PainWeek

ADVANCED EDUCATION

CERTIFICATION SERIES

Opioid Conversion Calculations

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Disclosures

Learning Objectives

- Describe the rationale for rotating patients from one opioid to another when treating pain
- Interpret recent research on retrospective opioid conversions and its impact on use of an equianalgesic opioid resource
- Given a simulated patient, calculate a new opioid regimen using the same opioid but with a different dosage formulation or route of administration
- Given a simulated patient, calculate a new opioid regimen that reflects switching between opioids, dosage formulations and/or routes of administration

Reasons for Changing Opioids

- Lack of therapeutic response
- Development of adverse effects
- Change in patient status
- Other considerations
  - Opioid/formulation availability
  - Formulary issues
  - Patient/family healthcare beliefs

- Opioid rotation
- Opioid substitution
- Opioid switching
- Opioid conversion calculation!

Equianalgesic Dosing Terminology

- Opioid responsiveness
  - The degree of analgesia achieved as the dose is titrated to an endpoint defined either by intolerable side effects or the occurrence of acceptable analgesia
- Potency
  - Intensity of the analgesic effect of a given dose
  - Dependent on access to the opioid receptor and binding affinity
- Equipotent doses = equianalgesic
- Equianalgesic opioid dosing

Converting Among Routes: Same Opioid

- Bioavailability
  - The rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action
- Oral bioavailability
  - Morphine 30%-40% (range 16%-68%)
  - Hydromorphone 50% (29%-95%)
  - Oxycodone 80%
  - Oxymorphone 10%

Equianalgesic Opioid Dosing

Opioid	Parenteral	Oral
Morphine	10	25
Fentanyl	0.15	NA
Hydrocodone	NA	25
Hydromorphone	2	5
Oxycodone	10 (not in US)	20

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NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

The Problem with “Those Charts”

- Source of equianalgesic data
- Patient-specific variables
- Unidirectional vs bidirectional equivalencies

5-Step OCC Process

1. Globally assess pain complaint (PQRSTU)
2. Determine TDD current opioid (LA and SA)
3. Decide which opioid analgesic will be used for the new agent and consult established conversion tables to determine new dose
4. Individualize dosage based on assessment information gathered in Step 1
5. Patient follow-up and continual reassessment (7-14 days)

TDD – total daily dose

Gammaitoni. *Clin J Pain*. 2003;19:286-297

Case 1

- HW is an 84-year-old man in a LTC facility with general debility on oxycodone 5 mg/acetaminophen 325 mg tabs, 6 per day, pain well controlled
- He can no longer swallow the tablets and his physician asks you convert him to an oral solution of oxycodone 5 mg per 5 ml

Case 1

1. Pain assessed; stable and controlled
2. 6 tabs x 5 mg oxycodone per day = 30 mg TDD oral oxycodone
3. Switching to 5 mg oxycodone by oral solution (5 mg/5 ml).
   Dose is 5 mg; volume is 5 ml (5 mg oxycodone/5 ml) q4h
4. Individualization – oxycodone is oxycodone; no need to change dose
5. Monitor response

Case 1 To Go Points

- Ignore contribution of acetaminophen
- You're going from oral oxycodone tablet (as oxycodone/acetaminophen) to oral oxycodone (oral solution)
  - The only thing you have to consider is the bioavailability difference between oxycodone as a tablet, and oxycodone as an oral solution
  - It's the same, so it's a 1:1 conversion

Case 2

- WP is a 62-year-old man with multiple myeloma and diffuse bony mets admitted to hospice
- Current analgesic regimen extended-release oral morphine 30 mg po q12h plus oral morphine solution 10 mg prn (takes six times per day), plus dexamethasone
- Admitted to inpatient to switch to IV morphine due to continued pain

Case 2

- Pain assessed
- TDD oral morphine = 30 mg po q12h = 60
- Oral morphine solution 10 mg x 6 = 60 mg
- TDD = 120 mg oral morphine
- Consult equianalgesic dosing chart for equivalency

