ORIGINAL ARTICLE

# EFFICACY OF A SINGLE-INJECTION SODIUM HYALURONATE TREATMENT IN LATERAL EPICONDYLITIS

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**Background:** Lateral epicondylitis or tennis elbow is a disease of tendons arising from common extensor origin at the lateral epicondyle of elbow and is commonly characterized by pain on supination of forearms as well as extension of fingers and wrists. **Methods:** This descriptive case series aims to determine the efficacy of a single-injection sodium hyaluronate treatment for lateral epicondylitis. The study was conducted at the Department of Orthopaedics. Ayub Teaching Hospital Abbottabad. From February 1 to August 31, 2014. Patients diagnosed with lateral epicondylitis were administered 1 cc of 1% Sodium hyaluronate 1 cm from the lateral epicondyle into the soft tissue. **Results:** Hyaluronic acid is more effective in patients with moderate pain of lateral epicondylitis (VAS score ≤7 than in patients with severe pain (VAS score >7). Paired sample *t*-test was used to compared the means of the pre- and post-procedure VAS score and the difference was found to be statistically very significant ($p$=0.00) with a mean±SD change in VAS of 2.31±1.35 at 4 weeks. **Conclusion:** A single injection of sodium hyaluronate is effective in management of moderate, but not severe pain of lateral epicondylitis.

**Keywords:** Elbow; Lateral epicondylitis; Pain; Sodium hyaluronate; Tennis; Corticosteroids

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## INTRODUCTION

The origin of common extensor tendons at the lateral epicondyle of elbow is frequently affected in lateral epicondylitis or tennis elbow.[1] Other terms that have also been used in literature for this condition include lateral elbow pain, tendonitis of common extensor origin, peritendinitis of the elbow and rowing elbow.[2] The most common presenting complaint by patients is a pain on wrist and finger extension and on supination of forearm. The annual incidence of lateral epicondylitis is 4–7 cases per 1000 patients, and it is mostly present in patients in the age bracket of 35–55 years.[3] The annual incidence of lateral epicondylitis is 1–3%.[4] Interestingly, a very small proportion of patients (5–8%) with lateral epicondylitis have ever played tennis, as much as half of all tennis players are known to have suffered from lateral epicondylitis at any point in their life.[4] The symptoms resolve in 6–24 months in many cases[1], although it can persist for more than a year in about 20% of the cases[3].

On clinical examination, there is usually a normal range of motion at the elbow joint, tenderness at the lateral epicondyle and pain on resisted movements (resisted third finger extension in particular).[1] The origin of extensor carpi radialis brevis is most commonly involved, however, the tendons of extensor carpi radialis longus and extensor digitorum communis are also known to have been affected in lateral epicondylitis.[5] It has been suggested that the alternating repetitive movements at the elbow play a major role in creating stress on the origin of extensor muscles.[1] Typically lateral epicondylitis affects people who become active after living a prolonged sedentary life and become involved in activities such as exercising at the gym, gardening, painting a room, lifting a new baby, or even just carry heavy luggage on a holiday.[1,3] Time spent in excess of 20 hours per week working at a computer increases the risk of lateral epicondylitis.[3] A number of treatment options for lateral epicondylitis have been explored with variable results: topical and oral non-steroidal anti-inflammatory drugs (NSAIDs) for short-term pain relief,[4] Corticosteroids alone[2] as well as in combination with the topical and oral NSAIDs[6,7]. Hyaluronic acid is a naturally occurring biologic compound which has been found to have a positive effect after intra articular administration for osteoarthritis.[8,9] The intra-articular administration of hyaluronic acid has resulted in reduction of pain and improvement of functional range, improvement in the soft tissue injury with high degree of patient satisfaction and few adverse events.[8,9] Hyaluronic acid may be useful in the long-term management of bursitis but as an adjuvant therapy and ankle sprain.[10,11] Hyaluronic acid serves to maintain their viscoelastic structural and functional characteristics of synovial cartilage and its surrounding structures.

Currently there are no local studies that have prospectively followed patients who were administered Hyaluronic Acid for the treatment of lateral epicondylitis. This study was designed hypothesizing

that administration of Hyaluronic acid for lateral epicondylitis will be well-tolerated in the soft tissues of elbow with comparatively fewer side effects.

