Invited Commentary

Another alternative to opioids for acute pain?

Raoul Daoust, MD, CSPQ, MSc*†‡; OPUM Study Group

In this issue of *CJEM*, Boucher and colleagues[1] report on a systematic review of the efficacy of calcitonin for treating acute pain associated with osteoporotic vertebral compression fracture, looking for an alternative to opioids. They searched a wide range of databases for randomized controlled trials that enrolled older adults (mean > 60 years of age) who suffered acute pain associated with a recent compression fracture (< 16 weeks). Although, their definition of acute pain related to compression fracture of less than 16 weeks is debatable because most authors consider 12 weeks of pain to be chronic pain. Efficacy of medications tend to vary whether used for the treatment of acute versus chronic pain. They conclude that "Calcitonin may be considered as an alternative to opioid and non-opioid analgesic in older adults with compression fractures in emergency and primary care settings."[1] This is a bold statement considering that the included studies suffered from significant statistical and clinical heterogeneity, using different types of calcitonin (salmon, eel, or synthetic), different dosages, different administration routes (intramuscular, subcutaneous injection, intravenous infusion, nasal spray, or suppository), and the low level of certainty regarding adverse events. Moreover, the use of calcitonin has been associated with an increased risk of cancer, and nasal calcitonin was withdrawn by Health Canada due to theses concerns. They acknowledge this fact in the interpretation section: "Research is required to clarify the safety of short-term use of calcitonin."[1] While we agree that calcitonin may one day be an interesting component of our therapeutic arsenal, its advantages compared with opioids or other analgesic for acute pain remain unclear. We understand the need to find alternatives to opioids in the context of the current opioid crisis. However, focusing on replacing opioids for acute pain treatment is not an ideal approach, and we should not adopt a drug (like calcitonin) with unclear benefits or risks on the basis that it is not an opioid.

Opioid prescriptions for acute pain represent less than 1% of all prescribed opioids in Canada and less than 5% in the United States.[2] However, some authors suggest that we, as emergency physicians, are the ones initiating the problem based mostly on studies of long-term use, an entity distinct from substance use disorder. Butler et al.[3] demonstrated in a small study that 19% of opioid substance-use disorder patients were first exposed to opioids through prescription. However, in this study, 80% of patients also said that they had a substance use disorder before they were exposed to opioids. Furthermore, in the same study, there was a delay of 6 months between the prescription and the first misuse. Because the vast majority of people who misuse opioids acquire them from friends or family and not from a drug dealer,[4,5] the availability of unused pills is one of the major determinants of the opioid crisis.[6] Additionally, in a post-surgery study[7] of 2,392 patients and in an emergency department (ED) study[8] of 627 patients, 42,692 (58%) and 16,049 (68%) opioid pills were left unused. The real problems seem to be the selection of patients and unused opioids in the medicine cabinet.

We are also facing a worrisome publication bias against opioids. For example, in 2015, *JAMA* published a study that evaluated the efficacy of adding opioids or cyclobenzaprine to nonsteroidal anti-inflammatory drugs (NSAIDs) for back pain and concluded that opioids are ineffective.[9] However, even though the analgesic effect provided by oxycodone does not last for 8 hours, the combination of oxycodone and acetaminophen was prescribed for only every 8 hours. The outcome of this study was predictable because the opioids

From the *Département de médecine de famille et médecine d'urgence, Université de Montréal, Montreal, QC; †Study Center in Emergency Medicine, Hôpital du Sacré-Coeur de Montréal, Montreal, QC; and the ‡CIUSSS Nord-de-l'ile, Montreal, QC.

Correspondence to: Dr. Raoul Daoust, Hôpital Sacré-Coeur de Montréal, 5400 boul. Gouin Ouest, Montreal, Québec, Canada, H4J 1C5; Email: raoul.daoust@umontreal.ca.

 CJEM 2020;22(3):273–274 DOI 10.1017/cem.2020.40

were prescribed without consideration to their pharmacokinetic properties. As shown in this study, combinations of opioids and acetaminophen are often used even though they prevent the optimal dosage of both medications.

Contrary to chronic pain syndromes where the efficacy of opioids is often questioned, stopping the prescription of opioids for acute pain may not be in the best interest of our patients. Instead, we should establish best practices for treatment of acute pain, which will allow us to use opioids more wisely. For example, we should avoid or use very small quantities of opioids in patients with substance-use disorder, optimize co-analgesia (acetaminophen, NSAIDs), and avoid combinations of medications. Separating acetaminophen from opioids allows patients to optimize the dosage of acetaminophen before requiring opioids. We should also prescribe the optimal quantity of opioids for the specific painful condition in order to adequately supply patients while limiting unused pills.

Because some patients consume only a few pills during the first 2 weeks after an ED visit,[8] we should consider partitioning our opioid prescription. According to the Controlled Drugs and Substances Act, refills of opioid prescriptions are not allowed in Canada, but partitioning is. Thus, physicians can instruct the pharmacist to supply only a portion of the total prescription at a time. Finally, acute pain typically resolves within 2 weeks. To further reduce excessive dispensing, storage, and potential diversion of opioids, physicians should include an expiration date on their prescription, after which pharmacists cannot fill or supply the remainder of the prescription, because the initial indication for its use is no longer present.[10]

These simple changes in how physicians write their opioids prescriptions should help individualize treatment and could decrease opioid unused pills and misuse without compromising analgesia. We should apply the same critical appraisal of the literature on alternatives to opioids as we would to any other medication before we start using them.

Acknowledgements: The authors would like to thank Martin Marquis and Megan Wes Martin for their contributions to manuscript revision.

Keywords: Anesthesia and analgesia, drugs and pharmacology, pain

Financial support: This study was funded by Canadian Institutes of Health Research (CIHR).

Competing interests: None declared.

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https://doi.org/10.1017/cem.2020.40 Published online by Cambridge University Press