TDD – total daily dose

Case 2

$$\frac{\text{“x” mg new opioid}}{\text{mg of current opioid}} = \frac{\text{equivalent mg new opioid}}{\text{equivalent mg current opioid}}$$

$$\frac{\text{“x” mg IV morphine}}{\text{120 mg oral morphine}} = \frac{\text{10 mg (IV morphine)}}{\text{25 mg (oral morphine)}}$$

(x)(25) = (10)(120)

X = 48 mg IV morphine per day

25%-50% increase → morphine 10 mg IV q4h (TDD 60 mg)

Case 2 To Go Points

- You're converting from morphine to morphine, BUT you're converting between routes of administration (oral to IV)
  - Morphine IV dose = ~ 1/3 of morphine PO dose
  - So, morphine IV dose is ~ 1/3 morphine PO dose (work in total daily doses for ease of calculation)

Case 2 To Go Points

- When you do a conversion calculation if you are SWITCHING from 1 opioid to a DIFFERENT opioid, you usually need to reduce the dose you calculated
  - This patient was going from morphine to morphine so you don't have to do that
- BUT he is in pain, so you need to increase the dose

Case 3

- Mrs. Smith is a 92-year-old woman with breast cancer, currently receiving MS Contin 60 mg po q12h, plus oral morphine solution 20 mg po q4h prn, taking on average 3 doses per day
- She has been on this dose for about 2 weeks, and her pain is well controlled, but she has developed visual hallucinations which she finds quite frightening

Case 3

- She has significant renal impairment (serum creatinine of 2.0 mg/dl) and this adverse effect may be due to accumulation of morphine metabolites
- Her physician would like to switch her to long-acting oxycodone
- What are the steps necessary to make this conversion?

Setting up the Conversion Equation

1. Calculate total daily dose of current opioids
2. Set up conversion ratio between old opioid (and route of administration) and new opioid (and route of administration) as follows:

$$\frac{\text{“x” mg new opioid}}{\text{mg of current opioid}} = \frac{\text{equivalent mg new opioid}}{\text{equivalent mg current opioid}}$$

Case 3

$$\frac{\text{“x” mg new opioid}}{\text{mg of current opioid}} = \frac{\text{equivalent mg new opioid}}{\text{equivalent mg current opioid}}$$

$$\frac{\text{“x” mg new opioid}}{\text{180 mg morphine}} = \frac{\text{20 mg (oxycodone)}}{\text{25 mg (morphine)}}$$

(x)(25) = (20)(180)

X = 144 mg oral oxycodone per day

Solving the Equation

- Cross multiply, solve for “x”
- Individualize dose for patient
  - Pain controlled; developed adverse effect
  - Reduce 25%-50%
  - Calculated oxycodone 144 mg po qd
  - Reduce to 72 - 108 mg po qd

Solving the Equation

- Reduce to 72 - 108 mg po oxycodone qd
- Decide how many times per day you're going to dose the new opioid; divide by the appropriate dosing interval and select a dosage that is available in that strength
- Oxycodone extended-release 30 mg po q12h (or 40 mg po q12h) with oxycodone IR 10 mg po q2h prn

Case 3 To Go Points

- In this case you are switching from 1 opioid to a DIFFERENT opioid
- Set up your ratio, calculate total daily dose of NEW opioid
  - If patient's pain was well controlled, REDUCE your calculated dose by 25%-50%
  - If patient was in pain at the time of the switch, go with calculated dose (or round down a little)
- Make sure you can GIVE the dose you recommend
  - With available tablets, capsules or oral solution

Switching

From 1 formulation or route to another of the SAME opioid

- Account for bioavailability
- Increase if patient in pain

From 1 opioid to another opioid

- Use ratios from equianalgesic chart
- If pain controlled, REDUCE calculated dose by 25%-50%
- If patient in pain, use calculated dose, or a little less

Case 4

- Mrs. Claytor is a 62-year-old woman with pancreatic cancer
- Her pain is well controlled, but she is unable to swallow the MS Contin tablets (200 mg po q12h) or even the oral morphine solution (40 mg q3h prn breakthrough pain, she uses about 1 dose per day)
- Her physician would like to switch her to a parenteral SQ morphine infusion. Recommendation?

