Periarticular Hyaluronic Acid in Acute Ankle Sprain

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Objectives: To determine the efficacy and safety of periarticular hyaluronic acid injections in acute lateral ankle sprain during 9 months at a sports injuries center.

Design: Randomized controlled prospective trial.

Setting: Primary sport medicine and emergency practice.

Patients: One hundred fifty-eight consecutive competitive athletes who suffered acute grade 1 or 2 lateral ankle sprains were randomized within 48 hours of injury.

Interventions: Patients were randomized at baseline to periarticular injection with hyaluronic acid (HA) + standard of care [rest, ice, compression, and elevation (RICE)] or placebo injection (PL) + standard of care (RICE) treatment at baseline assessment and on day 4 after injury.

Outcomes Measures: Assessments at baseline and days 4, 8, 30, and 90 included Visual Analogue Scale (VAS; 0–10 cm) pain on weight bearing and walking 20 m, patient global assessment of ankle injury (five-point categorical scale), patient satisfaction with treatment (five-point categorical scale), time to return to pain-free and disability-free sport, and adverse events. Differences between groups were determined using an intent-to-treat analysis of variance.

Results: About 30% of the ankle sprains were "first" events, and no differences in clinical assessments with those presenting but not volunteering for the study (n = 341) were observed. Time to intervention was 39 ± 4 hours, with no difference between groups. No serious adverse events were recorded during the 8-day treatment period. No difference in concomitant treatment or physical therapy was observed between groups. A significant reduction in VAS pain on both weight bearing and walking was observed at day 8 for HA compared with PL ($P < 0.05$). Significantly greater patient satisfaction was observed for HA versus PL at days 4 ($P < 0.05$), 8 ($P < 0.001$), 30 ($P < 0.001$), and 90 ($P < 0.05$). Patient global assessment of ankle injury was significantly better compared with baseline in the HA group at day 8, but this was not different between groups. Time to pain-free and disability-free return to sport was 11 (± 8) versus 17 (± 8) days for HA and PL, respectively ($P < 0.05$).

Conclusion: HA treatment for acute ankle sprain was highly satisfactory in the short term and the long term versus PL. This was associated with reduced pain and more rapid return to sport, with few associated adverse events.

Key Words: ankle sprain, hyaluronic acid

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INTRODUCTION

Ankle sprains are among the most common of all sports injuries, with approximately 2 million people per year seeking medical treatment.[1–3] An epidemiological study of professional, competitive, and recreational athletes found a prevalence of ankle sprain as high as 73%[4] or a crude incidence rate of at least 52.7 per 10,000.[5] Data from the National Hospital Ambulatory Medical Care Survey: 2000 emergency department (ED) summary list about 1.375 million ED visits in the United States attributable to ankle sprains, representing about 1.3% of ED visits.[5] Hence the economic impact of these injuries is also high.

Ankle sprains most commonly affect the lateral ligament complex (anterior talofibular, posterior talofibular, and calcaneofibular). Varus or inversion sprains include a spectrum of symptoms, and severity, which includes pain, swelling, tenderness, and loss of function, is described clinically as first-, second-, or third-degree. Most ankle sprains are described as first- or second-degree or of mild to moderate symptom intensity.[6–8]

Guidelines for the treatment of acute ankle sprain from the American Academy of Orthopaedic Surgeons recommend an initial rehabilitation program (up to 3 weeks) with nonsteroidal anti-inflammatory drugs (NSAIDs); rest, ice, compression, and elevation (RICE); protected weight bearing; early mobilization; and isometric exercise.[9] Conservative treatment may limit disability to an average of 8 days for a grade 1 sprain and 15 days for a grade 2 sprain.[3,4] However, even this approach may not modify the degree of disability or the recovery period. In one study of ankle sprain, pain and dysfunction were found to persist for 6 to 18 months (average 12.8 months) after initial ankle sprain in 73% of patients, with 40% reporting an inability to walk 1 mile and 11% continuing to use medications for ankle symptoms.[10] In a long-term follow-up study, nearly 40% of patients reported residual long-term symptoms and dysfunction 6.5 years after initial ankle sprain.[11] Also, long-term symptoms of ankle sprain have been noted by 40% of athletes 6 months after acute injury.[6]

NSAIDs effectively reduce the swelling, pain, and disability associated with acute ankle sprain,[12–16] but this may not alter the clinical course of ankle sprain regarding return to sport, and it may also cause significant adverse events,

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including gastrointestinal intolerance, and serious events, such as ulcers and bleeding.

