PSNet
PATIENT SAFETY NETWORK

Miscalculated Risk

August 1, 2006
Strassels SA. Miscalculated Risk. PSNet [internet]. 2006.
https://psnet.ahrq.gov/web-mm/miscalculated-risk

The Case

A healthy 36-year-old man was admitted to a teaching hospital for acute low back strain after lifting his 2-week-old infant. He received Vicodin (hydrocodone and acetaminophen) on an "as needed" basis. After 2 days, the intern was instructed to switch the patient to long-acting oral morphine in anticipation of discharge. After the first dose of MS Contin (controlled-release oral morphine), the patient was noted to be somnolent; 3 hours later, he was in respiratory distress. He was intubated and transferred to the intensive care unit. The ICU team evaluated his recent analgesic use and determined that he had received a dose of MS Contin that far exceeded his previous Vicodin requirement. The patient subsequently developed acute respiratory distress syndrome (ARDS) and sepsis, presumably related to aspiration. He remained in the ICU for 2 weeks and required pressors for blood pressure management. Eventually, the patient recovered fully and was discharged home.

The Commentary

High alert medications, opioids, and respiratory depression. As this case illustrates, oral opioids are high-risk drugs worthy of serious consideration when evaluating medication safety from an institutional perspective. Respiratory depression, the most serious opioid-related adverse effect, is most common within several days of beginning scheduled therapy and when converting from one regimen to another.(1,2) As in this case, somnolence often precedes hypoventilation; thus, vigilant monitoring for sedation (in addition to monitoring of respiratory status) is critically important in the routine care of patients receiving opioid therapy.

The error in this case was attributed to therapeutic conversion using a nonequivalent analgesic dose. Whether the error was caused by a calculation mistake when converting from Vicodin (hydrocodone and acetaminophen) to MS Contin (controlled-release oral morphine), a misunderstanding regarding the relative potencies of the two products, or some other cause, is not known. Regardless, it appears that there was a lack of understanding regarding the appropriate use of long-acting opiates, as well as a failure on the part of the pharmacist and nurse to appreciate the excessive dose relative to the patient's prior use of Vicodin.

The long-acting opioids (fentanyl transdermal system [Duragesic], controlled-release morphine [MS Contin], controlled-release oxycodone [OxyContin], extended-release morphine [Avinza, Kadian], and methadone) are generally reserved for use in persons who are not opioid-naïve, whose analgesic requirements are stable, and who are expected to need opioid analgesia for an extended period of time. In this case, if the patient's pain was not well controlled, use of a more potent immediate-release opioid would have been a reasonable step before switching to a long-acting drug.

Other types of errors reported in conjunction with use of opioids include name confusion, inappropriate use of adjunct medications, and use of a confusing array of overlapping analgesic regimens.(3-6) Reports of name confusion include using *opium tincture* (which contains 10 mg/mL of morphine) in place of *camphorated tincture of opium* (also known as paregoric), which contains 0.4 mg/mL of morphine.(5) Hydromorphone, meperidine, and morphine have also been erroneously interchanged, as have drugs with similar-sounding brand names, like Avinza (morphine sulfate extended release), Evista (raloxifene hydrochloride, a drug to prevent osteoporosis), and Invanz (ertapenem sodium, an antibiotic), or Roxanol (20 mg of morphine per mL), Roxicet (oxycodone with acetaminophen), and Roxicodone Intensol (20 mg of oxycodone per mL).(6) Inappropriate use of promethazine or hydroxyzine may contribute to sedation and other adverse effects without enhancing analgesia.(3) Another potential problem occurs when prescribers order different analgesic regimens depending on the patient's self-assessment of pain severity (eg, acetaminophen, 650 mg by mouth every 4 hours for pain scale ratings of 1-3; acetaminophen with codeine, 30 mg by mouth every 4 hours for pain ratings of 4-6; morphine, 2 mg IV every 3 hours for pain ratings of 7-8; and so on).(3) Inadvertent acetaminophen overdoses are another important concern, since this analgesic is present in many combination products.(7) The total amount of acetaminophen from all sources should not exceed 4 grams per day; lower ceiling doses (2 grams per day or less) are recommended in alcoholic persons and individuals with diminished hepatic or renal function.