Case 4

$$\frac{\text{“x” mg SQ morphine}}{\text{440 mg oral morphine}} = \frac{\text{10 mg SQ morphine}}{\text{25 mg oral morphine}}$$

Cross multiply and solve for “x” as follows:

(25)(x) = (10)(440)

25x = 4400

x = 176 mg SQ morphine per day

176 / 24 hours = 7.3 mg/hour

Recommend 7 mg/hour

Case 4

- Bolus dose?
  - 50%-100% of hourly infusion rate
  - 3.5 - 7 mg every 30 minutes SQ (could extend dosing interval once stable)
- When should the continuous infusion start relative to the last dose of MS Contin?

Case 4 To Go Points

- You are switching from oral morphine to IV morphine
  - But you've been asked to calculate a continuous infusion
- No need to dose reduce due to lack of cross-tolerance (morphine to morphine)
- No need to change dose you calculate (no mention of uncontrolled pain)
- Calculate infusion rate, AND bolus dose

Self-Assessment!

- If you're switching a patient from 1 formulation to a different formulation of the SAME opioid, which of the following should you account for?
  A. Comparative bioavailability of the 2 formulations
  B. Increased sensitivity to the new regimen
  C. Need to increase calculated dose due to pain control not at goal
  D. A and C
  E. A, B, and C

Self-Assessment!

- If you're switching a patient from 1 formulation to a different formulation of the SAME opioid, which of the following should you account for?
  - A. Comparative bioavailability of the 2 formulations
  - B. Increased sensitivity to the new regimen
  - C. Need to increase calculated dose due to pain control not at goal
  - D. A and C
  - E. A, B, and C

Case 5

- MJ is a 68-year-old man admitted for total hip replacement
- He was started on a PCA pump, hydromorphone 0.2 mg IV q10min
- From hours 49-60 he used a total of 7.2 mg IV hydromorphone
- Convert to shorting-acting AND long-acting oral morphine (at 50% of IV requirements)

Case 5

- 7.2 mg IV hydromorphone over 12 hours = 14.4 mg IV hydromorphone over 24 hours

$$\frac{\text{“x” mg PO morphine}}{\text{14.4 mg IV HM}} = \frac{\text{25 mg PO morphine}}{\text{2 mg IV HM}}$$

(2)(x) = (25)(14.4)

X = 180

Reduce by 50% - 90 mg oral morphine a day

90 mg/6 = 15 mg → MSIR 15 mg po q4h

LA MS

MS Contin 45 mg po q12h
Kadian 50 mg po q12h
Oramorph SR 30 mg po q8h

Case 5 To Go Points

- Going from IV to oral opioid
- This is ACUTE pain – should be getting better every day
- Consider giving as short-acting opioid
  - Unless pain expected to last a good while, then consider long-acting opioid

Case 6

- Mr. Crippen is a 58-year-old man who was admitted to an inpatient hospice facility for pain out of control
- Several days after admission, his pain is now well-controlled on a PCA IV morphine infusion at 1.5 mg/hour, plus 0.5 mg for breakthrough.
- On average he uses 8 doses of breakthrough per 24 hours

Case 6

- His physician would like to convert him to an oral opioid for discharge
- What do you recommend?
- Calculate an equivalent dose of oral morphine
- How about oral oxycodone?

