Letters

Psychoactive Properties of Opioids and the Experience of Pain

To the Editor:

A frequently held view in palliative care is that when patients in pain use opioids, they do not experience the psychoactive or euphoric effects of opioids. Furthermore, that those not in pain who use opioids do experience these euphoric effects that may lead to opioid-use disorder. Other than common clinical experience, there is scant evidence to support this view, and the contention awaits validation through empirical study. The following first-person example of this effect is shared to call for research on this important but neglected topic and to help demythologize and improve access to opioids for those in pain.

While working in hospice at a hospital in Northern California many years ago, I awoke at 2 AM at home in excruciating pain. My wife drove me to the emergency room at my hospital where I was greeted by staff to whom I offered the self-diagnosis of a likely kidney stone attack. The staff supportively said that they needed me to produce a urine sample to confirm my condition. Blood in my urine sample gave them the assurance that I was in severe pain and I was given 15 mg of intramuscular morphine.

The injection did not remove my pain but allowed me some ability to separate myself from the excruciating experience of the pain. There was no euphoria or any sense of pleasure. I waited until, some hours later, I was sent for an intravenous pyelogram (IVP) procedure to image the stone. Before administration of the IVP dye, I was given another injection of morphine. As the IVP contrast dye was injected, the stone moved from my kidney to my bladder.

As the stone moved to my bladder, the intense pressure pain I was experiencing dissolved. As the pain diminished, I began to feel the psychoactive effects of the morphine. Suddenly I felt high on the morphine. A warm sensation filled my body and I relaxed on the gurney. A sense of euphoria and deep contentment swept over me. I was put in a hallway to await results. At about 6 AM, the director of nursing on my hospice ward came to check on me (confidentiality for staff is not so much). Later, she said I looked very happy. I have not had any desire to repeat the experience.

The psychoactive properties of opioids are quite variable, and there is much variation in what is reinforcing from person to person. Severe pain will trump most of these psychoactive effects, but what one experiences when taking an opioid is affected by many complex factors including the type of pain, its intensity, short- or long-term use, which opioid is used, tolerance, genetic variations, the dose taken, patient characteristics, and so forth. It is surprising that more research on the difference between patients using opioids when in pain and not in pain does not exist, but given the complexities, it is understandable. Nevertheless, we really need this evidence.

Each year, an estimated 40 million people are in need of palliative care, 78% of whom live in low- and middle-income countries.[1] At present, over 80% of the world's population lacks adequate access to oral morphine.[2] Opioids are feared and avoided. Physicians are still taught that they are dangerous and will invariably lead to addiction, even when used for legitimate medical purposes. In most countries, the police monitor the medical use of opioids and prescribers fear going to jail even if they simply make documentation errors. The paperwork burdens are extensive. Opiophobia is alive and well throughout the world. There is a prevailing belief that a patient, even in severe pain, when prescribed an opioid will experience psychoactive effects that will likely transform the patient into an "addict." In palliative care, we rarely see opioid-use disorder in our patients. Time for our patients is usually short, and most die while still receiving opioids.

As I work internationally developing palliative care in many countries, I regularly confront opiophobia and counter this with our usual arguments, including the previously mentioned one, to advance the case for access to oral morphine, which is rarely available. Evidence for these arguments is lacking and would be very helpful to counter myths about opioids. What is

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needed is more rigorous research that effectively demonstrates what we see every day clinically: that our patients in moderate-to-severe pain, when started on an opioid, only experience relief of their pain.

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Subcutaneous Use of Lacosamide

To the Editor:

Epileptic seizures are one of the most common neurological emergencies and perceived as stress-related and fearful events by relatives and caregivers. Patients with brain tumors are at risk to develop epilepsy, with a prevalence of 30%−70%.[1] Status epilepticus can occur when endogenous mechanisms of seizure cessation fail or when mechanisms are initiated that lead to abnormally prolonged seizures.[2]

Not all the available antiepileptic drugs (AEDs) are suitable for use in palliative care. The drug of choice depends not only on local availability and costs but also on potential drug interactions, side effects, time of dose titration, and available formulations. Benzodiazepines, such as lorazepam or midazolam, are often used as emergency first-line treatment, but the sedating side effects might be undesirable, especially for long-term treatment. Although AEDs such as carbamazepine, oxcarbazepine, phenytoin, and valproic acid are known to be potent, widely available, and inexpensive, they have a high potential for drug interactions. Furthermore, the first two are not available in formulations for parenteral use, whereas phenytoin requires special precautions when administered parenterally and cannot be mixed with other drugs.[3] Newer AEDs, such as levetiracetam and lacosamide, are promising alternatives as they have a high efficacy, low potential for drug interactions, are well tolerated, have easy dose titration schemes, and are available in oral and parenteral formulations. As the intravenous route is not accessible for all patients who are unable to take oral medication, subcutaneous (SC) drug administration can be an important alternative in palliative care. Neither levetiracetam nor lacosamide are licensed for this route of administration. The successful use of levetiracetam SC has been reported previously.[4] Data on the SC use of lacosamide are still lacking, but, because of its pharmacological properties, potentially possible. We report our experiences with the use of SC lacosamide.

Case

A 41-year-old male patient suffered from a multifocal, left frontal, left mesiotemporal, and infratentorial anaplastic astrocytoma Grade III since he was 13 years old. After surgery in 1986, he had been asymptomatic for many years. In May 2012, a follow-up cerebral magnetic resonance imaging scan and subsequent biopsy confirmed tumor recurrence. Five weeks later, the patient experienced a first generalized tonic-clonic seizure, and treatment with levetiracetam was initiated. With the progression of his disease lacosamide, phenytoin, and zonisamide subsequently had to be added to his AED regimen over the following two years despite several tumor-modifying treatment approaches. In July 2015, he presented to our emergency unit because of significant deterioration with increasing weakness, dysphagia, and aphasic episodes. Progressive dysphagia led to tracheostomy. A nasogastric tube was placed. His antiepileptic treatment at this point comprised zonisamide 400 mg/d, levetiracetam 4 g/d, phenytoin 450 mg/d, and lacosamide 400 mg/d. He and his family decided to seek a palliative treatment approach, and he was transferred to our palliative care unit. As his seizures were well controlled, the antiepileptic regimen was revised, and we gradually withdrew phenytoin and zonisamide. Although swallowing was possible temporarily, it was obvious that this ability would not last for long. The patient refused the placement of a percutaneous endoscopic gastrostomy tube, and the nasogastric tube was removed because of increasing discomfort. He and his wife decided against intravenous (IV) access and favored SC drug administration only, when he would be unable to swallow. A literature search was performed, but no data on the SC use of lacosamide could be identified. Because of the physiochemical properties of the drug (pH 3.5−5; osmolality 290 ± 30 mOsmol/kg)[5] and the volume of administration (200 mg/20 mL), the SC route seemed