## MATERIAL AND METHODS

The descriptive case series was conducted at department of orthopaedics, Ayub Teaching Hospital, Abbottabad from from February 1 to August 31, 2014 with an aim to evaluate the efficacy of peri articular sodium hyaluronate injection in lateral epicondylitis. For the purpose of this research, lateral epicondylitis was defined as "tenderness over lateral epicondyle about 5 mm distal and anterior to the condyle. There is pain which increases with resisted dorsiflexion of wrist and supination of forearm and is also present on grasping objects".[2] The efficacy of hyaluronic acid was determined in terms of clinical pain reduction as described by the patients and as measured by the Visual Analogue Scale (VAS) before and after resisted wrist dorsiflexion after peri articular sodium hyaluronate injections. Efficacy was determined in terms of VAS $\leq 3$ from the pre-procedure VAS score.[12] A total of forty-five patients with lateral epicondylitis were enrolled into the study. The sample size was determined 3% prevalence of lateral epicondylitis in general population[4], 95% confidence interval and 0.05% absolute precision using WHO sample size calculations. Consecutive non-probability sampling technique was used and patients of either gender aged 35–60 years diagnosed as having tennis elbow or lateral epicondylitis for at least 3 weeks and with a baseline VAS value at least 7 were included in the study. At the same time, patients with fracture or dislocation of the same upper limb, who needed to take NSAIDs regularly for some medical reason (except patients taking Aspirin 75 mg OD for cardiovascular prophylaxis), patients regularly taking corticosteroids for any medical reasons, patients treated for elbow pain during the past 6 months, bilateral elbow involvement, cervical radiculopathy and peripheral nerve disease were excluded from the study. The above-mentioned conditions could act as confounders and if included were likely to introduce bias in the study results. The study was conducted after approval from hospitals ethical and research committee. All patients meeting the inclusion criteria were included in the study through the OPD of orthopaedic department. The procedure was explained to patients and an informed written consent was obtained before enrolling the patients into this study. Treatment course consisted of 2 injections (first one at baseline and a second one at day 7) of sodium hyaluronate which were injected as 1cc of 1% sodium hyaluronate taken from a 5-cc vial. Injection were administered using a sterile disposable syringe affixed to a 27 gauge, 1-inch needle. Skin was prepared using Povidone Iodine solution. Injections were administered using a standard approach along the lateral epicondyle with the affected arm flexed and resting on a firm surface. Injections were administered into the soft tissue 1 cm from the lateral epicondyle at the point of greatest pain in two planes using a fanning technique whereby contents were injected on withdrawal of the needle from the point of maximal tenderness in a single puncture. All patients were subjected to radiographic examination to exclude other pathologies at the discretion of the study physician (i.e., to exclude fracture). Assessment of patients included general demographics, co-morbidities and previous treatment. Patients were asked to rate their pain on a 10 cm Visual Analogue Scale, with 0 representing no pain and 10 representing maximal pain at rest and after a resisted dorsiflexion at wrist joint. Follow-up examination was completed at Day 28. Patients were again asked to assess pain on the VAS at rest and after resisted dorsiflexion at wrist joint. During the study, including the follow up period, the patients were not allowed to use any topical analgesics, NSAIDs or corticosteroids. However, Aspirin in a dose of 75 mg per day for cardiovascular prophylaxis was allowed in patients who were already be taking it. The response of the patients was recorded duly on a pre-designed *pro forma*. All the data was collected on the predesignated *pro forma* and analysed in SPSS version 21. Mean±SD were calculated for numerical variables like age. Frequencies and percentages were calculated for categorical variables like gender and VAS responses. Efficacy was stratified among age, gender and baseline grade of pain as recorded on VAS to see the effect modifications. $p$ value less than 0.05 was taken as significant. Additionally, independent sample $t$-test as well as paired sample $t$-test were also employed to determine significance of difference in the VAS score.

## RESULTS

The study was conducted at the Department of Orthopaedics, Ayub Teaching Hospital, Abbottabad. Forty-five patients were included in the study after an informed consent was obtained from them. Of these 45 patients, 27 (60%) were males and 18 (40%) were females (Table-1). Age of the patients ranged from 37–60 (48.60±7.13) years (Table-2). The baseline VAS score ranged from 7–10 (8.73±1.07) while the post procedure VAS score ranged 5–8 (6.42±1.06) (Table-2). A base line visual analogue score of a minimum 7 was required for inclusion in the study. A total of 7 (15.6%) patients had a baseline VAS score of 7. 12 (26.7%) patients had a baseline score of 8, and another 12 (26.7%) patients had a baseline VAS of 9. 14 (31.1%) patients assessed their baseline VAS to be 10 (Table-3). After injection of Sodium Hyaluronate, 11 (24.4%) patients assessed their pain on the VAS as 5. 12 (26.7%) patients assessed their pain score to be 6. 14 (31.1%) patients reported the pain score to be 7 and 8 (17.8%)