Case 6

- 1.5 mg/hour IV morphine x 24 hours = 36 mg IV morphine per day
- Plus 8 x 0.5 mg bolus = 4 mg IV morphine
- TOTAL daily IV morphine dose = 40 mg
- Total daily oral morphine dose = 100 mg
  - MS Contin 45 mg po q12h
  - MSIR 15 mg po q2h prn

Case 6

- TOTAL daily IV morphine dose = 40 mg

$$\frac{\text{“x” mg po oxycodone}}{\text{40 mg IV morphine}} = \frac{\text{20 mg po oxycodone}}{\text{10 mg SQ morphine}}$$

80 mg oral oxycodone total daily dose

Reduce 25%-50% to 40-60 mg oxycodone per day

Case 6 To Go Points

- This is a patient with advanced illness – pain will NOT be improving (will likely worsen)
- Going from parenteral to oral morphine – account for bioavailability, but otherwise no need to adjust
- Going from parenteral morphine to oral oxycodone – need to account for bioavailability AND dose reduce because his pain was controlled

Case 7

- Mr. Johnson is a 62-year-old cancer pain patient who is unable to swallow tablets or oral solution
- He refuses rectal administration of medications and is not interested in a parenteral infusion
- He is currently receiving Oramorph SR 30 mg po q8h with oral morphine solution 10 mg po q3h prn (taking about 4 doses per day)

Case 7

- His pain is well controlled on this regimen
- What do you need to consider before converting him to transdermal fentanyl (TDF)?
- How do you make this conversion?

Case 7

- Calculate total daily dose of morphine:
  - Oramorph 30 mg po q8h = 90
  - Oral morphine solution 10 mg x 4 per day = 40
  - TDD = 130 mg oral morphine
- Generally give 50% of total daily morphine dose as transdermal fentanyl
  - TDF in mcg/hour ~ 50% of oral morphine TDD
- 65 mcg – need to round up or down
  - Transdermal fentanyl 50 mcg/hour q3days
- Considerations? Timing?

Case 7 To Go Points

- You CANNOT start transdermal fentanyl is an opioid-naïve patient (must meet FDA definition)
- If patient not on oral morphine, convert to oral morphine total daily dose
- Take 50% of oral morphine TDD and that's ~ the mcg/h TDF patch strength

Breakthrough Pain

- Spontaneous
  - Idiopathic, occurring with no known stimulus
- Incident
  - Secondary to a stimulus which the patient may or may not be able to control
- End-of-dose failure
  - Pain at the end of the dosing interval of a long-acting opioid

Types of Breakthrough Pain

	Characteristics	Management Strategies
Spontaneous	•Pain that requires no precipitating stimulus. •Can occur without warning and be acutely severe. •Spontaneous pain commonly has a neuropathic component.	•Immediate-release opioid on an as-needed basis. •Consider use of a co-analgesic (particularly if neuropathic).
Incident pain; volitional	•Consistent temporal causal relationship with identifiable causes that are under the patient's control such as patient-precipitated movement, wound, or personal care.	•Nonopioid or immediate-release opioid, on an as-needed basis .prophylactically; rest; ice; patient education.
Incident pain; nonvolitional	•Consistent temporal causal relationship with identifiable causes that are NOT under the patient's control such as sneezing, bladder spasm, or coughing.	•Immediate-release opioid on an as-needed basis.
End-of-dose	•Pain that recurs before the next scheduled dose of the around-the-clock analgesic. •Likely due to a subtherapeutic dose of analgesic.	•Increase in dose and/or frequency of around-the-clock analgesic.

McPherson ML. *Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing*. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2009.

BTP Assessment Questions

- Do you have episodes of severe pain or BTP?
- How many episodes of BTP do you have each week? Each day?
- How long is it from the time the pain first occurs to when the pain is at its worst?
- How long does each episode of BTP last (minutes, hours)?
- On a scale of 0 to 10, with 0 being no pain and 10 being the worst pain you can imagine, how much does an episode of BTP hurt when it occurs?
- Describe where the BTP occurs. What does it feel like?
- Is the BTP similar to or different from your baseline persistent pain?
- Does your BTP occur with movement or other activity, spontaneously (not associated with any activity), or just before you are supposed to take your next dose of pain medicine?

Bennett. *P&T.* 2005;30:354-361.

