65)       | 160.65 (1.62)     | 0.3615    |
| P - value                   | <0.0001             | <0.0001           |           |
| **Abduction**               |                     |                   |           |
| Baseline                    | 91.74 (2.65)        | 92.00 (2.73)      | 0.6500    |
| Week 3                      | 126.46 (10.06)      | 125.86 (8.99)     | 0.7671    |
| Week 6                      | 145.87 (6.89)       | 144.19 (7.24)     | 0.2659    |
| Week 12                     | 161.09 (4.98)       | 161.58 (5.01)     | 0.6449    |
| Week 18                     | 171.70 (4.38)       | 171.95 (4.65)     | 0.6449    |
| Week 24                     | 176.83 (1.87)       | 177.67 (2.00)     | 0.0441    |
| P - value                   | <0.0001             | <0.0001           |           |
| **External rotation**       |                     |                   |           |
| Baseline                    | 31.78 (2.74)        | 32.19 (2.86)      | 0.4942    |
| Week 3                      | 41.00 (5.19)        | 40.70 (5.16)      | 0.7863    |
| Week 6                      | 50.30 (3.48)        | 50.09 (3.90)      | 0.7905    |
| Week 12                     | 60.00 (2.27)        | 60.00 (2.89)      | 0.9990    |
| Week 18                     | 64.13 (2.47)        | 63.95 (3.01)      | 0.7599    |
| Week 24                     | 67.57 (1.06)        | 67.91 (1.80)      | 0.2840    |
| P - value                   | <0.0001             | <0.0001           |           |
| **Internal rotation**       |                     |                   |           |
| Baseline                    | 2.93 (1.06)         | 2.93 (0.91)       | 0.9999    |
| Week 3                      | 7.43 (1.05)         | 7.65 (1.04)       | 0.3262    |
| Week 6                      | 10.00 (1.01)        | 10.14 (0.97)      | 0.5909    |
| Week 12                     | 12.33 (1.03)        | 12.23 (1.07)      | 0.6563    |
| Week 18                     | 14.15 (0.84)        | 14.26 (0.88)      | 0.5502    |
| Week 24                     | 14.93 (0.95)        | 14.88 (1.03)      | 0.8135    |
| P - value                   | <0.0001             | <0.0001           |           |

Values are mean (standard deviation), Fisher exact test applied.

### References:

1. Picavet, H.S. & Schouten, J.S. 2003. “Musculoskeletal pain in the Netherlands: prevalences, consequences and risk groups, the DMC(3) study”. Pain, vol.102, no.1-2, pp.167-178
2. van der Windt, D.A., Koes, B.W., de Jong, B.A. & Bouter, L.M. 1995. “Shoulder disorders in general practice: incidence, patient characteristics, and management”. Annals of the Rheumatic Diseases, vol.54, no.12, pp.959-964.
3. Blair B, Rokito AS, Cuomo F, Jarolem K, Zuckerman JD. Efficacy of injections of corticosteroids for subacromial impingement syndrome. J Bone Joint Surg Am 1996; 78: 1685-1689
4. Darlington LG, Coomes EN. The effects of local steroid injection for supraspinatus tears. Rheumatol Rehabil 1977; 16: 172-179
5. White RH, Paul DM, Fleming KW. Rotator cuff tendinitis: comparison of subacromial injection of a long acting corticosteroid versus oral indomethacin therapy. J Rheumatol 1986; 13: 608-613
6. Crawshaw DP, Hellwell PS, Hensor EM, et al. Exercise therapy after corticosteroid injection for moderate to severe shoulder pain: large pragmatic randomised trial. BMJ 2010;340:3037
7. Kirkley A, Litchfield R, Alvarez C, Herbert S, Griffin S. Prospective double blind randomized clinical trial of subacromial injection of betamethasone and xylocaine versus xylocaine alone in rotator cuff tendinitis. J Bone Joint Surg [Br] 1999;81-B(Supp 1):107.
8. Gruson KI, Ruchelsman DE, Zuckerman JD. Subacromial corticosteroid injections. J Shoulder Elbow Surg 2008;17(Suppl):118–130.
9. Alvarez CM, Litchfield R, Jackowski D, Griffin S, Kirkley A. A prospective, double-blind, randomized clinical trial comparing subacromial injection of betamethasone and xylocaine to xylocaine alone in chronic rotator cuff tendinitis. Am J Sports Med 2005;33:255–262.
10. Winters JC, Van der Windt DAWM, Spinnewijn WEM, et al. NHG-Standaard Schouderklachten (Tweede herziening). Huisarts Wet 2008;51:555–565.
11. Shibata Y, Midorikawa K, Emoto G, Naito M. Clinical evaluation of sodium hyaluronate for the treatment of patients with rotator cuff tear. J Shoulder Elbow Surg 2001;10:209–216.
12. Itokazu M, Matsunaga T. Clinical evaluation of high-molecular-weight sodium hyaluronate for the treatment of patients with periarthritis of the shoulder. Clin Ther 1995;17:946–955.
13. Funk L. Hyaluronan vs. steroid
injections for subacromial impingement of the shoulder. Osteoarthritis Cartilage 2005;13(Suppl A):S80.

