Power Doppler Sonography and Clinical Monitoring for Hyaluronic Acid Treatment of Rhizarthrosis: A Pilot Study

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Abstract Trapeziometacarpal (TMC) joint osteoarthritis (OA) is a common disabling condition in which the impact of visco-supplementation has to be ascertained. We aim to evaluate the efficacy of high molecular weight hyaluronic acid (HA) ultrasound (US)-guided intra-articular injection of TMC joints in OA. 32 TMC joints of 16 patients with symptomatic thumb base OA were treated with three injections of high molecular weight HA at 1-week intervals. Before injection, at week 0, 1, 2, and 24 all patients underwent clinical and US examination. A significant clinical improvement was obtained by the decrease in visual analog scale for pain after 2 weeks of treatment ($p=0.0003$) and this result is maintained at week 24 ($p=0.009$). The Dreiser's index also decreased after week 2 and remain stable after 6 months. Power Doppler signal significantly decreased after 2 weeks of treatment ($p=0.02$), even if this result was not maintained at week 24. No significant decrease in the synovial hypertrophy score was observed during the study. Our preliminary study suggests that US-guided TMC injections by high molecular weight HA may be effective in decreasing local inflammation and pain.

Keywords Rhizarthrosis · Hyaluronic acid · Ultrasonography

Introduction

Trapeziometacarpal (TMC) joint osteoarthritis (OA) is a common disabling condition presenting with pain at the base of the thumb, instability, deformity, and impairment of hand function. The disability is caused predominantly by local pain in the early stages of the disease, and by restricted movements of the thumb in the late stages [1].

Hyaluronic acid (HA) is responsible for the viscoelastic component of synovial fluid, because it is an effective lubricant, shock absorber, and fluid retainer [2]. Moreover, HA is not only a relevant component of normal synovial fluid of the diarthrodial joints, but also its decrease has a crucial role in the OA process [2].

Based on these findings, injection of HA in the TMC joints should be considered a possible treatment options, both because of its pivotal role in the homeostasis of joints and because its replacement in OA restores rheological properties of the synovial fluid and improves symptoms. Nevertheless, a few studies have been designed to ascertain the impact of visco-supplementation for the treatment of TMC joint OA [3–9].

It has been shown that Hyalubrix®, a sterile non-pyrogenic viscoelastic solution of HA sodium salt obtained by bacterial fermentation with a molecular-weight of 3,200 kDa, reduces joint friction, improves joint function, restores viscoelasticity of the synovial fluid, and also relieves pain on movement in knee and hip OA [10].

With this as background, we prospectively investigate the short term effects of biological viscosupplementation of TMC joints with high-weight HA, using clinical and ultrasonography (US) variables to ascertain the impact of this treatment in patients with OA of the thumb base.

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Methods

The study involved 32 TMC joints of 16 consecutive patients between January and June 2009, all of whom fulfilled the ACR (American College of Rheumatology) hand OA classification criteria [11].

The subjects were considered eligible for inclusion in the study if they had been diagnosed as having symptomatic thumb base OA, which was defined using both radiographic criteria on the hand radiographs (i.e. grade 3 or 4 by Kellgren-Lawrence) [12, 13] and clinical criteria (i.e. visual analogue scale—VAS—for pain score ≥ 40 mm). The study was approved by the local review board and informed consent was obtained from all patients.

Furthermore, all patients had failed prior treatment with NSAIDs, physical therapy, and splinting. Patients were free of any joint injection in the last 6 months and free of any pain medication in the last 1 week. Patients with major trauma history to the hand, wrist, and elbow were also excluded. Other exclusion criteria included pregnancy, prior surgery on the thumb or wrist, history of infection in the affected joint, history of inflammatory arthritis, coagulation disorders, skin disease or eruption at the joint injection site and history of adverse reaction to HA.

All the TMC joints were treated with three US-guided intra-articular injections of high molecular weight HA (Hyalubrix®, Fidia 0.5 ml) at 1-week intervals. Hyalubrix® was instilled after visualization of the needle tip within the joint.

US-guided injections were performed with a GE LOGIQ 9 unit (General Electric Medical Systems; Milwaukee, Wisconsin, USA) using a high-frequency 9–14 MHz linear array transducer. The setting for grey-scale US was 14 MHz and the pulse repetition frequency for the power Doppler signal (PDS) was set at 500 Hz.

All subjects during the same consultation, were referred to one physician who collected at baseline (week 0), after 2 and 24 weeks the following data: 1) VAS for pain; 2) hand function with Dreiser's index for the OA of the hand [14]; and 3) US examination assessing TMC joints for synovial hypertrophy and PDS, scored from 0 to 3 according to the preliminary scoring tool for hand OA [15].

Statistical Analysis

The descriptive statistics are reported as median and interquartile range (25th and 75th percentiles). Statistical analysis was performed by non-parametric tests for paired samples when the effect of treatment was assessed (Wilcoxon). Significance level was set at $P < 0.05$. Data were analyzed using the GraphPad Prism version 4.00 (GraphPad Software, San Diego California USA).