BTP Assessment Questions

- What impact does BTP have on your daily responsibilities at home/work? Are you able to do the things that you want/need to do?
- Are there any things that you avoid doing or that you are unable to do only with severe pain?
- What do you do to relieve the pain?
- What types of treatments have you used? How long did you use them? Were they effective? Are they still effective?
- What drugs have you used to relieve the BTP? What were the doses? Were they effective? Are they still effective?

Bennett. *P&T.* 2005;30:354-361.

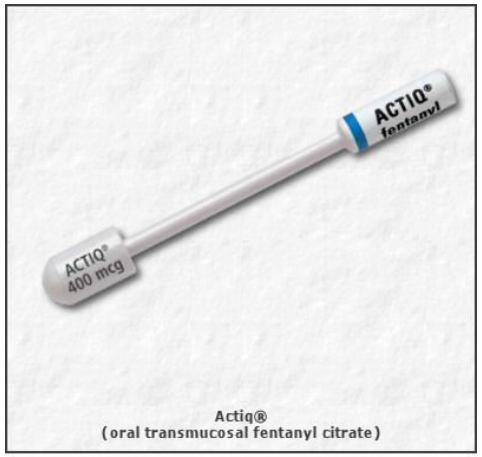
Pharmacokinetics of IR Opioids

Solubility	IR Opioids	Onset of analgesia	Duration of effect
Hydrophilic	Morphine (oral)	30-40 minutes	4 hours
	Oxycodone (oral)	30 minutes	4 hours
	Oxymorphone (oral)	30 minutes	4-6 hours
	Hydromorphone (oral)	30 minutes	4 hours
	Methadone (oral)	10-15 minutes	4-8 hours
Lipophilic	Fentanyl (transmucosal)	5-10 minutes	1-2 hours

Bennett. *P&T.* 2005;30:354-361.

Dose of Rescue Opioid

- OTFC (Actiq)
  - Opioid tolerant patients: initial dose is 200 mcg
  - If BTP not relieved in 15 minutes after completing previous dose (30 minutes after the start of the previous dose), an additional 200 mcg may be used. Do not use more than 2 units for each BTP episode.
  - Higher strengths are available:
    200, 400, 600, 800, 1200, 1600 mcg
    lozenges



Actiq®
(oral transmucosal fentanyl citrate)
Photo: usdoj.gov

www.accessdata.fda.gov/drugsatfda_docs/label/2016/020747s043s044lbl.pdf.

Dose of Rescue Opioid

- Fentanyl buccal tablet (Fentora)
  - Opioid tolerant patients: Initial dose is 100 mcg
  - If BTP not relieved in 15 minutes after completing previous dose (30 minutes after the start of the previous dose), an additional 100 mcg may be used. Do not use more than 2 units for each BTP episode.
  - Higher strengths are available:
    200, 300, 400, 600, 800 mcg

www.accessdata.fda.gov/drugsatfda_docs/label/2016/021947s024s025lbl.pdf.

Dose of Rescue Opioid

- Fentanyl buccal soluble film (Onsolis)
  - Opioid tolerant patients: Initial dose is 200 mcg
  - Single doses should be separated by at least 2 hours. Onsolis should only be used once per BTP episode
  - If one 200 mcg Onsolis film does not relieve pain, use multiples of the 200 mcg film in subsequent BTP episodes
  - Higher strengths are available:
    400, 600, 800 and 1200 mcg

www.accessdata.fda.gov/drugsatfda_docs/label/2009/022266s000lbl.pdf.

Other Transmucosal Fentanyl Products

- Sublingual fentanyl tablet (Abstral)
- Sublingual fentanyl spray (Subsys)
- Intranasal fentanyl spray (Lazanda)
- Approved FOR:
  - >18 years old, cancer breakthrough pain
  - Opioid tolerant patients (>60 mg oral morphine per day for at least 1 week)

www.accessdata.fda.gov/drugsatfda_docs/label/2016/022510s015lbl.pdf.
www.accessdata.fda.gov/drugsatfda_docs/label/2016/202788s016lbl.pdf.
www.accessdata.fda.gov/drugsatfda_docs/label/2011/022569s005lbl.pdf.