patients reported a VAS score of 8 (Table-4). The post-procedure VAS score was stratified according to gender, age and baseline score to see effect modification (Tables 6–8). When the efficacy of hyaluronic acid was stratified according to the age of patients a *p*-value of 0.094 was obtained rendering this result as non-significant (Table-6). Similarly, *p*-values for stratification of efficacy of hyaluronic acid administration with gender and pain severity as determined on baseline VAS score were 0.81 and 0.011 respectively (Table-7 and 8). Hyaluronic acid appeared to be more effective in patients with moderate pain of lateral epicondylitis (VAS score ≤7 than in patients with severe pain (VAS score >7) (Table-8). Paired sample *t*-test was used to compared the means of the pre- and post-procedure VAS score and the difference was found to be statistically very significant ($p$=0.00) with a mean±SD change in VAS of 2.31±1.35 at 4 weeks after injection of hyaluronic acid (Table-9). The independent sample *t*-test was applied to compare the means between the two sexes and among different age groups. It was observed that there was a significant difference between male and female study participants in terms of baseline intensity of pain measured on VAS score ($p$-0.018) (Table-10). This difference, however, disappeared after treatment with hyaluronic acid injections. There was no statistically significant difference between the age groups.

**Table-1: Sex of study participants**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | Male | 27 | 60.0 |
| | Female | 18 | 40.0 |
| | Total | 45 | 100.0 |

**Table-2: Descriptive statistics of study population**

| Variable | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|
| Age of patients | 48.60 | 7.13 | 37.00 | 60.00 |
| Baseline VAS at rest | 8.73 | 1.07 | 7.00 | 10.00 |
| Post procedure VAS | 6.42 | 1.06 | 5.00 | 8.00 |

**Table-3: Baseline score of patients on the Visual Analogue Scale**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | 7 | 7 | 15.6 |
| | 8 | 12 | 26.7 |
| | 9 | 12 | 26.7 |
| | 10 | 14 | 31.1 |
| | Total | 45 | 100.0 |
| | | | |

**Table-4: Visual analogue scale score recorded after injection of sodium hyaluronate**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | 5 | 11 | 24.4 |
| | 6 | 12 | 26.7 |
| | 7 | 14 | 31.1 |
| | 8 | 8 | 17.8 |
| | Total | 45 | 100.0 |

**Table-5: VAS groups according to the pre-procedure VAS score**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | Moderate pain | 23 | 51.1 |
| | Severe Pain | 22 | 48.9 |
| | Total | 45 | 100.0 |

**Table-6: cross-tabulation of efficacy of hyaluronic acid with the age of study population.**

| Age of patients | Efficacy of hyaluronic acid | | Total | *p*- value |
|---|---|---|---|---|
| | Yes | No | | |
| upto 48 | 7.00 | 14.00 | 21.00 | 0.094 |

**Table-7: cross tabulation of efficacy with the sex of patients**

| Sex of patients | Efficacy of hyaluronic acid | | Total | *p*-value |
|---|---|---|---|---|
| | Yes | No | | |
| Female | 8.00 | 10.00 | 18.00 | 0.81 |
| Male | 13.00 | 14.00 | 27.00 | |
| Total | 21.00 | 24.00 | 45.00 | |

*p* value <0.05

**Table-8: Cross tabulation of efficacy with pain severity in study population**

| Pain Severity | Efficacy of hyaluronic acid | | Total | *p*-value |
|---|---|---|---|---|
| | Yes | No | | |
| Moderate pain | 15.00 | 8.00 | 23.00 | 0.011 |
| Severe Pain | 6.00 | 16.00 | 22.00 | |
| Total | 21.00 | 24.00 | 45.00 | |

*p* value <0.05

**Table-9: Paired sample-test**

| | Paired Differences | | | | | t | df | Sig. (2-tailed) |
|---|---|---|---|---|---|---|---|---|
| | | | | 95% Confidence interval of the difference | | | | |
| Pair 1 | Mean | SD | Std. Error Mean | Lower | Upper | | | |
| Baseline VAS at rest - Post procedure VAS | 2.31 | 1.35 | .20 | 1.91 | 2.72 | 11.52 | 44 | .000 |

**Table-10: Independent Sample t-test comparing the means of VAS scores with respect to age of study participants**

| | | Levene's test for equality of variances | | t-test for equality of means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| Baseline VAS at rest | Equal variances assumed | .27 | .604 | -.66 | 43.00 | .511 | -.21 | .32 | -.87 | .44 |
| | Equal variances not assumed | | | -.67 | 42.94 | .508 | -.21 | .32 | -.86 | .43 |
| Post procedure VAS | Equal variances assumed | 4.49 | .040 | 1.18 | 43.00 | .246 | .37 | .31 | -.26 | 1.00 |
| | Equal variances not assumed | | | 1.15 | 36.64 | .256 | .37 | .32 | -.28 | 1.02 |

