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Commentary: The dose makes the poison: A look at opioid-free analgesia

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The dose makes the poison. This common adage in toxicology is a condensed version of the statement attributed to Paracelsus from the 16th century: All things are poison and nothing (is) without poison; only the dose makes that a thing is no poison. For those interested in pharmacology, this is a fascinating truth. Extreme examples such as water, required for life, but deadly in large enough quantities or digoxin, a valuable medication with a painfully narrow therapeutic index, demonstrate this truth. Grant and colleagues¹ describe the adverse consequences of the use of high-dose opioids for patients undergoing cardiac surgery and suggest potential alternatives in their article.

The goal in providing analgesia to patients undergoing cardiac surgery is to provide comfort from pain and allow patients to perform activities that will aid in their rehabilitation. It is ideal to minimize negative side effects of opioids, which include nausea and vomiting, sedation, itching, sedation, ileus, and respiratory depression. Grant and colleagues¹ provide a list of potential alternatives to opioids to be used in a multimodal approach with the suggestion that opioids may be eliminated entirely. It is important to recognize that with each agent introduced to reduce or eliminate opioids, new side effects and adverse events are possible. A great deal of enthusiasm surrounded the use of pregabalin and gabapentin for use in opioid-sparing regimens; however, the data have been mixed. Some data suggest the potential to reduce postoperative chronic pain;

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Disclosures: The author reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication April 14, 2021; revisions received April 14, 2021; accepted for publication April 15, 2021; available ahead of print May 8, 2021.

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JTCVS Open 2021;7:253-4
2666-2736

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<https://doi.org/10.1016/j.jtc.2021.04.007>



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CENTRAL MESSAGE

Should opioids be eliminated from cardiac surgery? Let's look at the alternative options available and discuss the lack of data to support an opioid-free approach to cardiac surgery.

however, side effects such as diplopia, potentially dangerous for an elderly cardiac surgical population, have been noted.²⁻⁴ Similarly, ketamine and dexmedetomidine have shown promise for use in patients undergoing cardiac surgery, but increasingly data have been disappointing. A single, subanesthetic dose of ketamine was not effective in reducing pain or delirium postoperatively in a large, multicenter trial.⁵ The ideal dosing of ketamine that may provide analgesic benefit and minimize side effects is unknown and more research is needed. Similarly, the effect of dexmedetomidine on analgesia after cardiac surgery is unclear. In spine surgery, it was shown to not reduce pain and opioid consumption.⁶ Previously, it was believed that dexmedetomidine would be of benefit for delirium and atrial fibrillation, but the Dexmedetomidine for Reduction of Atrial Fibrillation and Delirium after Cardiac Surgery study refutes these ideas.⁷ Very little data exist to suggest the use of intravenous lidocaine is of analgesic benefit in patients undergoing cardiac surgery.⁸ It is imperative to have further research into the use of these adjuncts in patients undergoing cardiac surgery to determine which combinations and at what doses may provide analgesic benefit. Study designs must also include evaluation of the known side effects for these agents (presented in Table 1 in the article by Grant and colleagues¹). Nerve blocks are being pursued in patients undergoing cardiac surgery with positive outcomes; however, further data are needed regarding which adjuncts may be useful with the local anesthetic and the most efficacious blocks.

Examples of opioid-free analgesia are provided by the authors who acknowledge the limited value of the case reports and case series they present. However, it was also pointed out that even when the hospital course was opioid-free, the patients often received opioid prescriptions going home. A significant consequence to the use of opioids in surgery, in particular high-dose opioids, is chronic opioid use/abuse. In 1 study, the rate of chronic opioid use in opioid naïve patients after cardiac surgery was 5.7%.⁹ Grant and colleagues¹ make the excellent point that posthospital management is crucial and care must be paid to opioid prescribing at the time of discharge. A recent review shows existing data do not support opioid-free being exceptional to opioid-sparing approaches.¹⁰

It remains to be determined whether or not opioid-free analgesia for cardiac surgery is superior to the use of opioids in low doses in combination with appropriate adjunct agents. The key points in the article by Grant and colleagues¹ are undeniable: opioid-only and high-dose opioid techniques are harmful, alternative medications are available, influencing analgesic practice often requires a culture change, and posthospital analgesia must be considered. As research moves forward on this topic, it will be crucial to determine what doses of the various analgesic medications provide effect without becoming a poison.

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