

Evidence-based answers from the  
Family Physicians Inquiries Network

## CLINICAL INQUIRIES

# Q/Do NSAIDs impede fracture healing?

**EVIDENCE-BASED ANSWER**

**A/NO, ALTHOUGH THE EVIDENCE VARIES.** Nonsteroidal anti-inflammatory drugs (NSAIDs) don't appear to impair clinical fracture healing (strength of recommendation [SOR]: **B**, inconsistent evidence from a randomized controlled

trial [RCT] and retrospective studies). Even though animal studies show delayed healing and nonunion with NSAID use, evidence in humans doesn't merit avoiding NSAIDs in patients with fractures who need the drugs' analgesic and anti-inflammatory benefits.

**Evidence summary**

NSAIDs are commonly prescribed to control pain in patients with fractures. Laboratory studies have found that their antiprostaglandin properties delay callus formation and subsequent healing.<sup>1</sup> However, human studies evaluating the effects of NSAIDs on fracture healing have found variable results (TABLE).

**An RCT finds no delay in healing**

An RCT of 42 postmenopausal women with displaced Colles' fractures who were given piroxicam or placebo found no difference in the rate of healing between the intervention and control groups.<sup>2</sup> After 8 weeks, the bone mineral content of the radius and ulna, measured by bone density, was similar in both groups. Patients in the piroxicam group had significantly less pain at 10 days and 4 weeks, and used significantly less rescue medication.

**Other studies beg to differ**

Three observational studies of patients with different types of fractures found an increase in nonunion associated with NSAIDs.<sup>3-5</sup> Two retrospective studies of patients with long-bone fractures reported a higher rate of nonunion among patients taking indomethacin, diclofenac, or ibuprofen.<sup>3,4</sup> The third study, a retrospective analysis of postoperative spinal fusion patients who took ketorolac, also found an association between increased risk of nonunion and NSAIDs<sup>5</sup> (TABLE).

A retrospective study of 94 patients with tibial fractures reported delayed healing in patients who had taken any NSAID. This association persisted after elimination for age, sex, fracture severity, and high-energy injuries.<sup>6</sup>

**A relationship, but is it causal?**

A larger retrospective cohort study of 9995 patients with humeral shaft fractures found an increased risk of nonunion in patients exposed to NSAIDs during the 90 days after the fracture. On further analysis, however, only NSAID exposure 60 to 90 days after the fracture was significantly associated with nonunion. Because patients with painful nonunion fractures are likely to use more NSAIDs, the relationship may not be causal.<sup>7</sup>

**Benefits of NSAIDs outweigh concerns**

Three reviews of the effect of NSAIDs on fracture healing all come to the same conclusion: Although animal studies raise theoretical concerns that NSAIDs affect fracture healing, no conclusive evidence supports denying patients the analgesic benefits of these drugs for managing fractures.<sup>8-10</sup>

**Recommendations**

The American Academy of Family Physicians recommends using NSAIDs temporarily along with other measures—such as stretching, ice, and a steady return to the aggravating exer-

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**NSAIDs don't appear to impair clinical fracture healing.**

**TABLE**  
**Fracture healing with NSAIDs: What the studies show**

Type of study	Population	Intervention	Outcome and results
Randomized controlled trial <sup>2</sup>	Postmenopausal women with Colles' fractures (N=42)	Piroxicam	No delay in fracture healing
Retrospective <sup>3</sup>	Patients with long-bone fractures (N=112)	Indomethacin	Rate of nonunion 29% vs 7% (P=.004)
Retrospective <sup>4</sup>	Patients with femoral shaft fractures (N=99)	Diclofenac or ibuprofen	OR for nonunion=10.7 (95% CI, 3.5-33.2)
Retrospective <sup>5</sup>	Postoperative spinal fusion patients (N=288)	Ketoralac	OR for nonunion=4.9 (95% CI, 1.8-16.6)
Retrospective <sup>6</sup>	Patients with tibial fractures (N=94)	Multiple NSAIDs	Increased mean time to union of 7.6 wk (P=.0003)
Retrospective <sup>7</sup>	Patients with humeral shaft fractures (N=9995)	Multiple NSAIDs	Increased risk of nonunion with exposure to NSAIDs 60-90 days postfracture (RR=3.9; 95% CI, 2.0-6.2)

CI, confidence interval; OR, odds ratio; RR, relative risk.

➤ Although animal studies raise theoretical concerns, no conclusive evidence supports denying patients the analgesic benefits of NSAIDs for managing fractures.

cise—to relieve the pain of stress fractures until the patient is pain-free.<sup>11</sup>

The American College of Sports Medicine, The American Academy of Orthopedic Sur-

geons, and the American Academy of Physical Medicine and Rehabilitation haven't issued definitive guidelines concerning whether to use NSAIDs in managing fractures. **JFP**

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