14. Chou WY, Ko JY, Wang FS, et al. Effect of sodium hyaluronate treatment on rotator cuff lesions without complete tears: a randomized, double-blind, placebo-controlled study. J Shoulder Elbow Surg 2010;19:557–563.

15. Iwata H. Pharmacologic and clinical aspects of intraarticular injection of hyaluronate. Clin Orthop Relat Res 1993;289:285–291.

16. Kuiper-Geertsma DG, Bijlsma JW. Intra-articular injection of hyaluronic acid as an alternative option to corticosteroid injections for arthrosis. Ned Tijdschr Geenekd 2000;144:2188–2192 (in Dutch).

17. Cho KH, Gee SJ, Lee HJ, Hwang SH. Comparison of blind technique and ultrasonography guided technique of subacromial subdeltoid bursa injection. J Korean Acad Rehab Med 2010; 34: 209-213

18. Tillander B, Franzen LE, Karlsson MH, Norlin R. Effect of steroid injections on the rotator cuff: an experimental study in rats. J Shoulder Elbow Surg 1999; 8: 271-274

19. Akpinar S, Hersekli MA, Demirors H, Tandogan RN, Kayasecuk F. Effects of methylprednisolone and betamethasone injections on the rotator cuff: an experimental study in rats. Adv Ther 2002; 19: 194-201

20. Yoon SH, Kwack KS, Rah UW, Cho KH. Ultra sonography-guided subacromial bursal injection of corticosteroid: a comparative study of two dose regimens. J Korean Acad Rehab Med 2009; 33: 402-407

21. Byun SD, Park DH, Jo DH, Choi WD, Lee ZI. Effect of three consecutive steroid injection on blood glucose and cortisol level in diabetic patients with hemiplegic shoulder pain. Clin Pain 2010;9:82-9.

22. van Den Ende CH, Rozing PM, Dijkmans BA, Verhof JA, Voogt-van der Harst EM, Hazes JM. Assessment of shoulder function in rheumatoid arthritis. J Rheumatol 1996;23:2043-8.

23. Kim C, Park YB, Youn JE, Kim DY. Treatment of adhesive capsulitis with steroid injection followed by hyaluronic acid injection. J Korean Acad Rehabil Med 2010;34:310-5.

24. Yoshimi T, Kikuchi T, Obara T, Yamaguchi T, Sakakibara Y, Itoh H, Iwata H, Miura T. Effects of high-molecular-weight sodium hyaluronate on experimental osteoarthrosis induced by the resection of rabbit anterior cruciate ligament. Clin Orthop Relat Res 1994; 298: 296-304.

25. Leardini G, Perbellini A, Franceschini M, Mattara L. Intra-articular injections of hyaluronic acid in the treatment of painful shoulder. Clin Ther 1988; 10: 521-526.

26. Rosier RN, Okeef RJ. Hyaluronic acid therapy. Instr Course Lect 2000; 49: 495-502.

27. Tamai K, Mashitori H, Ohno W, Hamada J, Sakai H, Saotome K. Synovial response to intraarticular injections of hyaluronate in frozen shoulder: a quantitative assessment with dynamic magnetic resonance imaging. J Orthop Sci 2004; 9: 230-234.

28. Midorikawa Ket al. Clinical evaluation of sodium hyaluronate for the treatment of patients with rotator cuff tear. J shoulder elbow surg 2001;10:209-216.

29. Penning LIF, de Bie RA, Walenkamp GHIM. The effectiveness of injections of hyaluronic acid in patients with subacromial impingement. J Bone Joint Surg Br 2012;94-B:1246–52.