Hyaluronic acid (HA) is a naturally occurring biological substance that has been shown to have a positive clinical impact in intra-articular and intradermal indications.[17] Because HA relieves pain and stiffness related to its rheologic modification of intra-articular matrix, as well as "filling" intradermal space, it may be hypothesized to have a similar effect on the extra-articular complex, including ligamentous structures affected by acute ankle sprain, such as structural and inflammatory interruption. Further, HA injected locally at the site of injury would not precipitate systemic risk of adverse events. Previously, we have described significant improvements in pain and functioning in a pilot study of seven patients with grade 1 or 2 ankle sprain who were given periarticular HA therapy for 4 days.[18] Although we are aware of the efficacy of local and oral NSAIDs in the treatment of acute ankle sprain, we are unaware of any other studies of local periarticular HA treatment for acute ankle sprain.

Hence, the aim of the current randomized controlled trial was to assess the efficacy and tolerability of periarticular HA versus placebo (PL) in the treatment of acute ankle sprain. Because there is no consensus on the treatment of ankle sprain, and because ankle sprain often responds without medication at a similar rate as that experienced with other treatment modalities, HA versus PL periarticular injection was compared with standard-of-care RICE in a representative treatment facility during the short- and longer-term recovery of these patients.

METHODS

This randomized, controlled study was conducted between March 2003 and December 2005 in three primary care sport medicine facilities in Ontario, Canada. The total number of sprains seen at these facilities during the 2 years before the study was 1063. All study physicians and personnel attended a prestudy investigator meeting to ensure standardization of study procedures, data collection, and management. The study was approved by the institutional ethics committee and was conducted according to the Declaration of Helsinki good clinical practice guidelines. All patients signed informed consent before participation.

The study included a screening phase where patients were assessed according to selected inclusion and exclusion criteria (below). Before enrollment, a diagnosis of first- or second-degree ankle sprain was made by athletic trainers affiliated with university athletic programs, emergency physicians at affiliated local hospitals, and family physicians in the referral base for the three sport medicine clinics. Patients were then asked to participate in the study and were required to report to the sport medicine clinics within 48 hours of injury. This was followed by provision of informed consent and then a screening assessment and physical examination by a study physician to confirm entry. Pain severity at enrollment was assessed using a pain Visual Analogue Scale (VAS); it included eligibility of a VAS at rest of more than 4.5 cm (0–10 cm). After enrollment, patients were randomized (1:1) to one of the two treatment groups, using a computer-generated randomization schedule: periarticular HA (MW range 750 to 1 million kilodaltons, 20 mg) + usual standard care RICE, or periarticular PL + usual standard of care RICE. The first dose of study treatment was administered on day 1 (within 48 hours of injury), and the second dose was administered on day 4 (± 1 day).

Assessments were done at baseline and on days 4, 8, 30, and 90 (Table 1). Efficacy measures included patients' VAS of pain on weight bearing (0–10 cm) and walking 20 m (0–10 cm), patients' global assessment of ankle injury (five-point categorical scale), patients' assessment of return to normal function/activity in sport (five-point categorical scale), patients' satisfaction assessment (10-point categorical scale), and adverse events as defined by the World Health Organization.