**Table-11: Independent sample t test comparing the mean of VAS score with respect to the sex of study population**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| Baseline VAS at rest | Equal variances assumed | .00 | .958 | -2.45 | 43.00 | .018 | -.76 | .31 | -1.38 | -.13 |
| | Equal variances not assumed | | | -2.45 | 36.60 | .019 | -.76 | .31 | -1.39 | -.13 |
| Post procedure VAS | Equal variances assumed | 1.21 | .277 | -.46 | 43.00 | .650 | -.15 | .32 | -.80 | .51 |
| | Equal variances not assumed | | | -.47 | 40.03 | .640 | -.15 | .31 | -.78 | .49 |

## DISCUSSION

The aetiology of tennis elbow remains unidentified despite it being a common clinical disorder. However, it is commonly believed that it results from a "repetitive over-use" of tendons leading to development of microscopic tears and an increasing degeneration of the tendon due to imperfect repair process.[13] It has been suggested that the degeneration of tendons is due both to auto-phagy and apoptosis.[14] Another theory proposes a combination of factors such as an altered threshold for pain, changed neuro-muscular function and pathology involving tendon itself.[15]

Hyaluronic acid is known to significantly affect a number of process such as development, healing of wounds and regenerative processes in addition to possessing anti-inflammatory characteristics and a possible role in restoration of normal function of injured tissues.[16,17] Hyaluronic acid increases the recruitment of progenitor cells and prevents premature fusion of myotubes during the repair process.[18]

Currently, there is a lack of consensus on the management of lateral epicondylitis. Various therapies with systemic or local targets for intervention have been studied.

A search for related literature on www.pakmedinet.com using the terms "tennis elbow" and "lateral epicondylitis" yielded no local studies that could have determined the role of sodium hyluronate in the management of lateral epicondylitis.

A recent study by Kumai and colleagues reported that Hyaluronic acid was effective in bringing about symptomatic improvement in patients with enthesopathies such as lateral epicondylitis, patellar tendinopathy, Achilles tendinopathy and plantar fasciitis. [19] The authors reported that the mean±SD change in VAS score for lateral epicondylitis after an injection of sodium hyaluronate was −2.55±2.43. The authors followed up the patients one week following the injection.[19] On the other hand, the follow-up period in our study was 4 weeks following a single injection of sodium hyaluronic acid.

In a single-site palcebo-controlled trial which was published fairly recently, it was demonstrated that a single injection of sodium-hyaluronate was superior to placebo in bringing about improvement in pain of lateral epicondylitis at rest and after grip testing.[20] The patients were followed up at one and three months and it was noted on inter-group comparison that there were significant differences in favour of SH group at 30 and 90 days ($p$<0.05).[20]

A recent study by Petrella *et al.* reported that hyaluronic acid was significantly better than control in improving pain at rest and after maximal grip testing in patients with lateral epicondylitis when administered in peri-articular manner. They also noted that treatment with HA produced a higher degree of satisfaction by the patients and physicians alike and it resulted in a better return to pain-free activities than the control group.[4]

A recently published meta-analysis that compared the reported efficacy of a number of injection therapies for lateral epicondylitis reported that hyaluronic acid injection might be more effective than other injection therapies such as autologous blood injection , platelet rich plasma, injection of botulinum toxin and the placebo.[21] There are promising reports about the efficacy of Hyaluronic acid in the symptomatic management of lateral epicondylitis, this study was found that hyaluronic acid was effective symptomatic management of lateral epicondylitis. However, large randomized studies are needed for establishing a definitive role for hyaluronic acid in the symptomatic management of lateral epicondylitis.

**Study limitations:**

This was a small hospital based study and included only those patients with lateral epicondylitis who

presented to the out-patient department or our unit for consultation. The sample size was small and therefore the results cannot be generalized to a larger population. No effort was done to compare hyaluronic acid with other treatment modalities or placebo in the management of lateral epicondylitis was done and no effort was made to stratify patients according to the duration of symptoms and to see effect modification according to duration of symptoms after administration of hyaluronic acid.

## CONCLUSION

A single injection of Sodium hyaluronate can effectively ameliorate moderate pain of lateral epicondylitis

## AUTHORS' CONTRIBUTION

IUK, ASA: Conceived the idea, data collection, write-up. ASK, IM: write-up, data analysis. MATERIAL AND METHODS: Data collection, literature search, write-up.

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