Equianalgesic conversion. Changing from one opioid analgesic to an alternative drug may be necessary when pain persists despite increasing doses, when a patient develops an adverse event (eg, an allergic reaction or intolerable side effect), when converting between routes of administration, or when changing between long-acting and short-acting agents based on the goals of pain management. Clinicians must understand the basic concepts of equianalgesic conversion. Importantly, conversions are not exact, and cross tolerance between opioids is incomplete. For these reasons, the calculated dose of the new opioid is often reduced by 25%-50% depending on how well pain is controlled. In addition, rescue medications must be made available for breakthrough pain.

To calculate an equianalgesic dose, the following steps should be followed:

- First, add up the patient's total 24-hour analgesic requirement, including all doses for breakthrough pain.(1,2)
- Second, convert that total amount to the drug and route desired using a conversion table, such as the Table below.
- Third, divide the total 24-hour dose of the new drug by the number of daily doses to be administered. The duration of action values in the Table are helpful in this regard.
- Fourth, consider reducing the calculated dose of the new drug by 25%-50%. The specific reduction often depends on how well the patient's pain is controlled. For example, if pain is well controlled, the

dose of the new drug may be reduced by 50%, and liberal doses for breakthrough pain would be ordered.

- Finally, calculate a rescue dose for breakthrough pain. This amount is generally up to 20% of the total daily opioid dose, given every 3 to 4 hours as needed.

As an example, assume that a person has required 54 mg of IV morphine during the previous 24 hours and that a switch to immediate-release oxycodone is planned in preparation for hospital discharge. Using the Table, 10 mg of IV morphine is roughly equivalent to 20 mg of oral oxycodone. Multiplying 54 mg by the dose ratio from the conversion table (20/10, or 2), the total expected 24-hour dose of oxycodone is 108 mg. Immediate-release oxycodone is dosed every 2 to 4 hours. At the full conversion rate, two options for dosing are 9 mg of oxycodone every 2 hours or 18 mg of oxycodone every 4 hours. These amounts would likely be rounded to 10 or 20 mg per dose (depending on whether the 2-hour or 4-hour dosing interval is chosen) to take advantage of 5-mg tablets. If this expected dose is reduced by 50% to account for possible incomplete cross-tolerance, dosing schedules of 5 mg every 2 hours or 10 mg every 4 hours could be recommended. The dose for breakthrough pain would be up to 20% of the daily dose (about 10 mg). It is important to note that other analgesic conversion methods are available and that equianalgesic doses may differ depending on which conversion method is used.(8,9) In addition, equianalgesic dose ratios different from those shown in the Table may be appropriate for patients on long-term opioid therapy.(10)

Preventing opioid errors. Strategies to prevent opioid errors are not substantially different from those used for other types of medication errors, with a few exceptions. For example, a new order for a long-acting opioid should be accompanied by a check to determine whether the person is opioid-naïve. Similarly, equianalgesic requirements can be calculated when the route of administration is changed or when a more potent drug is started. Computerized prescriber order entry (CPOE) is a promising technology for its potential to reduce medication errors.(11) CPOE might improve analgesic safety by preventing prescribers from ordering drugs not on the institution formulary or alerting the prescriber that use of a drug for a given patient is not recommended. Also, equianalgesic conversion algorithms could be programmed into CPOE software to help prescribers choose drugs and doses. Although this tool could be potentially useful, it is important to acknowledge that opioid dosing is very flexible and that a single algorithm would likely not be appropriate for all clinical situations. In this regard, another important system approach to enhance analgesic safety is to ensure that prescribers, nurses, and pharmacists are all comfortable with equianalgesic calculation methods, independent of any computerized system.

