Are Opioid-tolerant Patients Resistant to Local Anesthetic Nerve Blockade?

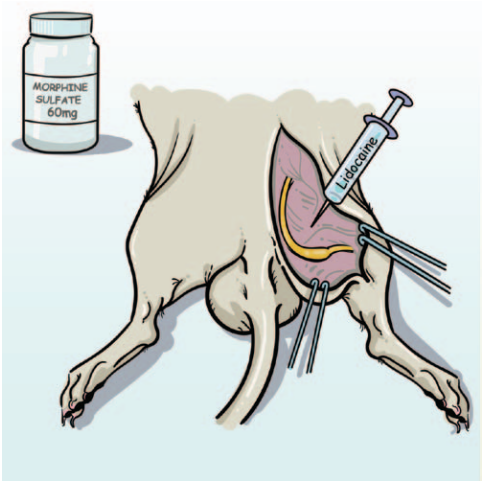
We Need More Information

Timothy J. Brennan, M.D., Ph.D., Richard C. Lennertz, M.D., Ph.D., Sinyoung Kang, M.D., Ph.D.

THE management of acute pain in the opioid-tolerant patients is an important topic in perioperative medicine. In this issue of Anesthesiology, Liu and Gold[1] demonstrate that morphine administration that induces morphine tolerance in rats produces resistance to lidocaine-induced nerve blockade *ex vivo*.

Acute pain management can be quite challenging in opioid-tolerant patients.[2] Opioids remain the most potent analgesic medications for treating acute pain and yet require greater dosages in patients with long-term use.[3] Administering larger doses of opioids not only leads to undesirable side effects,[3] but often fails to provide adequate analgesia based on patient report.[4] Further, multimodal analgesia with nonopioid analgesics such as ketamine,[5] acetaminophen, nonsteroidal antiinflammatory drugs, and local anesthetics has become the cornerstone of perioperative pain management in opioid-tolerant patients.[6] Rotating the opioid medication to a different opiate can improve efficacy by taking advantage of incomplete cross-tolerance among these medications, but the clinical evidence is limited.[7]

In this preclinical study, Liu and Gold[1] nicely demonstrate that the *ex vivo* potency of lidocaine is reduced in a dose-dependent and time-dependent manner by repeated morphine injections in adult rats. Loss of lidocaine potency requires exposure of the central nervous system to morphine; thus, morphine is not acting in the periphery. However, the loss of lidocaine potency is peripheral, at the axon. Surprisingly, after morphine is discontinued, the reduced potency of lidocaine is sustained for more than 30 days after morphine stoppage.



"...morphine tolerance in rats produces resistance to lidocaine-induced nerve blockade* ex vivo*...[but] we need...clinical data to determine if opiate-tolerant patients are...resistant to local anesthetic peripheral nerve blockade."

Preclinical studies have limitations that affect the clinical utility of the results to some degree. Recognizing such limitations enables us to better understand clinical relevance and propose additional experiments that may enable us to take advantage of this very well-performed study with succinct new information. For example, the methods to induce morphine tolerance are not typically seen in most opioid-tolerant patients preparing for surgery; most develop tolerance to low doses of opioids and gradually escalate dosing over several months or longer. Second, most opioid-tolerant patients presenting preoperatively have a chronic pain problem for which they are being treated. Third, these opioid-tolerant patients frequently have associated medical and psychologic comorbidities, such as anxiety or depression, and are prescribed other medications, such as benzodiazepines, that can make acute pain difficult to manage.[8] Finally, some patients are prescribed drugs, such as methadone and buprenorphine, that have markedly different pharmacokinetic and pharmacodynamic profiles compared to morphine.[9]

We should recognize that the morphine tolerance paradigm used in the current study may have similarities to that used in patients who are exposed to high doses of opioids for several days. An example might be those patients with postoperative pain who are sedated with opiates and are mechanically ventilated in the intensive care unit until they can be extubated.

Image: John Ursino, ImagePower Productions.

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Accepted for publication June 13, 2016. From the Department of Anesthesia, University of Iowa Hospitals and Clinics, Iowa City, Iowa.

 Anesthesiology 2016; 125:625-6

<zdoi;10.1097/ALN.0000000000001240>

Currently, clinical evidence for resistance to local anesthetics in opioid-tolerant patients is sparse. There have been a few case–control studies in patients who had a history of opioid abuse and underwent spinal anesthesia or digital nerve blocks.[10–12] While possible resistance to local anesthetics was suggested in these studies, these data require caution in extrapolation to the larger population of opioid-tolerant patients: these cases were selected solely based on the patient-reported history of opioid addiction and withdrawal, and the presence and degree of opioid tolerance were not examined. Moreover, currently available evidence is limited to a single country, and information regarding race and ethnicity was lacking from these reports.

Given the limited evidence, we need more clinical data to determine if opioid-tolerant patients are indeed resistant to local anesthetic peripheral nerve blockade. Admittedly, this is a somewhat difficult patient population to study. Short durations of hospital stay limit collection of detailed postoperative data. Postoperative pain management is procedure specific, and the pain problem for which the opioids are prescribed may be the indication for surgery with some resolution of the pain problem postoperatively, or the chronic pain problem for which opioids are prescribed may have no relation to the surgery (*i.e.*, the patient with chronic low back pain undergoing hip replacement surgery). The exact dosages and the length of time patients have been taking opioids are sometimes difficult to determine.

Furthermore, additional preclinical studies are needed. Can investigators bring the succinct basic science experiments closer to the chronic pain and opioid-tolerant patients undergoing surgery? Does the loss of local anesthetic potency also occur with local anesthetics that are used more often, such as bupivacaine and ropivacaine?

How should this study affect our patient care? We will continue to use opioids for acute pain management of the opioid-tolerant patients. Nonopioid analgesic adjuncts should be trialed in an attempt to limit opioid dosages. We should continue to use local anesthetics for perioperative pain management in the opioid-tolerant patients as a part of multimodal analgesia. If greater doses are considered, we must administer within a safe dosing range to avoid toxicity. We look forward to more information on acute pain management in the opioid-tolerant patients.

Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

Correspondence

Address correspondence to Dr. Brennan: tim-brennan@uiowa.edu

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