Opioids for Chronic Pain: Can Opioids Make Pain Worse?

Dr. Rachel Seib

The therapeutic use of opioids in North America has experienced a boom since the late 1990s. In the United States, the use of hydrocodone, methadone and oxycodone has increased 280%, 1293% and 866%, respectively, from 1997 to 2007.[1] According to data from the International Narcotics Control Board (INCB), in 2009 Canada consumed more morphine (76.75mg/person) than any other country in the world.[2] In part, this reflects the efforts of physicians and organizations advocating for more liberal laws governing the use of opioids to treat chronic pain. The result is that as many as 90% of patients in pain clinics receive opioids for management of their pain.[3]

The idea of using opioids to treat chronic pain is a non-validated extension of their established utility in the acute pain setting. This rationale has come under a great deal of criticism in recent years owing to a rising number of abuse issues, which are set against a backdrop of questionable effectiveness and well known side effects. To complicate matters, there is ongoing controversy about whether long-term opioid administration can actually make pain worse – a phenomenon referred to in the medical literature as "opioid-induced hyperalgesia" (OIH).

OIH represents a paradoxical response to an opioid, whereby instead of pain relief occurring, there is enhanced pain perception. [4] Clinical experience suggests this phenomenon occurs mainly in patients on very high doses of opioids for long periods of time.[5] This paradoxical reaction has been scientifically demonstrated in animals but the evidence in humans is, as yet, confined mostly to healthy volunteers undergoing opioid infusions.[6] Still, there is vast clinical experience showing a diminishing return of opioid therapy in patients with chronic pain. Attempts to gather definitive evidence are limited by the difficulty conducting randomized control trials (RCTs) in this patient population, the lack of consensus as to what the operational definition of OIH is, and the difficulty extending this laboratory-derived operational definition into real life.

It is important to appreciate that OIH is different from opioid tolerance. The latter is a state of reduced opioid efficacy which can be overcome by increasing the dose.[5] It reflects a dampening or down-regulation of the opioid-dependent systems in the central nervous system (CNS). This is in contrast to OIH where pain will actually get worse or remain unchanged when the dose of opioid is increased. There is no simple test or exam that can distinguish these clinical syndromes apart. If pain is unresponsive to increased opioid doses, pain physicians have several options. There is some evidence that rotating an opioid from one type to another can overcome OIH.[7] However, opioid rotation can also be effective in treating opioid tolerance, so while this may be effective, it will not necessarily help diagnose OIH from opioid tolerance. Switching to a drug that
contains a combination of opioid and opioid-antagonist, such as buprenorphine, is also widely practiced, with moderate evidence of effectiveness.[8] Another option is to antagonize the N-methyl D-aspartate (NMDA) receptor which is implicated in the mechanism of OIH.[5] In addition to being an opioid, methadone is a weak NMDA antagonist [9] and is thought to have some benefit in situations where escalating opioid doses are ineffective.[10]

The first-line management of OIH is the simplest and most obvious solution: avoid using opioids for chronic pain in the first place. There is weak evidence that opioids for chronic pain (i.e. over 6 months) results in lower pain scores and disability.[3] A large study performed in Denmark, where opioids are prescribed with great liberality, showed worse pain, higher healthcare utilization and lower activity levels in patients treated with opioids compared with chronic pain patients who were not.[11] There is also a higher occurrence of depression in patients on opioids. [12] This isn’t to say that opioids may not be effective in the short-term, but as a long-term treatment strategy, there may too little gain and much to lose. An exit strategy for patients with persistent pain on opioids should always be discussed with prescribing physicians.

References


Bio

Dr. Rachael Seib is a Chronic Pain Fellow with joint appointments at the Wasser Pain Management Centre at Mt. Sinai Hospital and the Department of Anesthesia at Toronto Western Hospital. She completed her medical degree at McMaster University and her anesthesia residency training at University of Toronto. She has a Masters of Arts from the University of Toronto. She has published articles on the use of gabapentin for postoperative pain, as well as on the use of ultrasound to perform peripheral nerve blocks for the management of chronic pain. In addition to her interest in ultrasound-guided interventions for chronic pain, she has research interests in sciatica in pregnancy, as well as in the use of ketamine infusions to treat neuropathic pain syndromes.