Clinical Question: Do non-steroidal anti-inflammatory drugs (NSAIDs) increase the risk of fracture non-union or impede healing?

Bottom-line: Limited RCT data suggests that NSAIDs do not impair fracture healing. Cohort studies associating NSAID use with fracture non-union are likely demonstrating that patients with non-healing (and painful) fractures are just using more analgesics. As NSAIDs provide equivalent or superior acute pain relief to other common analgesics often with fewer adverse effects, patients should not be denied their short-term use in fracture management.

Evidence:
- Randomized Controlled Trials (RCTs):
  - Adults: Two placebo controlled RCTs (140 patients total, predominantly or all middle aged women) with Colles fractures randomized to flurbiprofen x 14 days\(^1\) or piroxicam 20mg/day x eight weeks\(^2\):
    - No difference in recovery time, physiotherapy requirement, mal- or non-union,\(^1\) or functional recovery or healing.\(^2\)
    - Superior pain relief with NSAIDs (both arms allowed acetaminophen if required).
    - Limitations: ~20% lost to follow up, small numbers.
  - Children: One RCT (336 children)\(^3\) with arm fractures randomized to ibuprofen or acetaminophen + codeine:
    - No difference in fracture non-union at one year.
    - Ibuprofen provided equivalent pain relief with less functional impairment and adverse effects.
- Quasi-RCT of adults with acetabular fractures requiring heterotopic ossification (HO) prophylaxis\(^4\) is misleading. Patients with less significant injuries and different surgical approach (whom were not randomized to NSAIDs or radiation for HO prophylaxis) were analyzed in the "non-NSAID" arm.

Context:
- Retrospective cohort and case control studies suggesting that NSAIDs are associated with fracture non-union\(^5,6,7,8\) are:
Confounded by patients differing in initial injuries, smoking rates, or receiving different treatments. Demonstrating association (not causation): Opioid use is also associated with increased non-union rates, likely demonstrating that patients with non-healing (and painful) fractures are just more likely to be using analgesics.

- Non-union of long bone fractures is 1-6%. NSAIDs provide good post-surgical pain relief in adults, and are superior to acetaminophen or codeine and equivalent to acetaminophen plus codeine (with less adverse events) in pediatric musculoskeletal injury (including fractures).
- Some animal studies demonstrate supra-normal doses of NSAIDs impair bone healing.

Authors:
Ian C Taylor MD, Michael R Kolber BSc MD CCFP MSc

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References:

Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline.

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