Combination of ibuprofen and acetaminophen is no different than low-dose opioid analgesic preparations in relieving short-term acute extremity pain

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Context

The epidemic of opioid overdoses in the USA has not abated despite recent decreases in the number of opioid analgesics prescribed by US providers.1 Despite millions of patient-years of use, there are relatively few studies comparing the effectiveness and safety of commonly prescribed analgesics for acute pain in the emergency department (ED). Emerging data suggest that opioids initiated for acute pain may carry a substantial risk of opioid use disorders,2-3 emphasising the need for prudent opioid prescribing in acute care settings.

Methods

This was a blinded, randomised-controlled trial comparing single doses of four different oral analgesic preparations (non-opioid and opioid) for the treatment of acute extremity pain in the ED.4 The study was conducted in the USA at two large urban academic EDs. Eligible patients included those with strains, sprains, fractures or contusions of the upper or lower extremity. Patients were randomised to receive (1) 400 mg of ibuprofen and 1000 mg of acetaminophen; (2) 5 mg of oxycodone and 325 mg of acetaminophen; (3) 5 mg of hydrocodone and 300 mg of acetaminophen or (4) 30 mg of codeine and 300 mg of acetaminophen. The primary outcome of this four-arm study was the change in pain intensity (numerical rating scores (NRS)) over the 2-hour study period. Receipt of rescue analgesia (in morphine equivalents) was reported as a secondary outcome and subanalyses were performed in patients with fractures and maximum baseline pain scores.

Findings

In total, 416 patients were randomised; 411 were included in the final analyses. The sample comprised roughly half women (48%), but also tended to be younger (mean age 37 (SD, 12)) and predominantly Latino (60%). On average, patients in the sample reported severe baseline pain (mean NRS score=8.7 (SD, 1.3)). At 2 hours, the mean NRS pain score decreased by 4.3 (95% CI 3.6 to 4.9) in the ibuprofen and acetaminophen group, by 4.4 (95% CI 3.7 to 5.0) in the oxycodone and acetaminophen group, by 3.5 (95% CI 2.9 to 4.2) in the hydrocodone and acetaminophen group and by 3.9 (95% CI 3.2 to 4.5) in the codeine and acetaminophen group (p=0.053). The codeine and acetaminophen group had the highest proportion of participants that received rescue analgesia (21.4%) and the oxycodone and acetaminophen group had the lowest (12.5%), but differences in rescue analgesia across groups were not significant.

Commentary

Although the USA has seen declines in opioid prescribing since 2012, there were still enough opioids dispensed in 2016 to supply roughly two-thirds of the population with an opioid prescription, and opioid overdose deaths are at an all-time high.5 On the surface, the study findings would seem to support the equivalence of non-opioid analgesics in the treatment of acute extremity pain, but key limitations about the study question and methods limit broad implementation of the study findings. As acknowledged by the authors, the opioid doses studied are at the lower end of an initial dose range and may not reflect clinical practice or an adequate analgesic dose for some patients. Although a subanalysis in patients with fractures yielded similar results, lack of accounting for injury severity, a heterogeneous base sample and use of non-pharmacological adjuncts potentially bias results towards the null. In addition, failure to more rigorously account for the timing and receipt of rescue analgesia could potentially impact the study’s main findings. Lastly, we must be reminded that the study results are on average—there are likely both responders and non-responders within each of the treatment groups. While the study methodology is generally sound, it stops short of answering two key questions: (1) does receipt of non-opioid analgesics in the ED reduce opioid prescribing at ED discharge, and (2) what is the impact of various analgesic regimens on pain outcomes beyond 2 hours (in the ED and more importantly, postdischarge)?

Implications for practice

On average, a single dose of commonly prescribed analgesic formulations results in similar changes in pain. This finding could be used in the EDs with triage-based pain protocols whereby patients receive a single dose of analgesia in advance of seeing a physician. More work is needed to determine the long-term impact of opioid and non-opioid analgesic prescribing in the ED.

Competing interests None declared.

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References

Commentary: Emergency care


