

Petrella R, Ekman EF, Schuller R, Fort JG. Efficacy of Celecoxib, a COX-2-Specific Inhibitor, and Naproxen in the Management of Acute Ankle Sprain. *Clin J Sport Med*. 2004;14:225-231.

For decades now, clinicians have been following strict guidelines in the treatment of acute ankle sprains, including the use of nonsteroidal anti-inflammatory drugs (NSAIDs). In the past, NSAIDs have been proven to effectively reduce the primary and secondary effects of the acute inflammatory response. However, NSAIDs inhibit COX-2, which is associated with gastrointestinal (GI) tolerability and having no effect on platelet function when compared with more traditional NSAIDs. Therefore, the purpose of this study was to compare the efficacy and safety of celecoxib, a COX-2-specific inhibitor, with naproxen in the management of grade 1 and 2 acute ankle sprains.

This study used a multicenter, double-blind, parallel group, randomized controlled study design in which patients (n=397) with acute ankle sprains underwent a screening assessment that included a physical examination. Following inclusion into the study, patients were randomized using a computer-generated randomization schedule to 1 of 2 oral treatment groups: celecoxib 200 mg BID or naproxen 500 mg BID for 7 days. Clinical assessments were performed at baseline, day 4, and day 8. The primary measures of efficacy (Patient's Assessment of Ankle Pain VAS on weight bearing and Patient's Global Assessment of Ankle Injury) were taken at day 4 and day 8. The secondary measures of efficacy (Physician's Global Assessment (PGA), Patients' and Physicians' Satisfaction Assessments, and Patient's Assessment of Normal Function/Activity) were taken at day 8, with the PGA also being taken on day 4.

Significant differences were only noted at day 4 from the PGA, showing a significantly greater improvement at day 4 with naproxen ( $p=0.025$ ) compared with celecoxib. However, this difference was no longer observed at day 8 ( $p=0.96$ ). All other assessments did not show statistical significant differences. However, both of the primary efficacy measures, including the Patient's VAS with a treatment difference of 2.86 mm (with the upper 95% CI at 5.79 mm,  $p = .01$ ) and the PGA with responder rates of 71% (celecoxib) and 72% (naproxen) were within prespecified minimal clinical important differences. In addition, dyspepsia was significantly greater in patients on naproxen (6%,  $p=0.032$ ) compared to celecoxib (2%,  $p=0.032$ ).

As the study design was previously reported, the level of evidence was determined with the *AAOS Levels of Evidence for Primary Research Question*. This study used a double-blind, randomized controlled design and statistical analyses with narrow CI's, therefore this study was determined to be Level 1, Therapeutic. In addition, this article accumulated a Critical Appraisal Checklist score of 40/48.

NSAIDs are commonly used in clinical athletic training practice, particularly for acute injuries. It's imperative that, if clinicians are administering NSAIDs to any age group, they understand the potential adverse events to the patient, whether it be the NSAIDs effect on the acute inflammatory response or the patient's GI system. Though there doesn't appear to be a difference in the clinical effects of celecoxib or naproxen, it is clinically significant that naproxen causes greater GI discomfort. This is also important to patients, as they may purchase over-the-counter NSAIDs at their own discretion before or after consulting with their athletic trainer or physician.