Eligibility

Inclusion criteria included the following: 18 years and older, first- or second-degree lateral ankle sprain within 48 hours of administration of the study drug, reported moderate (>4.5 cm) or greater ankle pain on full weight bearing on the Patient's Assessment of Ankle Pain using a 10-cm VAS, and availability for the duration of the study (90 days). Exclusion criteria included bilateral ankle sprain; ipsilateral knee injury; third-degree sprain; previous ankle sprain within 6 months; patients who had recently used anti-inflammatory medications, muscle relaxants, or psychotropic medications that could confound the results; patients with a history of severe gastrointestinal, renal, or hepatic disease; patients with rheumatic diseases, including osteoarthritis; history of drug or alcohol abuse; pregnant or lactating, or a woman of childbearing potential not willing to use an acceptable method of contraception during the study; or having received the investigational product within 30 days of the day 1 visit. The study consisted of a screening phase, a treatment phase, and a follow-up phase, as described below.

TABLE 1. Schedule of Time and Events

Evaluations	Baseline/ Day 1	Day 4	Day 8	Day 30	Day 90
Informed consent	X				
Medical history	X				
Vital signs and physical exam	X				
X-ray evaluation	X				
Patient's VAS of pain on weight bearing	X		X	X	X
Patient's VAS of pain on walking (20 m)	X		X	X	X
Patient's global assessment of ankle injury	X		X	X	X
Patient's assessment of normal function/activity	X		X	X	X
Patient's satisfaction assessment			X	X	X
HA administration	X	X			
Concomitant medications	X	X	X	X	X
Adverse events		X	X	X	X

VAS, Visual Analogue Scale; HA, hyaluronic acid.

Screening Phase

On day 1 (within 48 hours of the injury), patients underwent an examination to confirm whether they met all the inclusion and exclusion criteria, including the diagnosis of first- or second-degree sprain made on clinical grounds and VAS pain at rest >4.5 cm. An x-ray of the ankle joint was performed to exclude other pathologies at the discretion of the study physician, as well as medical history and physical examination. Patients were then assessed using the VAS for pain on weight bearing and after walking 20 m, where 0 cm represented no pain and 10 cm represented maximal pain. This was followed by the patient's global assessment of ankle injury (five-point categorical scale), the patient's assessment of return to normal function/activity in sport (five-point categorical scale), the patient's satisfaction with treatment (10-point categorical scale), and a record of concomitant treatment.

Treatment Phase

After outcome assessments, those randomized to HA treatment received a single injection of HA (0.7–1.2 mL) or PL (normal saline 0.7–1.2 mL).

Injections were performed using previously[19,20] described blinded syringes affixed to a 27-gauge, 1-inch needle. Skin was prepped using betadine 1%. Injections were delivered by the study physician using a standard approach along the anterior talofibular ligament, using clinical landmarks. The injection (1.2 mL total) was delivered during a single penetration along three planes (steps 1–3): anteroposterior, medial, and lateral to the proximal ligamentous landmark (Fig. 1). All study physicians attended a training session to ensure standardization of injection technique, including video review of a sample of three randomly selected patients during the study.

Assessments and injections were repeated on day 4 (± 1 day). All randomized patients received standard care consisting of RICE; assistive devices as determined by the study physician, including crutches, taping, or bracing, but not physiotherapy; and oral or topical medications, such as NSAIDs. These latter interventions could be used after day 8, at the patient's discretion.

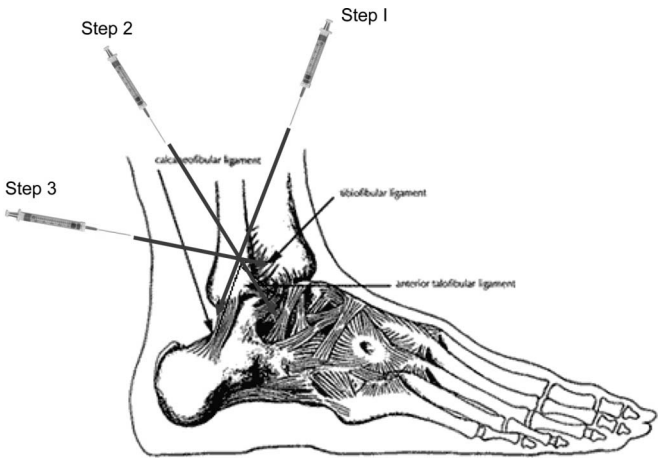

FIGURE 1. Injection location and direction.

