ARTICLE:
• Country: Hong Kong
• Funding Sources: Health and Health Services Research Grant Committee of the Hong Kong Government

PURPOSE:
• Research Question(s): Investigate the equivalence in pain reduction and differences in safety between corticosteroids and NSAIDs in the management of patients with acute gout.
• Hypothesis: Null hypothesis: no difference between corticosteroids and NSAIDs

DESIGN:
• Study Design: Prospective, multicenter, double-blind, randomized trial
• Dependent / outcome Variable(s): Pain reduction, adverse events
• Independent / research Variable: treatment with NSAIDs or corticosteroids

SETTING / SUBJECTS:
• Research Setting: Four EDs in Hong Kong

• Subjects:
  o Study population: Patients 18 or older with acute arthritis suggestive of gout who presented between 9AM-4PM, Mon-Fri.
  o Inclusion / Exclusion criteria:
    • Inclusion:
      • Rapid onset of severe pain, swelling, tenderness, and erythema of the affected joint (maximal by 6-12 hrs), AND
      • At least one of:
        o MTP joint involvement, or
        o Knee, ankle, wrist or elbow involvement with gouty tophi, previous arthrocentesis confirming gout,
hyperuricemia, or hx of clinical gouty arthritis
attacks
  o If the above not met, aspirated fluid with MSU
crystals

- Exclusion:
  - Received steroids or indomethacin w/in 24 hrs prior to
    presentation
  - Hx of bleeding disorders or anticoagulant use
  - Allergy to study drug
  - Suspected other joint pathology
  - No MSU crystals if arthrocentesis
  - Unstable cardiac conditions
  - Comorbidities that would interfere with assessment
  - Cr >2.26 or GFR <30

  o Number (control / intervention groups): 208 in each group
  o Demographics: Mostly male, mean age 65
  o Attrition: 40 patients lost to follow up

METHODS:
- Interventions: Randomized to receive either indomethacin or prednisolone for 5
days plus Tylenol 1 g q6hrs PRN
  o Indomethacin group: 50 mg TID x2 days, then 25 mg TID x3 days (plus 6
tables of placebo prednisolone daily)
  o Prednisolone: 30 mg daily x5 days (plus placebo indomethacin in the same
dosing as the indomethacin group)
- Study Groups: Indomethacin or Prednisolone
- Outcomes:
  o Primary: Joint Pain at rest and with activity
  o Secondary: Adverse events (dizziness, sleepiness, n/v, abd pain,
  indigestion, rash, dry mouth, other), considered major if requiring
  hospitalization
  o Tenderness, redness, swelling of joint
  o Time to resolution of symptoms
  o Use of Tylenol
  o Length of ED stay
  o Patient satisfaction
  o Adherence to study medication
  o Additional GP or ED visit
  o Functional activity
  o Score on short form health survey
  o Demographics
  o Medical history
- **Instruments:** Pain assessed using a visual analog scale (0-100 mm) with 13 mm or greater difference considered significant; joint redness and tenderness measured using likert scales

- **Data Collection:**
  - Outcomes assessed in the ED by a research investigator at baseline, and every 30 minutes for 2 hours after the patient took the first two tablets
  - Patients kept a diary and recorded data once daily x14 days
  - Patients were interviewed and examined by a research nurse on day 5, then contacted by phone on day 14

**DATA ANALYSIS:**
- **Level of Data:** Pain relief was categorized as yes or no based on a cutoff of 13 mm difference in the visual analog pain scale
- **Statistics Used:** T-test for means and SD, chi-squared or fisher test for counts and percentages. Data analyzed for both per-protocol (including only patients who completed follow-up), and intention to treat (all patients who were randomized).
- **What, if any, variables were controlled for?:** Confounding was adequately controlled through randomization

**RESULTS:**
- **Brief answers to research questions:**
  - No baseline differences in the treatment groups
  - No difference between the groups for pain reduction
    - Both groups showed significant pain reduction over the 2 hour ED course and over the 2 week follow up with the greatest improvement from days 1-5
  - There were no serious adverse events (table 2)
    - 8 patients required discontinuation of treatment for suspected serious clinical signs or symptoms, 7 of whom were in the indomethacin group (3 abd pain, 3 dizziness, 1 lethargy)
    - Significantly greater minor adverse events in the indomethacin group
    - More in the prednisolone group had rashes
  - No difference in joint redness, tenderness, tylenol use, patient satisfaction
  - Indomethacin patients were more likely to seek further care

- **Other possible explanation for findings:** Low incidence of complications in the indomethacin group may be due to exclusion of patients with history of upper GIB, significant CKD.

- **Limitations:**
  - Diagnosis was based on clinical criteria, not arthrocentesis (though the criteria seem fairly specific, and realistic)
Patients were only recruited mon-fri during the day, potentially missing many patients, possibly with higher severity who had to come to the ED emergently

- Only looks at indomethacin, not other NSAIDs
- No examination of cost effectiveness
- No placebo (though this is probably unethical)

IMPLICATIONS FOR PRACTICE:
- Applicable to this clinical practice: Yes this is applicable to our ED practice. Though it would be nice to see similar data from a US population, the demographics are otherwise similar to the patients we see with gout.

- Feasible (cost, resources, etc): Easily feasible to use corticosteroids

- Clinically Relevant: Provides a great option for the many older patients in whom we should be hesitant to use NSAIDs

LEVEL OF EVIDENCE / DECISION FOR USE:
- Ready for use

- Level of Evidence: Ib Evidence obtained from at least one RCT