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Q/ How do oral NSAIDs compare to other oral analgesics right after an acute musculoskeletal injury?

EVIDENCE-BASED ANSWER

A/ NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) are at least as effective as other oral analgesics (opioids, acetaminophen) in relieving pain in the first few days after an acute musculoskeletal injury. Evidence also indicates that us-

ing NSAIDs results in fewer adverse events than using narcotics (strength of recommendation [SOR]: **A**, systematic review of randomized controlled trials [RCTs], as well as individual RCTs).

Evidence summary

A Cochrane review of 16 RCTs (2144 patients) compared pain relief and return to function with oral NSAIDs and other oral analgesics (acetaminophen, opioids, or opioids plus acetaminophen) in patients who had suffered a soft tissue injury within the past 48 hours.¹ No differences between NSAIDs and acetaminophen were seen in pain relief at fewer than 24 hours on a 100-point visual analog scale (VAS) (4 trials; 359 patients; mean difference [MD]=1.56; 95% confidence interval [CI], -3.9 to 7.0). Nor were differences observed in return to function at 7 days (3 trials, 386 patients; risk ratio [RR]=0.99; 95% CI, 0.90-1.09).

No differences in pain relief between NSAIDs and oral opioids were seen at fewer than 24 hours (2 trials, 757 patients; MD=-0.02; 95% CI, -3.71 to 3.68) nor at days 4 to 6 (one trial, 706 patients; MD=-2.9; 95% CI, -6.06 to 0.26). Compared with NSAIDs, opioids showed a small increase in return to function at 7 days (2 trials, 749 patients; RR=1.13; 95% CI, 1.03-1.25), but the combination of acetaminophen and opioids didn't show a difference (one trial, 89 patients; RR= 1.28; 95% CI, 0.90-1.81).

Adverse gastrointestinal events (not defined) were no different between NSAIDs

and acetaminophen (7 trials, 627 patients; RR=1.76; 95% CI, 0.99-3.14) and occurred less often with NSAIDs than with oral opioids (2 trials, 769 patients; RR=0.51; 95% CI, 0.37-0.69). Overall, the authors concluded that low-quality evidence consistently showed NSAIDs were at least equal to other oral analgesics in efficacy of pain relief and return to function.

Naproxen vs oxycodone:

The opioid has more adverse effects

A double-blind, noninferiority, randomized trial (published after the Cochrane review search date) compared the effects of treatment with a single dose of oxycodone with a single dose of naproxen in 150 adult emergency department (ED) patients in a tertiary care academic center who had acute soft tissue injury and pain scores between 3 and 7 (on a 1-to-10 scale).² Injuries included sprains, strains, contusions, low-back injury, and intervertebral disk problems. The authors didn't clearly define "acute" with regard to time from injury.

Patients were randomized and given a single dose of oxycodone 10 mg or naproxen 250 mg with water. Pain scores and adverse effects were reassessed at 30 minutes and

60 minutes after administration, and a follow-up phone call was placed at 24 hours to evaluate further need for analgesics and adverse effects.

Baseline pain scores before medication administration were similar in the 2 groups (6.21 for the oxycodone group, 6 for the naproxen group). No difference in pain scores between oxycodone and naproxen was seen at 30 minutes (4.5 vs 4.4; $P=.76$) or 60 minutes (2.5 vs 2.6; $P=.45$). The number of patients who required more analgesics within 24 hours after administration didn't differ significantly between the oxycodone group and the naproxen group (12 patients vs 5 patients; $P=.07$).

The study evaluated adverse effects, including nausea, vomiting, dizziness, drowsiness, pruritus, and epigastric pain. Overall, 22% of patients (33) from both groups combined experienced at least one adverse effect. The oxycodone group reported more adverse effects overall (36% vs 8%; $RR=4.5$; 95% CI, 2.0-10.2;). Ten patients experienced nausea, 6 vomiting, 4 dizziness, 3 drowsiness, and 2 pruritus. In the naproxen group, 4 patients experienced nausea; no other adverse effects were reported.

Acetaminophen, indomethacin, and diclofenac are equivalent

A double-blind RCT in a university hospital ED in Hong Kong compared patients older than 16 years with "isolated painful limb injury" after trauma who received combinations of analgesics or placebo.³ Patients were recruited during typical work-week hours (Monday to Friday, 9 am to 5 pm) and randomized into 4 groups: acetaminophen 1 g plus placebo (66 patients), placebo plus indomethacin 25 mg (71 patients), placebo plus diclofenac 25 mg (69 patients), or acetaminophen 1 g plus diclofenac 25 mg (94 patients).

Each patient was given the group's designated combination of analgesics in the ED and asked to rate pain on a 0-to-100 visual analog pain scale (VAPS) at 0, 30, 60, 90, and

120 minutes after administration. Patients then left the ED with a 3-day course of their analgesic combination and were instructed to take the medication 4 times daily on the first day and 3 times daily thereafter. Patients recorded pain scores on the VAPS 3 times daily after discharge and at follow-up 5 to 8 days after initial presentation. Intention-to-treat analysis was done for patients lost to follow-up. A change in VAPS of 13 was considered clinically significant.

All groups started with similar pain scores (30 at rest and 70 with activity) and didn't achieve clinically significant pain relief within the first hour (mean change in VAPS <13). At 90 minutes, all groups achieved a mean change in VAPS >13, with no statistically significant difference between the groups. Adverse effects were rare (7% total), and none were severe (no gastrointestinal hemorrhage or renal damage).

Outside the ED, the acetaminophen-diclofenac combination group showed the greatest pain score reduction at every time point at rest and with activity, but none of the reductions were statistically or clinically significant (results presented graphically). No difference was found between the groups in number of patients who completed the course of analgesics, took additional analgesia, tried Chinese medicine, or returned to the ED within 30 days.

Limitations to the study included that the medication dosages may be much lower than typical dosages given in the United States and therefore lack applicability. The study also didn't include a true placebo arm. **JFP**

References

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NSAIDs are at least as effective as opioids and acetaminophen in relieving pain from acute musculoskeletal injury.



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