

Nonopioids and opioids gave similar relief for back pain or osteoarthritis, but nonopioids had fewer adverse effects

Krebs EE, Gravelly A, Nugent S, et al. **Effect of opioid vs nonopioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain: the SPACE randomized clinical trial.** JAMA. 2018;319:872-82.

Clinical impact ratings: ★★★★★☆ ★★★★★☆

Question

Do opioids reduce severe chronic back pain or knee or hip osteoarthritis pain more than nonopioid medications?

Methods

Design: Randomized controlled trial (Strategies for Prescribing Analgesics Comparative Effectiveness [SPACE] trial). ClinicalTrials.gov NCT01583985.

Allocation: {Concealed}*.[†]

Blinding: Blinded[†] (outcome assessors).

Follow-up period: 12 months.

Setting: Clinics affiliated with the Minneapolis Veterans Affairs (VA) Health Care System in the USA.

Patients: 240 patients (mean age 58 y, 87% men, 65% with back pain) who had chronic back pain or hip or knee osteoarthritis pain that was moderate to severe despite analgesic use. Exclusion criteria included long-term opioid therapy, contraindication to all drug classes in either treatment group, or conditions that could interfere with outcome assessment.

Intervention: Opioids, titrated to a maximum of 100 morphine-equivalent (ME) mg/d ($n = 120$), or nonopioids ($n = 120$), following a treat-to-target strategy. Opioid treatments included immediate-release morphine, hydrocodone/acetaminophen, and oxycodone (step 1); sustained-action morphine and oxycodone (step 2); and transdermal fentanyl (step 3). The opioid used was changed when 60 ME mg/d was ineffective. Nonopioid treatments included acetaminophen and nonsteroidal anti-inflammatory drugs (step 1); adjuvant oral medications and topical analgesics (step 2); and drugs requiring authorization from the VA health system (pregabalin and duloxetine) and tramadol (step 3).

Outcomes: Pain-related function (Brief Pain Inventory [BPI] interference scale). Secondary outcomes included pain intensity (BPI severity scale) and adverse medication-related symptoms. 230 patients would provide 80% power to detect a 1-point difference (minimum clinically important difference [MCID]) between groups in the primary outcome at 12 months, assuming a standard deviation of 2.7 (2-sided $\alpha = 0.05$); the initial target was 276 randomized patients. Recruitment was stopped when 240 patients were randomized due to recruitment difficulty and better-than-expected patient retention.

Patient follow-up: 98% (intention-to-treat analysis).

Main results

Groups did not differ for pain-related function at 12 months (Table) or across all follow-up assessments ($P = 0.58$). Nonopioids reduced pain intensity more than opioids over 12 months (Table) and across all follow-up assessments ($P = 0.03$), but differences did not reach the MCID of 1.0. Opioids increased risk for adverse treatment-related symptoms at each assessment (12-mo results in Table) and across all follow-up assessments ($P = 0.03$).

Conclusion

Nonopioids and opioids had similar benefits for moderate to severe chronic back pain or knee or hip osteoarthritis pain, but nonopioids had fewer adverse treatment-related symptoms.

*Information provided by author.

[†]See Glossary.

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Commentary

There is a dearth of evidence to support the widespread belief that opioids are more effective analgesics than nonopioids. Further, despite the widespread use of long-term opioids, there has been no robust evidence that long-term opioid treatment is safe and effective. Treating chronic nonmalignant pain with opioids is an example of how wide adoption of a treatment lacking robust evidence of effectiveness can be problematic. So, kudos to Krebs and colleagues and the Minneapolis VA Healthcare System for doing the challenging and valuable SPACE trial.

The SPACE trial showed that patients in the opioid group achieved similar, not superior, improvement in function and nearly equivalent improvement in pain compared with the nonopioid group, while opioids caused more adverse effects. Thus, for chronic pain, nonopioid treatment should be preferred when possible. However, opioid treatment can reduce chronic pain and remains an option when carefully used, such as when nonsteroidal antiinflammatory drugs are contraindicated or poorly tolerated.

When possible, opioid-based treatment of chronic pain should be avoided or minimized, but follow Dr. Moore and colleagues' wisdom: When treating pain, expect failure while striving for success (1).

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Opioids vs nonopioids in patients with moderate to severe chronic back pain or knee or hip osteoarthritis pain at 12 mo[‡]

Outcomes	Mean scores		Between-group difference in mean score (95% CI)
	Opioids	Nonopioids	
Pain-related function (BPI interference scale) [§]	3.4	3.3	0.1 (−0.5 to 0.7)
Pain intensity (BPI severity scale) [§]	4.0	3.5	0.5 (0.0 to 1.0)
Adverse medication-related symptoms	1.8	0.9	0.9 (0.3 to 1.5)

[‡]BPI = Brief Pain Inventory; CI defined in Glossary.

[§]Score range 0 to 10 (higher score indicates worse function/intensity).

^{||}Score range 0 to 19 (higher score indicates worse symptoms).

Reference

1. Moore A, Derry S, Eccleston C, Kalso E. Expect analgesic failure; pursue analgesic success. BMJ. 2013;346:f2690.