Rescue medication (500-mg acetaminophen tablets, up to four tablets daily) was allowed in both groups, but not for the 24 hours before study visit. Patients were free to withdraw at any time during the trial.

Follow-up Phase

Follow-up assessments were completed at days 8 (± 2 days), 30 (± 7 days), and 90 (± 7 days).

Adverse events and concomitant medications were assessed throughout the patient's participation in the study.

Outcome Measures

The primary efficacy outcome (Appendix 1) was VAS of pain on weight bearing at day 8. The secondary efficacy outcomes were VAS of pain on walking (20 m), patient's global assessment of ankle injury, patient's assessment of return to normal function/activity in sport, and patient's satisfaction assessments.

Study Materials

HA was supplied in a single-dose vial containing 1% HA sodium salt solution with an average molecular weight of 800 to 1200 kd, in enough excipient to make a total volume of 1.2 mL. Vials were stored at room temperature (10–30°C). The normal saline volume was 0.7 to 1.2 mL.

Safety Assessment

During the treatment and follow-up phases, to evaluate safety, assessments of adverse events (throughout the study) and vital signs were conducted on all patients who received at least one dose of study products.

Statistical Analysis

The sample size was determined to allow the detection of a 20-mm difference in weight-bearing VAS (18) on day 8, assuming a standard deviation ≤10 mm of the mean distribution, an α of 5%, and a β level of 10%, giving a statistical power of 90%. With a potential dropout rate of 10%, we estimated a sample size of 150 patients.

Demographic and baseline data were compared within the two groups using the Student t tests for continuous variables and χ^2 statistics for noncontinuous variables. Statistical analysis was based on the intent-to-treat (ITT) population. Efficacy and safety variables were analyzed between groups using appropriate statistical methods, including the Student t test for quantitative variables, χ^2 test for nominal variables, and Mann–Whitney U test for ordinal variables. The data analysis was performed using SAS version 8.2 (SAS Institute, Cary, NC). All statistical tests were two tailed, with a 5% level of significance.

The primary efficacy endpoints were the decrease in pain (weight bearing) by day 8. Adverse events (AEs) were listed individually and were summarized by body system.

RESULTS

A total of 499 patients were screened, and the ITT population was 158 patients (Figure 2). Reasons for nonparticipation included not being available for the study period (27%), concomitant injury (16%), use of NSAIDs (13%),

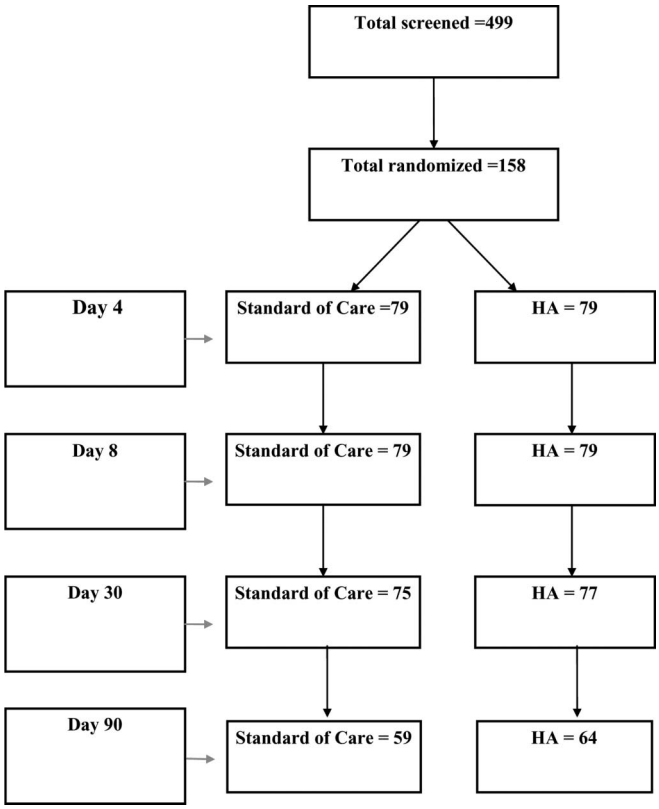

FIGURE 2. Study schema.

