

Case Report

Overdose Deaths Demand a New Paradigm for Opioid Rotation

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Abstract

Objective. An increasing number of deaths have been inferred to be associated with current opioid rotation practices and evidence is mounting that the use of widely accepted protocols for opioid rotation is an important contributing factor. Based on the findings of a literature review published in conjunction with this article, we propose a new paradigm for a potentially safer method of opioid rotation and present a case study illustrating the paradigm. This

new paradigm suggests three easy-to-remember steps in opioid rotation and obviates the need to use a conversion table.

Design. Report of a clinical case of a patient undergoing opioid rotation using this new paradigm.

Summary. The patient was successfully rotated from extended-release oxycodone to extended-release hydromorphone. The dose of oxycodone was slowly decreased, while the hydromorphone dose was slowly titrated. A critical element to this approach involved providing sufficient immediate-release opioid to treat breakthrough pain and to reverse acute abstinence signs and symptoms if the dosing changes prove insufficient.

Conclusion. A safer new paradigm for opioid rotation may provide an important incremental step forward in reducing adverse public health consequences of inappropriate opioid dosing.

Key Words. Opioid Rotation; Equianalgesic Dose Tables; Opioid Dose Conversion

Introduction

Opioid rotation is a common practice for patients suffering from chronic pain and has been shown to be useful in up to 50–80% of patients [1,2]. Unfortunately, an increasing number of deaths have been associated with current opioid prescribing practices [3–6] and evidence is mounting that the use of dose conversion ratios published in equianalgesic dose tables are an important contributing factor [7,8]. A literature review on deaths or near misses during opioid rotation revealed important flaws in the current protocol for opioid rotation [9]. These flaws included not only the use of outdated equianalgesic tables and inadequate prescriber competence, but, more importantly, a system that is not working. Overdoses were found to occur even when prescribers used published opioid rotation guidelines due to the large variability in interpatient response to opioids.

A New Paradigm for Opioid Rotation Is Necessary

Given the evidence that the current paradigm used for opioid rotation can be dangerous and lead to potentially fatal outcomes, a new paradigm for opioid rotation is necessary. Table 1 presents recommendations for a new

Table 1 Recommendations for a new paradigm for opioid rotation

Begin a downward titration of the original opioid by reducing the current dose by about 10–30% while beginning the new opioid at a dose that would normally be used in an opioid-naïve patient or at the lowest available dose for the formulation.

Slowly reduce the dose of the original total daily opioid dose by about 10–25% per week while increasing the dose of the new daily opioid dose by about 10–20% based on clinical need and safety. In most instances, the complete switch can occur within 3–4 weeks.

Provide sufficient immediate-release opioid throughout the rotation to prevent withdrawal and/or increased pain if the dosing changes prove insufficient. This minimizes the risk of the patient self-medicating due to inadequate relief, which can be fatal.

paradigm for opioid rotation *in unmonitored settings* in which the previous opioid dose is slowly tapered while the new opioid dose is slowly increased. The new paradigm suggests three easy-to-remember steps in opioid rotation and obviates the need to use a conversion table. In this proposed paradigm, the dose of the new opioid should be started at the lowest available dose rather than at a putative equianalgesic dose.

An important premise in developing this paradigm is that in the vast majority of patients, opioid rotation is an *elective* process, not an *emergent* one, and that safety is the leading health-related concern. Therefore, a more protracted period of time can and should be allowed for complete conversion. In cases where more immediate switching is needed due to overwhelming adverse side effects or inaccessibility of a previously available delivery route (e.g., the oral route is no longer available), a more closely supervised or monitored setting is advised, or the patient/caregiver(s) should be counseled in much greater detail about the risks, and those risks, on balance, should be viewed as acceptable compared with all other reasonable alternatives.

The essence of the equianalgesic (dosing) table-free approach is that the conversion process will occur slowly over a period of 3–4 weeks, and sufficient immediate-release opioid must be provided throughout the rotation to prevent withdrawal and/or intolerable pain.

Case Study

A 42-year-old man with a 12-year history of poorly controlled low back pain had undergone three spine operations, including a fusion, which left him with more pain. As a component of his overall rehabilitation-oriented treatment plan, this adherent patient was eventually titrated to 80 mg extended-release (ER) oxycodone three times daily (TID) as well as 10 mg hydrocodone/acetaminophen 325 mg not to exceed 6/day, along with gabapentin 400 mg TID and trazadone 100 mg for sleep. This regimen reduced his pain from 8/10 to 5/10 on a 0–10 verbal analog scale during the first 3 months, but then the pain returned to 8/10, seemingly due to tolerance. Function improved as pain improved. After 6 months of opioid therapy, the decision was made to switch from ER oxyc-

odone to ER hydromorphone by slowly discontinuing the ER oxycodone while slowly initiating the ER hydromorphone. The first step was to decrease his ER oxycodone of 80 mg TID to 60 mg TID and begin 8 mg ER hydromorphone each morning. The patient was scheduled to be seen weekly until the switch was completed and side effects, if any, were controlled. Hydrocodone 10 mg/APAP 325 mg was continued. At the second visit, the patient said his pain had worsened so the ER hydromorphone dose was increased to 12 mg every morning, while no change was made in the ER oxycodone dose. He was asked to return to the clinic in 1 week and instructed to stop his pain medications if he experienced sluggishness or became drowsy and to call the clinic immediately. This message was conveyed to his spouse as well. She was advised to call for help if the patient began to snore heavily and call 911 if he was unable to be awakened. On his third weekly visit, the patient reported better pain control, so the ER oxycodone was further decreased to 20 mg TID and the ER hydromorphone dosage was increased to 16 mg each morning. The patient returned for a fourth visit after 1 week during which he reported stable pain with full routine activities and no symptoms of withdrawal. Therefore, ER oxycodone was discontinued and ER hydromorphone was not changed. He was instructed to follow up in 2 weeks for reassessment of pain management and further adjustments to medications if necessary. After 6 months, the patient reported his pain at 6–8/10 but with an activity level greater than before he started on opioids or while he was taking 80 mg of ER oxycodone. Hydrocodone 10 mg/APAP 325 mg was continued for breakthrough pain but not to exceed 6/day.

