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Brief Communication

Sudden Discontinuation of Chronic High Dose Intrathecal Hydromorphone and Its Withdrawal Implications

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Intrathecal (IT) therapies have become increasingly utilized since their inception in the 1980s. Clinical research into their effectiveness has been ongoing since that time. Morphine has had the most robust evidence with multiple clinical trials. However, many IT agents are used clinically despite the lack of US Food and Drug Administration approval. Use of these agents is based upon personal clinical experience and consensus recommendations. Dosages for these IT agents also vary greatly and can make instances in which they are quickly stopped challenging. The optimal dose range for hydromorphone has a wide range, with current dose range recommendations up to a maximum of 10 mg/d (1). This is an increase compared to a previous recommendation made in 2007, in which the maximum dose range was 4 mg/d (2). The increase in dose range occurred despite new randomized clinical trials. This case report describes a 67-year-old patient on high dose IT hydromorphone that was emergently stopped due to wound dehiscence and infection. The patient was additionally on IT bupivacaine and clonidine. No time was available to wean down any of the IT medications.

The patient is a 67-year-old female with an IT pump infusing 9.4 mg/d hydromorphone, 1.6 mg/d bupivacaine, and 47 mcg/d clonidine for back pain. Despite this, the patient continued to take oxycodone controlled-release (CR) 40 mg twice daily with 5-10 mg oxycodone immediate-release 4 times a day as needed. The patient presented to the emergency department with an infected pocket site and the decision was made by the surgical team to explant the pump and catheter that night. Preoperatively, a 150 mcg fentanyl patch was started and immediately postop hydromorphone patient-controlled analgesia (PCA) was started using a continuous infusion of 5 mg/h with a bolus dose of 1 mg every 6 minutes with no lockout. The patient was monitored in the intensive care unit (ICU) for signs and symptoms of withdrawal. During the 24 hour time frame from the evening on postoperative day (POD) #0 and POD #1, the patient used 104.7 mg of intravenous (IV) hydromorphone with no signs and symptoms of withdrawal. The continuous infusion of hydromorphone was decreased to 3 mg/h during POD #1; this subsequently decreased the total hydromorphone dose to 46.1 mg for the 24 hour period for POD #2. The PCA continued to be weaned in an aggressive fashion such that the total dose of IV hydromorphone was 12.5 mg for POD #4. One episode of hypertension with chest pain occurred POD #5 requiring readmission to the ICU, which was not thought to be secondary to opioid withdrawal. The patient had a rash caused by the fentanyl patch and was started on oxycodone CR/oxycodone immediate-release as needed that was gradually increased as PCA was weaned off. The patient was discharged on 60 mg oxycodone CR 3 times a day and oxycodone 15 mg every 6 hours as needed.

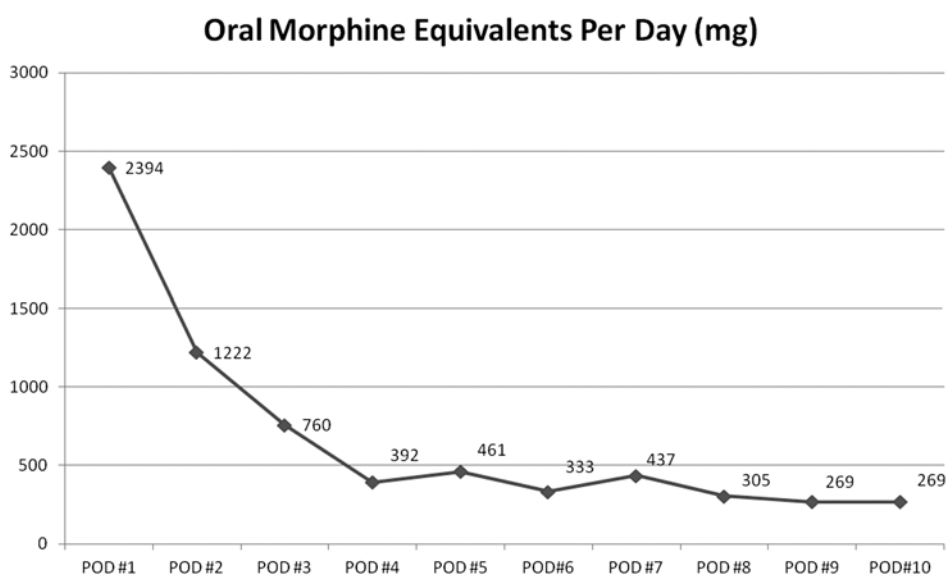

Fig. 1. *The daily use of oral morphine equivalents in milligrams.*

The conversion of IT hydromorphone can be challenging. Although it is debated, the approximate conversion of IT hydromorphone to IT morphine is 5:1 (3). Additionally, the conversion of intrathecal morphine to its oral form is challenging as well, with ratios of IT to oral morphine ranging from 300:1 to 12:1 (4,5). Some of these conversion factors are extrapolated from animal data. This wide conversion factor range creates clinical situations in which they are used troubling since they differ by such a large factor. For the sake of simplicity, a commonly accepted conversion factor of 100:1 IT morphine to IV morphine is used here. Intravenous morphine can then be converted to oral morphine at a value of 3:1 (9.4 mg of IT hydromorphone/d x 5 x 100 x 3). This yields an approximate value of 14,000 mg oral morphine equivalents (OME) per day. This commonly accepted dosing conversion may be more accurate for opioid naïve patients than for patients with opioid tolerance on chronic therapy.

Starting a replacement regimen to prevent withdrawal given such a high dosing requirement presents obvious challenges as there is no evidence in the literature of how to wean down from such high doses. Opioid withdrawal after cessation of intrathecal opioid therapy is a known clinical entity with one case report demonstrating withdrawal after a one-time dose of IT morphine (6). Case reports exist in which high dose IT therapies were stopped due to complications from pump failure or granuloma formation, but these reports did not examine the regimen to prevent withdrawal (7, 8). The initial combination of hydromorphone PCA and fentanyl patch could provide a theoretical maximum of 7,360 mg of OME per day if the patient is able to hit the button every 6 minutes during a 24-hour period. The patient used less than 20% of the initial PCA settings and still nursing reported that the patient had mental status changes at night and the PCA button was removed with no side effects of withdrawal. This allowed for a very aggressive weaning schedule. Common thinking is patients must be weaned down slowly in order to prevent withdrawal, but this patient weaned very quickly. The authors suspect that there is a certain threshold of opioid consumption that can prevent any withdrawal regardless of starting dose. This suspicion is based on the patient not withdrawing on a fraction of the previous dose but still receiving a large dose of opioids. This may also be a reason to question the conversion factor of IT to IV opioids.

This patient also demonstrates a problem with using high dose IT opioids despite the lack of good randomized clinical data. The patient continued to use oral opioids that were but a small fraction of the large amounts of IT therapies calling into question the true efficacy of using such a high dosing regimen of IT opioids. Interestingly, the patient reports that her pain is better now without the IT pump. The authors believe

that the use of oral high dose opioids for chronic non-malignant pain does not have good evidence and perhaps it is time to call into question the use of high dose IT opioids for chronic non-malignant pain as well (9).

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