previous ankle sprain within 6 months (18%), and aversion to injections (8%). Average age was 26 ± 7 and 24 ± 8 years for the HA and PL groups, respectively, with equal male:female representation between groups. Thirty percent of sprains were first events, and 65% were grade 1, with no difference between groups. There was no difference between the groups at baseline, nor were there any differences in administration of the injections between the groups. We obtained 100% compliance with the injection series throughout the treatment phase. Time to intervention was not different between groups (39 ± 4 hours). Only 6 and 35 subjects did not return for follow-up at 30 and 90 days. Of the six who did not return at day 30, three claimed nonefficacy of the treatment (1 HA and 2 PL), and three had moved away. Those who did not return at day 90 had all moved away from the study location (transient students).

Efficacy

The primary criterion was the decrease from baseline to visit 2 (day 8 ± 1) in weight-bearing pain calculated in the ITT population (Table 2). This and changes in walking pain were −3.16 ± 1.18 and −1.83 ± 1.1 cm (%) (weight-bearing pain) and −4.99 ± 2.02 and −3.76 ± 2.43 cm (%) (walking pain) in the HA and PL groups, respectively ($P < 0.0001$), giving an intergroup difference of 1.31 and 1.23 cm in favor of treatment.

The differences between groups were also significant at visit 3 (day 30) and visit 4 (day 90) in favor of the treatment group (Table 2).

Globally, all efficacy parameters improved during the study in both groups. However, intergroup comparisons showed a statistically significant difference in favor of HA after visit 1 on most efficacy parameters (Table 2). For parameters where such a difference was not obtained for all visits, the improvement was more marked in the HA than in the control. The results for the secondary efficacy variables were, therefore, globally consistent with those concerning the primary outcomes.

Global Therapeutic Response

Patient satisfaction with treatment scores among subjects showed that 75% versus 48% and 77% versus 57% were satisfied at days 4 and 8, whereas 95% versus 76% were satisfied at day 30 (χ^2 test, $P < 0.001$) (Table 2). These results were consistent with the findings in the efficacy analyses.

Tolerance

Three AEs were observed among all subjects and consisted of pain requiring self-medication with NSAIDs (2 HA, 1 PL), including one mild erythema and pain (HA) at the injection site not requiring further intervention at day 4 and three pain and one mild erythema at the injection site in the HA versus two erythema, one pain, and one swelling at day 8 in PL (Table 2). The pain AEs in the two groups did not differ in intensity. No further AEs were reported at days 30 or 90. There were no serious adverse AEs. Sixteen subjects (7 versus 8; intervention versus control) took oral NSAIDs after day 8 for 14 (± 9) days. Physical therapy was used by 33 patients (18 versus 14; intervention versus control) but for only 4 (± 3) sessions for ankle indications during the 90-day follow-up. No difference in concomitant treatment or physical therapy was observed between groups.

DISCUSSION

The emphasis of therapy in ankle sprains is centered on reducing the swelling and pain rapidly after injury,[6,8] including early mobilization and isometrics.[9] Whereas conservative treatment may limit disability to an average of 8 days for a grade 1 sprain and 15 days for a grade 2 sprain,[3,4] failure to provide adequate therapy can limit a patient's efforts in rehabilitation and can prolong the recovery period and participation in sport. Studies have shown large numbers of patients reporting ongoing disability after the acute sprain, potentially impacting sport performance and quality of life. Hence, the implications of ankle sprain may extend beyond the acute injury and have longer-term impact on disability and performance, making adherence of effective, timely treatment important to clinicians and patients.

Although NSAIDs effectively reduce the inflammation, pain, and disability associated with acute ankle sprain,[12–16] they are nonselective and may cause significant adverse events, including gastrointestinal intolerance, serious events such as ulcers and bleeding, and potentially negative cardiorenal effects. Hence, therapeutic options for ankle sprains may be limited, whereas the short- and long-term implications may be significant, such that further search for novel, safe, and effective alternative treatment is warranted.

