Oral Prednisolone in the Treatment of Acute Gout

BACKGROUND:

- Currently, three conflicting guidelines exist for the treatment of acute gout.
- The use of prednisolone for the treatment of acute gout has been previously studied but only in two small randomized controlled trials.

OBJECTIVE:

- To assess the efficacy and safety of prednisolone versus indomethacin for the treatment of acute gout.

METHODS

- **Design:** Randomized, parallel, double blind, double-dummy, placebo-controlled trial.
- **Duration of study:** 14 days
- **Inclusion criteria:** At least 18 years old, presented to the emergency department (ED) within 3 days of symptom onset, considered to have gout by a specialist emergency physician, and have the following two criteria: rapid onset of severe pain, swelling, tenderness, and erythema of an affected joint AND at least one of the following, metatarsophalangeal (MTP) joint involvement OR knee/ankle/wrist/elbow involvement with gouty tophi, previous joint aspiration confirming gout, hyperuricemia, or clinical history of 1 or more clinical gouty arthritis attacks.
- **Exclusion criteria**: Received corticosteroids or indomethacin within the past 24 hours, history of bleeding disorders/anticoagulation use, allergic to study drug, septic arthritis, rheumatoid arthritis, no MSU crystals on join aspiration, unstable cardiac conditions, significant comorbidities, SCr > 2.26 mg/dL or GFR < 30 mL/min.
- 416 patients total (208 per group) either received:
    - Two Indomethacin 25 mg tablets three times daily plus 6 tablets of placebo prednisolone once daily for 2 days
        - Then 1 indomethacin 25 mg tablet three times daily plus 6 tablets of placebo prednisolone once daily for 5 days

      OR
    - Three prednisolone 10 mg tablets once daily plus 2 tablets of placebo indomethacin three times daily for 2 days
        - Then 3 prednisolone 10 mg tablets once daily plus 1 tablet of placebo indomethacin three times daily for 3 days
    - All subjects received paracetamol 1 gram every 6 hours as needed.
- **Primary outcome measures:** Analgesic effectiveness using a visual analog scale (VAS) 0-100 mm
- **Secondary outcomes measures:** Presence or absence of adverse events
- 100 individuals (50 in each group) was required to calculate a power of 80%
- Data handling method was intent-to-treat and per-protocol.

RESULTS

- 376 patients completed the study (189 in the indomethacin group and 187 in the prednisolone group)
- **Primary outcome measure:** No significant difference was detected in the mean pain reduction during the first 2 hours in the ED at rest (-1.15 (95% CI 0.83 to – 3.14) p = 0.79) or with activity (0.10 (95% CI 2.10 to -1.91) p = 0.52). No significant difference was detected in the mean pain reduction during days 1-14 at rest (-0.15 (95% CI 0.26 to -0.56) p = 0.92) or with activity (0.12 (95% CI 0.58 -0.35) p = 0.15). A significant

difference was detected in the mean pain reduction between groups during days 1-5 (-1.30 (95% CI -0.38 to -2.22)) but a P value was not reported.

- **Secondary outcome measure:** A statistically significant difference was observed in the first 2 hours of the ED in: one or more adverse events occurred in 39 patients receiving indomethacin and 13 of those receiving prednisolone ($p < 0.001$), dizziness was reported in 19 patients receiving indomethacin and in 0 patients receiving prednisolone ($p < 0.001$), sleepiness was reported in 15 patients receiving indomethacin and 3 patients receiving prednisolone ($p = 0.004$), and nausea was reported in 7 patients receiving indomethacin and 0 patients receiving prednisolone ($p = 0.015$). A statistically significant difference was also observed in days 1-14 for the following: nausea was reported in 15 patients receiving indomethacin and 4 patients receiving prednisolone ($p = 0.009$), vomiting was reported in 10 patients receiving indomethacin and 1 patient receiving prednisolone ($p =0.006$), and a skin rash was reported in 2 patients receiving indomethacin and in 11 patients receiving prednisolone ($p=0.011$).
- **Authors' conclusion**: Oral corticosteroids are as effective at treating pain and as acceptable to patients as NSAIDs and hey should be considered as a first line alternative to NSAIDs in the treatment of patients with acute gout.

STRENGTHS

- Randomized, multi-center, placebo-controlled trial design
- Compared study drugs at appropriate dose for the treatment of acute gout
- Adherence was assessed

LIMITATIONS

- Patients were only recruited at EDs from 9 am – 4 pm thus limiting potential candidates
- Indomethacin was the NSAID of choice and may not be able to extrapolate these findings to other NSAIDs
- Cost effectiveness was not assessed
- Paracetamol 1 g every 6 hours as needed was prescribed for both groups
- Baseline at rest pain ratings were low
- Over the counter NSAID use was not accounted for or limited in the study design
- Patients were not instructed on various measures on how to counteract typical GI side effects of the study drugs, such as taking the medication with food.

CONCLUSIONS

- Overall, this study does support the use of prednisone as a viable option for the treatment of acute gout due to its pain resolution and relatively low side effects.
- Future research:
    - Since short course steroids has been said to cause recurrent acute gout flare ups, further evaluations of 5 day courses of steroids cause a statistically significant difference in recurrent gout flare ups compared to NSAIDs.

Reference: Rainer, T., Cheng, C., Jassens, H., Man, C., Tam, L., Choi, Y., & Yau, W. (2016, February). Oral prednisolone in the treatment of acute gout. *Annal of Internal Medicine, 164*, 464-471.

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