

Review: Opioids are more effective than placebo but not other analgesics for chronic noncancer pain

Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. CMAJ. 2006;174:1589-94.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Hospitalists ★★★★★☆ Geriatrics ★★★★★☆ Neurology ★★★★★☆ Phys Med & Rehab ★★★★★☆ Rheumatology ★★★★★☆

QUESTION

In patients with chronic noncancer pain (CNCP), are opioids more effective than placebo or other analgesics for relieving pain and improving functional outcomes?

METHODS

Data sources: 6 databases and bibliographies of relevant studies.

Study selection and assessment: Randomized controlled trials (RCTs) in English, French, or Spanish that compared oral, transdermal, or rectal opioids given for ≥ 7 days with placebo or other analgesics for treatment of CNCP (> 6 mo) (neuropathic pain, osteoarthritis, rheumatoid arthritis, fibromyalgia, and back and musculoskeletal pain). Studies on migraines, dental pain, abdominal pain, and ischemic pain from vascular disease and studies comparing different opioids were excluded. 41 RCTs ($n = 6019$, age range 40 to 71 y, 63% women, 85% white) met the selection criteria; 34 RCTs were included in the meta-analysis. Weak opioids (codeine, tramadol, and propoxyphene) and strong opioids (morphine and oxycodone) were compared with placebo (28 RCTs) and other analgesics (nonsteroidal antiinflammatory drugs or tricyclic antidepressants) (8 RCTs). All opioids were given orally, and the mean duration of treatment was 5 weeks (range 1 to 16 wk). Individual study quality was assessed using the Jadad scale. 87% of studies had quality assessment scores ≥ 3 out of 5.

Outcomes: Pain relief, functional outcomes, and side effects.

MAIN RESULTS

Opioids were more effective than placebo for relieving pain and improving functional outcomes; opioids were less effective than other analgesics for improving functional outcomes (Table). Opioids and other analgesics did not differ for pain relief, although a sensitivity analysis showed differences favoring strong opioids (Table). The mean dropout rate was 37% in the opioid groups and 38% in the control groups. 6 of 10 side effects were more frequent with opioids than with placebo (constipation; nausea; dizziness or vertigo; somnolence or drowsiness; vomiting; and dry skin, itching, or pruritus), and 3 were more frequent with opioids than with other anal-

gesics (nausea, constipation, and somnolence or drowsiness).

CONCLUSIONS

In patients with chronic noncancer pain, weak and strong opioids are more effective than placebo for relieving pain and improving functional outcomes, although they are less effective than other analgesics for improving functional outcomes. Strong opioids are more effective than other analgesics for relieving pain.

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Opioids (codeine, tramadol, propoxyphene, morphine, oxycodone) vs placebo or other analgesics (nonsteroidal antiinflammatory drugs or tricyclic antidepressants) for chronic noncancer pain*

Outcomes	Number of trials (n)	Comparisons	Standardized mean difference (95% CI)
Pain relief	28 (3741)	Opioids vs placebo	-0.60 (-0.69 to -0.50)
	8 (1079)	Opioids vs other analgesics	-0.05 (-0.32 to 0.21)‡
	2 (146)	Strong opioids† vs other analgesics	-0.34 (-0.67 to -0.01)
Functional outcomes	20 (3221)	Opioids vs placebo	-0.31 (-0.41 to -0.22)
	3 (892)	Opioids vs other analgesics	0.16 (0.03 to 0.30)§
	1 (123)	Strong opioids† vs other analgesics	0.00 (-0.35 to 0.35)‡

*CI defined in Glossary; a random-effects model was used.
 †Morphine or oxycodone.
 ‡Not significant.
 §Favors other analgesics.

COMMENTARY

Over 100 years of clinical experience has shown that opioids are useful for acute pain relief. The systematic review by Furlan and colleagues provides reassurance that oral opioids are more effective than placebo for CNCP in the short term, with a modest magnitude of benefit. Unfortunately, the review cannot answer the question that physicians really need to know: How do opioids compare with other treatments for long-term pain relief and functional outcome improvement?

The findings on pain and functional outcomes for opioids compared with nonopioid agents are of limited strength. The extensive use of quantitative meta-analysis may be misleading. We do not agree with the conclusion that strong opioids outperformed other analgesics for pain relief based on meta-analysis of 2 trials. One of the trials was a crossover study that reported more responders for titrated morphine than for nortriptyline (52% vs 34%), but also 3-fold more dropouts in the morphine group (1). The other trial was an open-label study that showed small between-group differences in endpoint pain scores (scale 0 to 100) between naproxen alone (65.5), fixed-dose oxycodone (59.8), and titrated sustained-release morphine plus oxycodone (54.9) (2). The adverse effects of long-term opioid use are underestimated by a review that included only RCTs; most excluded patients with a history of substance abuse. Diversion of prescription opioids toward street use is also

an important problem (3).

While opioids may be an option for treating CNCP, they should not be considered the first or best option. Adequately powered, long-term, head-to-head trials comparing opioids with nonopioid drugs as well as with such nonpharmacologic treatments as structured exercise programs are still needed. As long as such evidence is lacking, prescribing opioids for CNCP will continue to be controversial.

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