TABLE 2. Subject Characteristics, Efficacy and Safety Outcomes

	Double-Blind Treatment Phase				
Characteristics	**Baseline (n = 158)**	**Day 4 (n = 158)**	**Day 8 (n = 158)**	**Day 30 (n = 152)**	**Day 90 (n = 123)**
VAS pain of weight bearing change in centimeters, mean (SD)					
HA		−3.16 (1.18)*†	−4.11 (1.81)*†	−4.04 (1.16)*†	−4.07 (1.27)*†
PL		−1.83 (1.12)	−2.38 (1.72)*	−2.42 (1.09)*	−2.67 (1.47)*
VAS pain on walking change in centimeters, mean (SD)					
HA		−4.99 (2.02)*†	−5.62 (2.54)*†	−5.68 (2.55)*	−5.10 (1.92)*
PL		−3.76 (2.43)*	−4.2 (2.16)*	−4.67 (1.89)*	−4.78 (1.99)*
Patient global assessment of ankle injury, mean (SD)*					
HA	1.3 (1.8)	3.8 (1.8)*	4.8 (0.3)*	4.9 (1.8)*	4.9 (1.3)*
PL	1.5 (1.5)	2.1 (2.4)	3.5 (1.8)*	3.8 (2.7)*	4.8 (1.5)*
Patient assessment of return to normal activity in sport, mean (SD)*					
HA	1.4 (1.1)	2.1 (2.6)	4.7 (1.4)*	4.5 (1.2)*	4.6 (0.7)*
PL	1.3 (1.8)	1.6 (1.8)	3.7 (1.9)*	3.6 (1.8)*	4.6 (1.4)*
Patient satisfaction with treatment, mean (SD)					
HA	NA	7.4 (2.8)*†	7.7 (2.4)*†	9.5 (1.2)*	9.6 (0.7)*
PL	NA	4.8 (2.9)*	5.7 (1.7)*	7.6 (1.6)*	9.6 (1.1)*
Adverse events (n)					
Erythema		1/0	1/2	0/0	0/0
Pain		2/1	3/1	0/0	0/0
Swelling		0/0	0/1	0/0	0/0
Other		0/0	0/0	0/0	0/0

VAS, Visual Analogue Scale; HA, hyaluronic acid group; PL, usual care group.

Sprain grade is percent presenting with grade 1 sprain; VAS pain on weight bearing is the score decrease from baseline in centimeters on a 10-point Likert scale; VAS pain on walking is the score decrease from baseline in centimeters on a 10-cm Likert scale; patient global assessment of ankle injury is self-reported score from 1 to 5, where 1 = very poor assessment of injury on health and 5 = very good assessment of injury on health; patient assessment of return to normal activity in sport is self-reported score from 1 = severely restricted to 5 = normal activity; patient satisfaction with treatment is self-reported score from 1 = not satisfied to 10 = completely satisfied with treatment; adverse events are the self-reported adverse events at each study visit.

*Statistically significant differences within treatment groups for these parameters.

†Statistically significant difference between treatment groups for these parameters.

Conversely, HA is a naturally occurring biological substance, representing an unbranched, high–molecular weight polysaccharide as a major component of ligamentous, cartilaginous, and synovial ultrastructure.[17] It has no demonstrated effect on gastrointestinal and platelet function; this could add to its positive attributes as a potential treatment option in soft-tissue trauma.

The primary goal of the present study was to determine the efficacy of HA versus PL + RICE in the treatment of ankle sprain. The primary efficacy criterion was a decrease in pain during the first 8 days in the ITT population. On the basis of this criterion, periarticular HA was found to be significantly more effective than PL + RICE. This change of 3 cm is considered clinically significant.[15] Furthermore, almost all the secondary criteria, including patient global satisfaction, were improved during the trial compared with controls, even up to 90 days.

