



## Article Appraisal

**Article:** Oral Prednisolone in the Treatment of Acute Gout: A Pragmatic, Multicenter, Double Blind, Randomized Trial

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**Resident Reviewer Name(s) and Residency Affiliation:** James Powell (Kelowna), Baljeet Brar (Vancouver), UBC FRCP-EM Residency Program

**Faculty Methodology/Bio-statistics Resource Person:** Dr. Riyad Abu-Laban

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### Background and Study Objective(s):

Acute gouty arthritis is a common cause of inflammatory joint disease in patients presenting to the ED. Most guidelines suggest NSAIDs or colchicine as first line treatment. However, a recent Cochrane review, as well as two small RCTs have concluded an equivalent analgesic effect exists from steroids. This trial, larger in design than those prior, sought to determine if equivalence in pain reduction existed for prednisolone and indomethacin in the treatment of acute gout. In addition, the study was powered to detect hypothesized superiority in safety of prednisolone over indomethacin.

### Study Design:

This was a double-blind, double dummy multicentre RCT conducted in four large EDs in Hong Kong. Patients were enrolled if they presented within three days of symptom onset and fulfilled specific clinical criteria for the diagnosis of gout by a specialist emergency physician. In subjects who did not meet criteria, the diagnosis was confirmed by joint aspiration and fluid analysis. Enrollment occurred Monday through Friday 9am-4pm. Initially the randomization was stratified by both joint type (1st metatarsal or other) and study center, however stratification by joint type was subsequently dropped. The primary outcome was analgesic effectiveness, as defined by joint pain at rest and with activity as measured on a visual analogue scale (VAS) from 0-100mm. A difference of 13mm or more was defined a priori as the threshold for clinical significance. Analyses were done both by intention to treat and per protocol.

### Results:

416 subjects were enrolled. The baseline pain score in the indomethacin group was higher than in the prednisolone group (pain score of 37 mm vs. 27 mm respectively). Pain reduction in the ED and at 14 days was equivalent in both groups. There was a slightly greater pain decrease in the indomethacin group at rest from days 1-5 (99 vs. 76 patients with a decrease in pain >13mm). There were no major adverse events in either group. A slightly higher proportion in the indomethacin group had minor adverse events (62 vs. 15 in the ED and 380 vs. 353 at 14 days). There was no significant difference in the intention to treat and per protocol analyses.

## Validity of Results:

The consensus among journal club attendees was that the study addressed a clearly defined question and although stratification by joint type was dropped, this likely did not undermine the study as simple randomization (fortunately) resulted in relatively balanced study groups. The groups appeared to be treated equally and the patient characteristics in the two groups appeared to be similar. All patients were accounted for. It was noted that 80% power was relatively low for an equivalence trial (where a “negative trial” of no finding, is actually a “positive result” and in this case had a 20% probability of arising by chance), and typically such studies should be powered at 90% or more. Although the indomethacin group started with a higher pain score, this imbalance would likely favour the indomethacin group as higher pain scores generally show greater improvement from effective therapy, which further strengthens confidence that the conclusion of equivalence is correct.

## Generalizability of Results:

The characteristics of the patients in the Hong Kong EDs were felt to be similar to those seen in our hospitals in BC. The clinical approach taken in the trial to the diagnosis of gout was pragmatic, and thus arguably similar to what is done in Canadian EDs.

## The Bottom Line:

Prednisolone appears to be a safe and effective first line treatment for acute gout, with equivalent efficacy to indomethacin. The use of steroids as short term monotherapy in gout should be considered, particularly for patients with contraindications to the use of NSAIDs. The finding of equivalence between the two interventions will be practice-affirming for those EPs who have already adopted treatment with oral steroids for selected patients with gout, particularly the elderly where NSAIDs are known to be problematic. Those EPs who do not yet use steroids for gout should consider their selective use in appropriate patients.