Do NSAIDs impede fracture healing?

Evidence-BASED ANSWER

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. 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. 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. Two retrospective studies of patients with long-bone fractures reported a higher rate of nonunion among patients taking indomethacin, diclofenac, or ibuprofen. 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 (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.

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.

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.

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

References


**TABLE**

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome and results</th>
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</thead>
<tbody>
<tr>
<td>Randomized controlled trial²</td>
<td>Postmenopausal women with Colles’ fractures (N=42)</td>
<td>Piroxicam</td>
<td>No delay in fracture healing</td>
</tr>
<tr>
<td>Retrospective³</td>
<td>Patients with long-bone fractures (N=112)</td>
<td>Indomethacin</td>
<td>Rate of nonunion 29% vs 7% (P=.004)</td>
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<tr>
<td>Retrospective⁴</td>
<td>Patients with femoral shaft fractures (N=99)</td>
<td>Diclofenac or ibuprofen</td>
<td>OR for nonunion=10.7 (95% CI, 3.5-33.2)</td>
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<tr>
<td>Retrospective⁵</td>
<td>Postoperative spinal fusion patients (N=288)</td>
<td>Ketoralac</td>
<td>OR for nonunion=4.9 (95% CI, 1.8-16.6)</td>
</tr>
<tr>
<td>Retrospective⁶</td>
<td>Patients with tibial fractures (N=94)</td>
<td>Multiple NSAIDs</td>
<td>Increased mean time to union of 7.6 wk (P=.0003)</td>
</tr>
<tr>
<td>Retrospective⁷</td>
<td>Patients with humeral shaft fractures (N=9995)</td>
<td>Multiple NSAIDs</td>
<td>Increased risk of nonunion with exposure to NSAIDs 60-90 days postfracture (RR=3.9; 95% CI, 2.0-6.2)</td>
</tr>
</tbody>
</table>

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