Opioid Tapering Protocols Described in the Literature

Similar strategies for opioid rotation have been published, particularly with respect to conversion to methadone. Lynch performed a literature review of the methods used for opioid rotation from conventional opioids to methadone in patients with chronic noncancer pain [10]. Based on the finding that most authors recommended a process of progressive substitution, Lynch proposed a three-stage protocol of gradual substitution. At step 1, approximately 1/3 of the previous opioid dose is discontinued and replaced with the appropriate dose of methadone. At step

2, the previous opioid is decreased by a further 1/3 and replaced with methadone. At step 3, the previous opioid is discontinued and may or may not be replaced with methadone depending on pain control and side effects. A short-acting form of the previous opioid, morphine or hydromorphone, is used as rescue medication every 4 hours as necessary. Lynch also proposed increasing the length of time taken for opioid rotation from the 3-day schedule presented in many of the studies included in the review to a 9- to 15-day schedule using dose-adjusting intervals of 3–5 days depending on pain levels, adverse effects, and individual patient circumstances. Fredheim and colleagues also described a method of opioid switching using a stepwise substitution of the previous opioid with the new opioid [11]. These authors used a 3-day period, during which 1/3 of the morphine dose was substituted with the calculated putative equianalgesic dose of methadone each day. After the 3-day substitution period, the patients were followed closely for 1 week with the methadone dose titrated, if necessary. Of note, one patient experienced increasing drowsiness with methadone and was switched back to morphine, while another experienced sedation, which required an intravenous infusion of naloxone for 72 hours.

Reports of respiratory depression have been described when tapering protocols were used for opioid rotation; however, these events may have occurred because the opioids were switched too rapidly [12,13]. For example, Oneschuk and Bruera described a case of an 80-year-old man receiving hydromorphone 60 mg p.o./day plus 5 mg p.o. q1h prn for breakthrough pain who was being switched to methadone [12]. On the first day, his hydromorphone dose was decreased to 6 mg p.o. q4h and methadone liquid 1 mg p.o. q8h was commenced. Over the next 3 days, hydromorphone was incrementally reduced while the methadone dose was increased. By the fifth day of rotation, the methadone was increased to 10 mg p.o. q8h, the hydromorphone was stopped, and the hydromorphone breakthrough was increased to 6 mg p.o. q1h prn. That morning the patient was found to be unresponsive to verbal commands with a depressed respiratory rate and apneic periods lasting up to 30 seconds. Naloxone was administered and the patient recovered. Watanabe and colleagues reported a retrospective study of the charts of 50 patients who were converted from hydromorphone to methadone [13]. The authors noted that patients were converted by “gradually” increasing the methadone dose while reducing the dose of the original opioid over a number of days. Six instances of respiratory depression occurred with each treated by naloxone or temporary discontinuation of methadone. Five instances of respiratory depression occurred in a subset of 33 patients who were converted to methadone in less than 3 days and one instance occurred in a subset of 17 patients who had been converted in 3 or more days.

Conclusion

A new paradigm for opioid rotation is necessary. Guidelines for opioid rotation must minimize the risk of inadvert-

ent harm to ensure the safety of every patient—not just most of the patients most of the time. With an emphasis on safety, we propose a generalizable approach with three easy-to-remember steps in opioid rotation that obviates the need to use a conversion table. In this paradigm, one opioid is slowly decreased while the new opioid is slowly titrated from its lowest available dose. An immediate-release opioid must be provided to bridge the rotation to minimize risk that the patient might be tempted to self-medicate if pain is not adequately controlled or if withdrawal develops.

In order to optimize safety and mitigate potential harm, it is imperative that opioid rotation occurs slowly; a 1-week interval is practical and advisable between dose changes. Although this process takes a lot more time, the literature leads us to conclude that is likely to be much safer than switching all at once. In a study designed to determine the number of titration dose adjustments (“steps”) associated with attaining a stable dose of morphine and sequestered naltrexone extended-release capsules, 272 of 319 (85%) patients who achieved a stable dose did so in ≤ 2 titration steps and 305 (96%) did so in ≤ 4 steps [14]. Therefore, although opioids can be converted within 2 steps most of the time, some patients may require up to a month or longer when being rotated from one opioid to another.

Opioids may be a necessary component in the overall management of moderate to severe chronic pain. In light of increasing controversy over the use of opioids for chronic noncancer pain due to opioid-related morbidity and mortality, the goal should not be to eliminate these medications but to ensure their safe use. Current opioid prescribing practices must be examined and a concerted effort made to reduce the rising occurrences of unintentional overdose during opioid rotation. A new paradigm for potentially safer opioid rotation is proffered, but requires validation among a broad population of patients. Future research should include controlled trials testing our proposed model of opioid rotation and other techniques currently being used. Before this model or any other proposed model can be promoted as safe and effective, it must undergo rigorous studies to demonstrate the efficacy and safety. If successful, it may go a long way toward reducing adverse public health consequences of this particular cause of inappropriate opioid dosing.

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