

Wide Variation in Rates of Safety Events in Older Adults Using Opioids

Solomon DH, Rassen JA, Glynn RJ, et al. *The comparative safety of opioids for nonmalignant pain in older adults. Arch Intern Med* 2011;170:1979–86.

Objective: To examine the comparative safety of opioids commonly used to treat nonmalignant pain.

Design: Retrospective cohort study.

Setting and participants: The study examined Medicare beneficiaries who were new initiators of opioid therapy between 1 Jan 1996 and 31 Dec 2005 in 2 U.S. states that provide nonrestricted medication insurance coverage. Subjects were considered to be “opioid exposed” from the day after being dispensed an opioid through 7 days after the last available dose. The investigators excluded patients with cancer or enrolled in hospice or nursing homes. They also excluded patients on nonsteroidal anti-inflammatory drugs or who had been on opioids in the recent past. There were 6275 patients in the study sample taking either codeine, hydrocodone, oxycodone, propoxyphene, or tramadol. The patients were matched using propensity scoring, which estimates the probability of receiving a certain treatment compared with the reference group, to ensure comparability across the 5 opioid groups.

Main outcome measures: Incidence rates and risk ratios at 30 and 180 days for cardiovascular events, fractures, gastrointestinal or bowel obstruction adverse events, death during hospitalization for selected adverse events, all-cause mortality after opioid exposure, and composite end points.

Main results: While the risk of cardiovascular events 30 days after the start of opioid therapy was comparable across all opioid groups, it was increased at 180 days for codeine (risk ratio [RR], 1.62 [95% confidence interval {CI}, 1.27–2.06]).

The risk of fracture was significantly reduced for tramadol (RR, 0.21 [95% CI, 0.16–0.28]) and propoxyphene users (RR, 0.54 [95% CI, 0.44–0.66]) compared with hydrocodone users. Risk of gastrointestinal or bowel obstruction was similar across all opioid groups. Compared with hydrocodone users, all-cause mortality was increased at 30 days for oxycodone (RR, 2.43 [95% CI, 1.47–4.00]) and codeine users (RR, 2.05; [95% CI, 1.22–3.45]).

Conclusion: The findings suggest that there is wide variation in the rates of safety events among elderly patients who use opioids for noncancer pain.

Commentary

How to treat nonmalignant pain in the elderly remains highly controversial. While opioids are generally quite effective, clinicians worry about their safety profile due to studies that suggest that these drugs can lead to injuries and poor clinical outcomes. This had motivated many clinicians to avoid opioids altogether and use nonsteroidal anti-inflammatory (NSAIDs), although more recent evidence suggests that NSAIDs have a variety of toxic effects themselves [1]. Knowledge about the comparative safety of opioids in the elderly would be helpful in ensuring that clinicians are well armed to care for an aging population. In this context, the study by Solomon et al provides helpful data.

The study offers several important findings. First, it indicates that not all opioids are created equal. The overall safety profile of hydrocodone, propoxyphene, and tramadol seemed to be the best while codeine and oxycodone seemed to lag behind. In fact, the all-cause mortality for codeine

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and oxycodone was more than twice that of hydrocodone. The second important insight from the study is that there is tremendous variation in the types of adverse events that occur. Patients using propoxyphene and tramadol had dramatically lower rates of fractures than those using other opioids. Cardiovascular outcomes seemed particularly elevated among those taking codeine.

There are several important limitations of the study. The first and most important is the nonrandomized nature of the data. Physicians usually have reasons for choosing to use different medications for different patients. For example, it is possible that physicians might choose to use propoxyphene in patients they consider to be low risk for falls or codeine in patients who might be at high risk for cardiovascular disease. Alternatively, it might be that effective management of cardiovascular disease may be correlated with higher use of hydrocodone. Either way, the lack of randomization poses a problem. However, by using propensity score matching and examining subgroups, Solomon et al used as good of a

strategy as is available, and the patient populations seem to be quite comparable.

Applications for Clinical Practice

Despite its limitations, this study provides the best data to date on the variations in the safety profiles of opioid drugs. Clinicians should not assume that all opioid drugs are comparably safe, and in fact should consider tailoring their choice of pain medications based on patient risks to ensure that we deliver the highest quality pain relief to patients without causing harm.

—Review by Ashish K. Jha, MD, MPH

References

1. Trescot AM, Helm S, Hansen H, et al. Opioids in the management of chronic non-cancer pain: an update of American Society of the Interventional Pain Physicians' (ASIPP) Guidelines. *Pain Physician* 2008;11(2 Suppl):S5-S62.

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