Results

This study involved 16 subjects (15 women and 1 man), with a median age of 62.46 years (range 43.5 to 79.4 years) with symptomatic TMC joint OA.

As shown in Fig. 1, a significant clinical improvement was obtained by the decrease in VAS pain after 2 weeks of Hyalubrix® treatment ($p=0.0003$) and this result is maintained at week 24 ($p=0.009$). In fact, at baseline, VAS pain was higher, median 68.8 mm (interquartile range 50.5–80.0 mm), than after 2 and 24 weeks (median 40 mm, 20–68 mm and 55 mm, 45–70 mm respectively). The Dreiser's index also decreased from 9.0 (5.5–11.5) at baseline to 8.0 (4.0–9.0) at week 2; after 6 months, the median of Dreiser's index remain stable at 8.0 (5.0–9.0), but these differences did not reach statistical significance.

In our study, both hands of all the patients were treated with three US-guided intra-articular injections of Hyalubrix® at 1-week intervals. No adverse events occurred in our study.

In this study US examination analysing inflammatory parameters (i.e. synovial hypertrophy and PDS) of the TMC joints was performed in all the subjects, at baseline and during the follow-up period was performed. Interestingly, PDS significantly decreased after 2 weeks of treatment (median value from at baseline 0.5 to 0.0; $p=0.02$) (Fig. 2), even though this result was not maintained at week 24 (median 0.5). No significant decrease in the synovial hypertrophy score was observed during the study.

Discussion

Our preliminary study suggests the potential role of high molecular weight HA in decreasing local inflammation and pain of rizoarthrosis. This pilot open-label study involved a

Fig. 1 Box plot of the distribution of the visual analogue scale for pain at baseline and after 2 and 24 weeks of Hyalubrix® treatment

Fig. 2 Ultrasound longitudinal images of the left trapeziometacarpal joint of a patient with osteoarthritis of the thumb base. At baseline (**a**), anechoic fluid and power Doppler signal (*arrow*) were present, whereas these findings decreased after 2 weeks of treatment (**b**)

group of patients that reflects the common pattern of patients with TMC joint OA because most of the patients were women of postmenopausal age [1].

A significant clinical improvement was obtained by the decrease in VAS pain after 2 weeks of Hyalubrix® treatment and this result is maintained at week 24; such a result may be influenced by the ultrasound guidance injection. The exact mechanism through which intra-articular HA promotes pain relief is not clearly understood, although the upregulation of cartilage synthesis as well as the inhibition of inflammatory cytokines have been proposed [2].

Although previous studies differed either in the hyaluronan preparation (i.e. different molecular weight of HA and therefore, different regimen of intra-articular injections), or in the methodology, all the reports described a similar trend of improvement in pain relief after treatment [3–9]. Particularly, to date, there are only three randomized

clinical trials (RCTs) that have focus on use of HA for rhizarthrosis. These studies differences for several aspects such as: a) the use of different molecular weight HA; b) the different regimen of injections (i.e. one, two or three injections at weekly intervals); c) the presence of a placebo group (two of these have no placebo arm). On the other hand, all the RCTs have a control group treated with corticosteroid injections and showed a similar pain relief between steroid and HA [5, 6, 9].

Previous studies on the intra-articular injection of the TMC joint showed that the accuracy rate of the non-guided injection ranged between 58% and 91% [15]. Based on these findings and because an accurate needle placement is necessary for therapeutic injections, we performed US-guided injections. US provides an alternative means of ensuring accurate needle placement and has several noteworthy advantages because it has no contraindications, produces no radiation exposure to the patient or operator and does not require contrast.

It has been shown that sonographic needle guidance improves the performance, clinical outcomes, and cost-effectiveness of intraarticular injection [16, 17]. Therefore, because US-guided intra-articular HA injections are easily administered, safe and well tolerate, may be considered as an effective treatment option in the short-term.

To the best of our knowledge, this is the first study in which US examination analysing inflammatory parameters (i.e. synovial hypertrophy and PDS) of the TMC joints was performed in all the subjects, at baseline and during the follow-up period.

Although several complications have been reported after intra-articular HA injection for treatment of knee OA [18], such as pseudoseptic reactions or acute gouty attacks, no such reactions have yet been reported with use of HA in the thumb [18]. According to these previous findings, no adverse events occurred in our study. Even if the use of intra-articular HA displays some disadvantages, such as the need of multiple injections and higher cost than steroids, its use does not induce increase in blood glycemia, ligament or capsule weakening or cutaneous side effects. Moreover, the higher cost of HA treatment may be offset by the lower frequency of side effects [18].

Because a pilot study is burdened by major limitations, such as the inclusion of a relatively small number of patients, the lack of a control group and random allocation, the results have to be interpreted with caution.

Our preliminary study suggests that, in the short-term period, US-guided injections for thumb base OA by high molecular weight HA are effective in decreasing local inflammation and pain.

Disclosure statement None of authors have any conflict of interest with the subject matter or materials discussed in the manuscript.

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