Take-Home Points

- Respiratory depression is a potentially serious, but uncommon, adverse effect of opioid analgesics. Fear of respiratory depression should not interfere with provision of appropriate analgesia.
- Sedation typically precedes respiratory depression; thus, monitoring for sedation should be a routine part of caring for persons who receive opioid analgesics, particularly when starting treatment or changing doses.
- In general, use of long-acting opioid analgesics should be reserved for persons who are opioid-tolerant, who are expected to require opioid-level analgesia for an extended period, and whose analgesic requirements are relatively stable.

- Equianalgesic conversion methods are easily used, but the results are estimates. Reducing the "equipotent" dose of the new analgesic by up to 50% and allowing for liberal rescue doses to treat breakthrough pain may help avoid opioid overdoses. Importantly, patients whose pain is not well-controlled at the time of drug conversion may not need to have their dose decreased, or may even require an increased dose.
- Nurses and pharmacists should actively evaluate changes in prescribed opioid regimens and question orders that appear to represent a significant increase or decrease in dosage compared with a patient's prior stable analgesic requirement.

Scott A. Strassels, PharmD, PhD, BCPS Assistant Professor, Division of Pharmacy Practice University of Texas at Austin

References

1. Pasero C, Portenoy RK, McCaffery M. Opioid analgesics. In: McCaffery M, Pasero C, eds. Pain: Clinical Manual. 2nd ed. St. Louis, MO: Mosby; 1999:161-299.

2. Ashburn MA, Lipman AG, Carr D, et al. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain. 5th ed. Glenview, IL: American Pain Society; 2003.

3. Pain scales don't weigh every risk. ISMP Medication Safety Alert! Acute Care Edition. July 24, 2002. Available at: http://www.ismp.org/Newsletters/acutecare/articles/20020724.asp. Accessed July 31, 2006.

4. Special Edition: Drug Advisory. Confusion between opioid analgesics results in deaths. USP Quality Review No. 46. February 1995. Available at: http://www.usp.org/patientSafety/newsletters/qualityReview/qr461995-02-01a.html. Accessed July 31, 2006.

5. Opium. Facts & Comparisons 4.0. Available at: http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-hcp11543&book=dfc. Accessed 4/14/2006.

6. Action may be necessary to prevent confusion between Roxane's oral liquid opiate products. ISMP Medication Safety Alert! Acute Care Edition. December 18, 1996. Available at: http://www.ismp.org/Newsletters/acutecare/articles/19961218.asp. Accessed July 31, 2006.

7. Acetaminophen (N-Acetyl-P-Aminophenol, APAP). Facts & Comparisons 4.0. Available at: http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-hcp13078&&book=dfc. Accessed July 31, 2006.

8. Ready LB, Edwards WT, eds. The Management of Acute Pain: A Practical Guide. Seattle, WA: International Association for the Study of Pain; 1992.

9. Anderson R, Saiers JH, Abram S, Schlicht C. Accuracy in equianalgesic dosing: conversion dilemmas. J Pain Symptom Manage. 2001;21:397-406. [go to PubMed]

10. Souter KJ, Fitzgibbon D. Equianalgesic dose guidelines for long-term opioid use: theoretical and practical considerations. Seminars in Anesthesia, Perioperative Medicine and Pain. 2004;23:271-280.

11. Kilbridge PM, Welelob EM, Classen DC. Development of the Leapfrog methodology for evaluating hospital implemented inpatient computerized physician order entry systems. Qual Saf Health Care. 2006;15:81-84. [go to PubMed]

Table

Table. Opioid equianalgesic dosage conversion

Drug	Parenteral (mg)	Oral (mg)	Duration of action (hr)*
Codeine phosphate or sulfate	120	200	3-4
Hydromorphone hydrochloride	1.5	7.5	2-4
Meperidine hydrochloride	75	300	2-4
Methadone hydrochloride†	5	10	6-8
Morphine sulfate	10	30	2-4
Oxycodone hydrochloride	NA	20	2-4

*Values reflect immediate-release products.

†Substantial decreases in doses may be needed when converting to methadone (~90%) because of the drug's long elimination half-life and N-methyl-d-aspartate-receptor activity.

This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. View AHRQ Disclaimers