Because soft-tissue injuries may heal spontaneously,[3] the main criterion was assessed after 8 days—an important outcome, in our opinion, for return to sport. This seemed to be the best endpoint. Indeed, improvement in our primary efficacy variable was greatest at 8 days and persisted through the follow-up period, suggesting that periarticular HA injection was most effective as delivered in this indication. Further, the clinical implications of our results are confirmed by the fact that only a small number of patients in each group withdrew because of AEs or lack of efficacy, and our results are consistent with other treatments of ankle sprain with topical NSAIDs[14,21,22] and with oral NSAIDs and COX-2 inhibitors.[13,16] Importantly, we reported very low AEs, with high satisfaction, in this first report of HA injection in ankle sprain.

Another important consideration regarding the potential use of periarticular HA in ankle sprain would be the relative cost of this treatment versus the standard of care. Although this was beyond the scope of our investigation, and given that HA is not currently indicated or marketed for this indication, we note that a recent evaluation of the economic implications of HA in osteoarthritis versus conventional treatment was cost saving.[23,24] The comparative cost of HA for the two peri-injection series versus an 8- or 16-day course of naproxen would be approximately 15 to 30 Canadian dollars versus 4 to 8 Canadian dollars, respectively. Whether a cost savings is observed with periarticular HA versus oral NSAIDs awaits a further clinical trial directly comparing these treatments and performing a complete cost–benefit analysis.

In summary, the results of the assessment of the overall therapeutic response of periarticular HA by patients with acute ankle sprain were high. Most signs of pain, swelling, and disability were adequately controlled after only 8 days. Certainly, control patients also recovered, but this was less

efficacious or satisfactory compared with the HA group in both the short term and the long term. Whether this was implicated in better sport performance and recovery is unknown. In particular, return to sport was achieved in more than 90% of the HA group by 8 days compared with only 71% in the control group. This trial suggests that a two-injection course of periarticular HA may be useful in posttraumatic ankle sprain in the short and long term. Future studies are needed to compare this treatment with topical and oral NSAID/COX-2 treatments in ankle sprains using varying doses, molecular weights, and concentrations of HA in ankle sprains and other soft-tissue trauma.

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APPENDIX 1:

PAIN ASSESSMENT-PATIENT RECORD

Date of Visit: ____ ____ ____

day/month/year

Please Circle: Day no. 1 2 3 4 5 6 7 8 90 (follow-up)

Visit no. 1 2 3 4

PAIN ASSESSMENT (pain related to your ankle sprain)

This scale consists of a line that is 10cm in length and the line is anchored by two extremes of pain. The extremes are "no pain" and "pain as bad as it can be." Please put a stroke on the line that best represents how much pain you are feeling right now.

1. Pain on weight bearing:

The Visual Analogue Scale (VAS 0–10 cm)

No pain	———	Pain as bad as it can be

2. Pain after walking (20 m):

The Visual Analogue Scale (VAS 0–10 cm)

No pain	———	Pain as bad as it can be

PATIENT GLOBAL ASSESSMENT

Date of Visit: ____ ____ ____

Day month year

Please circle: Day no. 1 2 3 4 5 6 7 8 90 (follow-up)

Visit no. 1 2 3 4

Patients Global Assessment of Ankle Sprain:

Considering all the ways your ankle affects you, how are you doing today?

Check *one* box only:

☐ 1 Very Poor

☐ 2 Poor

☐ 3 Fair

☐ 4 Good

☐ 5 Very Good

Key to global assessment

Very Good = No symptoms and no limitation of normal activities*

Good = Mild symptoms and no limitation of normal activities

Fair = Moderate symptoms and limitation of some normal activities

Poor = Severe symptoms and inability to carry out most normal activities

Very Poor = Very severe symptoms which are intolerable and inability to carry out all normal activities

*Normal activities are defined as all activity that a patient does on a routine basis including work and recreation.

Patient's Assessment of Normal Function/Activity:

How does your condition affect your walking and normal activity?

Check *one* box only:

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5

Key to Normal Function/Activity

1 = Normal walking/activity and no pain

2 = Normal walking/activity with pain

3 = Mildly restricted walking due to pain and can't resume normal activities*

4 = Moderately restricted walking due to pain and can't resume normal activities

5 = Severely restricted walking due to pain and can't resume normal activities

*Normal activities are defined as all activity that a patient does on a routine basis, including work and recreation