Dose of SA Rescue Opioid

- ONE dose of rescue opioid (eg, oxycodone, oxymorphone, morphine) should be 10-15% of the TOTAL daily dose of oral long-acting opioid.
  - MS Contin 30 mg q12h
  - TDD = 60 mg
  - 10% - 6 mg; 15% - 9 mg
  - Oral morphine 5 or 10 mg q2h prn breakthrough pain
- Rate pain before and after rescue opioid

Case 8

- Mrs. Hendricks is a 54-year-old woman with end-stage esophageal cancer
- She is receiving TDF 75 mcg, every 72 hours for persistent pain
- You would like to use morphine oral solution (20 mg/ml) for breakthrough pain. What dose do you recommend?

Case 8

- TDF 75 mcg ~ 150 mg TDD oral morphine
  - 10% = 15 mg
  - 15% = 22.5 mg
- Morphine oral solution, 20 mg every 2 hours as needed for breakthrough pain
- Keep a pain diary, rate pain before and after rescue opioid

Case 8 To Go Points

- TDF mcg/h x 2 ~ total daily dose oral morphine
- Apply 10%-15% rule (10%-15% of total daily oral morphine dose = **1** dose of breakthrough short-acting opioid)

Opioid Dosage Escalation Strategies

- For moderate to severe pain, increase opioid TDD by 50%-100%, regardless of starting dose
- For mild-moderate pain, increase opioid TDD by 25%-50%, regardless of starting dose
- BUT USE SOME COMMON SENSE!
- Short-acting, immediate-release single-ingredient opioids (morphine, oxycodone, hydromorphone) can be safely dose-escalated every 2 hours
- Long-acting, sustained-release opioids can be increased every 24 hours (this does not include TDF or methadone)
- TDD = total daily dose; TDF = transdermal fentanyl

Self-Assessment!

- If a patient is receiving transdermal fentanyl 75 mcg/h (assume good body habitus) what would be an appropriate dose of short-acting morphine for breakthrough pain?
  A. SA morphine 5 mg po q2h prn
  B. SA morphine 10 mg po q3h prn
  C. SA morphine 15 mg po q2h prn
  D. SA morphine 20 mg po q6h prn
  E. SA morphine 30 mg po q2h prn

Self-Assessment!

- If a patient is receiving transdermal fentanyl 75 mcg/h (assume good body habitus) what would be an appropriate dose of short-acting morphine for breakthrough pain?
  - A. SA morphine 5 mg po q2h prn
  - B. SA morphine 10 mg po q3h prn
  - C. SA morphine 15 mg po q2h prn
  - D. SA morphine 20 mg po q6h prn
  - E. SA morphine 30 mg po q2h prn

Case 9

- HB is a 54-year-old secretary with severe osteoarthritis, receiving OxyContin 20 mg po q12h with Percocet (7.5 mg oxycodone/325 mg acetaminophen) for breakthrough pain
- She tells you this regimen, using 3 Percocet tablets per day, keeps her comfortable
- Do you make a change in her regimen?

Case 9

- OxyContin 20 mg po q12h = 40 mg
- Percocet – 3 x 7.5 mg oxycodone = 22.5 mg
- TDD oxycodone = 62.5 mg
- Change to OxyContin 30 mg po q12h with Percocet (7.5 mg oxycodone/325 mg acetaminophen), one tablet every 4 hours as needed for additional pain
- What if her pain had been an 8? A 3-4?

Additional References

- McPherson ML. *Demystifying opioid conversion calculations: a guide for effective dosing*, 2nd ed. Bethesda: ASHP; ©2018.
- Reddy, Akhila et al. The conversion ratio from intravenous hydromorphone to oral opioids in cancer patients. *J Pain Sympt Manag.* 2018;54(3):280-288. doi:10.1016/j.jpainsymman.2017.07.001
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