Use of Methadone as a Coanalgesic: Response to McKenna and Nicholson

To the Editor:

In response to McKenna and Nicholson’s report of the novel use of methadone as a coanalgesic, we would like to report our use of methadone as a coanalgesic with three patients over the last year at the Northern Ireland Hospice. All three patients had difficult to control neuropathic facial pain resulting from head and neck tumors despite multiple analgesics, coanalgesics, and opioid rotations. Methadone was introduced at a low dose, 2.5–5 mg at night, and titrated to a maximum dose of 10–20 mg at night over a period of nine to 15 days. All three patients responded well, and as the dose of methadone increased, each patient experienced significantly improved analgesia and developed symptoms of mild opioid toxicity, necessitating a reduction in their regular long-acting opioid medications. When doses were stabilized, all patients had greatly improved analgesia with fewer side effects from their medications.

Patient 1

This 70-year-old male was diagnosed with squamous cell cancer (SCC) of the buccal mucosa. He had uncontrolled left facial neuropathic pain despite continuous subcutaneous infusion of oxycodone 45 mg and ketamine 450 mg over 24 hours, amitriptyline 50 mg at night, clonazepam 1 mg at night, and pregabalin 300 mg twice a day. Despite multiple changes including opioid rotation, he was never pain free and regularly had symptoms of mild opioid toxicity and drowsiness with any attempt to increase his analgesics. He was titrated on methadone as follows: Day 1, 2.5 mg at night; Day 4, 5 mg; Day 9, 7.5 mg; and Day 13, 10 mg. The patient’s syringe driver with 45 mg oxycodone/24 hours was reduced as methadone was increased because of recurrent symptoms of opioid toxicity, and subsequently discontinued. He experienced regular pain-free episodes with no toxicity for the first time since his diagnosis, which continued until his death four weeks later.

Patient 2

Patient 2 was a 50-year-old male, diagnosed with SCC of the tonsil and base of the tongue. He had uncontrolled neuropathic facial pain despite modified-release morphine sulfate 200 mg twice a day, pregabalin 300 mg twice a day, diclofenac 50 mg three times a day, amitriptyline 70 mg at night, clonazepam 1 mg at night, and ketamine 200 mg four times a day via a percutaneous endoscopic gastrostomy (PEG) tube. He was unable to tolerate higher doses of any medications, having already been rotated to morphine sulfate from oxycodone. He was titrated on methadone as follows: Day 1, 2.5 mg at night (via his PEG); Day 4, (morphine reduced to 130 mg twice a day), 5 mg; Day 7, (morphine 80 mg twice a day), 7.5 mg; Day 10, 10 mg; Day 13, 15 mg (morphine 40 mg twice a day); and Day 15, 20 mg and morphine stopped. Methadone improved this patient’s pain considerably and was tolerated well, with morphine reductions resolving symptoms of opioid toxicity. His condition deteriorated because of advanced disease and he died with his pain well controlled for the last few days of his life.

Patient 3

This 51-year-old female, diagnosed with adenocarcinoma of the salivary...
gland, with uncontrolled neuropathic facial pain despite extended-release oxycodone 100 mg twice a day, gabapentin 300 mg three times a day, clonazepam 1.5 mg at night, and oral ketamine 60 mg four times a day. The patient was not able to tolerate dose increases in any of these medications because of drowsiness. She was titrated on methadone as follows: Day 1, 5 mg at night; Day 4, 7.5 mg (oxycodone 80 mg twice a day, ketamine 40 mg four times a day); Day 6, 10 mg (oxycodone 60 mg twice a day, ketamine 30 mg four times a day); Day 8, 15 mg (ketamine 30 mg twice a day); Day 10, ketamine stopped and oxycodone reduced to 50 mg twice a day; Day 11, methadone 20 mg (oxycodone 40 mg twice a day); Day 12, oxycodone reduced to 30 mg twice a day; and Day 13, oxycodone further reduced to 20 mg twice a day. She was discharged to home on Day 14, pain free (for the first time in months), and tolerating methadone 20 mg without evidence of toxicity.

Comment

All three patients experienced significant benefit with methadone, with self-reported pain levels dramatically reduced, and a reduction in the use of breakthrough analgesia. Its use as a coanalgesic was possible because introduction and subsequent dose titrations took place during inpatient stays at the Northern Ireland Hospice, where close monitoring for evidence of opioid toxicity could occur. All patients required a reduction in their other opioids as a result of symptoms of opioid toxicity as analgesia improved. Although our use of methadone remains limited, experience with these patients may suggest that it has a role in managing previously uncontrolled neuropathic pain in patients with head and neck tumors despite multiple analgesics, opioid rotations, and coanalgesics.

Our starting dose of 2.5–5 mg was lower than that described by McKenna and Nicholson1 (median 10 mg/day), whereas final doses correspond to the median of 20 mg/day in their 10 patients. As with their patients, methadone was well tolerated and our experience suggests that, with dose adjustment being possible over a period of nine to 15 days, admissions for titration of methadone would be a safer option for commencing this drug as a coanalgesic, unless very close monitoring is possible in the community.

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Reference


Sucrose During Single Painful Procedures—No Longer a State of Equipoise

To the Editor:

The recent study by Liaw et al.1 in the December 2011 issue showed that sucrose effectively reduced pain in newborn infants during a single, short-lasting, painful procedure. This is now the 145th published study of sweet solutions for infants and the 131st study where a placebo or no treatment group has been used (Harrison et al., unpublished data).

Liaw et al. conducted a high-quality randomized controlled trial. Aside from a lack of blinding, the methodological quality of the study was high and the study was at low risk of bias. The outcome measures comprised appropriate behavioral and physiological indicators, and the methods, analysis, and interpretation of results was exceptionally well written. The authors are to be congratulated on conducting such a rigorous, high-quality, well-presented study.

What, therefore, is the problem?

The problem is that to ethically conduct clinical research, there needs to be a state of uncertainty of the results, or equipoise: “a state of genuine uncertainty on the part of the clinical investigator regarding the comparative therapeutic merits of each arm in a trial.”3 (p. 141) In other words, we need to be uncertain of the outcome—that sucrose would be no better than the standard care of “gentle touch and verbal comfort” or non-nutritive sucking.

But, we have 145 single studies (Harrison et al., unpublished data), a large Cochrane systematic review, and even a review of systematic reviews that have shown us, beyond reasonable