


Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Opioids and Opioid Rotation



Mary Lynn McPherson, Pharm.D., BCPS
Professor, University of Maryland School of Pharmacy
mmcphers@rx.umaryland.edu

Objectives

- At the conclusion of this lecture, the participant will be able to:
 - Describe reasons why clinicians must rotate patients from one opioid to another.
 - Explain the development of the Equianalgesic Opioid Dosing chart, and limitations with the data.
 - Perform opioid dose conversions from one oral dosage formulation to another of the same opioid.
 - Perform conversions between opioids, and between routes of administration.
 - Perform conversions to and from fentanyl dosage formulations.

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 health care beliefs
- Opioid rotation, substitution, switching
- Opioid Conversion Calculations!

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

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Equianalgesic Opioid Dosing

Drug	Equianalgesic Doses (mg)	
	Parenteral	Oral
Morphine	10	30
Buprenorphine	0.3	0.4 (sl)
Codeine	100	200
Fentanyl	0.1	NA
Hydrocodone	NA	30
Hydromorphone	1.5	7.5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tramadol	100*	120

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010.

* - Not available in the US

Notes of Interest

- Morphine
 - Chronic morphine dosing, average relative potency of IV or SQ to PO morphine is between 1:2 and 1:3
 - Oral:rectal bioavailability is approximately equivalent
- Buprenorphine
 - 0.4 mg SL ~ 0.3 mg parenteral
 - 0.3 mg IM/IV ~ 10 mg IM/IV morphine
 - 4 and 7 day patch available in Europe
 - (100:1 morphine:buprenorphine)

Notes of Interest

- Fentanyl
 - Parenteral MS:Fentanyl shown to be 100:1, clinical practice shows its between 15-112.5:1
 - Many practitioners use an equivalency of 4 mg/hour IV morphine ~ 100 mcg/hr parenteral or transdermal fentanyl
 - TDF patch (in mcg/hr) is about 50% of TDD oral morphine (25 mcg TDF ~ 50 mg po MS TDD)
- Hydrocodone
 - Equivalence to oral morphine probably less than or equal to oxycodone

Notes of Interest

- Hydromorphone
 - Oral BAB may be as high as 60%, especially with chronic dosing (range 29-95%)
 - When switching from morphine to hydromorphone or vice versa (either oral or SQ), depends on direction
 - 5:1 (M:HM) going from morphine to hydromorphone
 - 3.7:1 (M:HM) going from hydromorphone to morphine
 - Oral: rectal bioavailability approximately equal
 - FDA dosing interval for rectal HM is 6 hours

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Notes of Interest

- Oxycodone
 - Oral morphine:oxycodone ratio is between 1:1 and 2:1. Most clinicians use 1.5:1.
 - Parenteral oxycodone not available in the US; 2 mg oral oxycodone ~ 1 mg parenteral oxycodone
- Oxymorphone
 - Oral morphine:oral oxymorphone – 30:10 – 18:10
 - Oral oxycodone:oral oxymorphone – 20:10 – 12:10

Source for all notes of interest: McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. American Society of Health-Systems Pharmacists, Bethesda, MD, 2010.

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)

Gammaitoni AR, et al. Clinical J Pain 2003;19:286-297

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%

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Case 1

- HW is an 84 year old man in a LTC facility with general debility on **oxycodone 5 mg/acetaminophen 325 mg tabs**, six 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/acetaminophen 325 mg per 5 ml.

Case 1

1. Pain assessed; stable and controlled
2. Six tabs x 5 mg oxycodone per day = 30 mg TDD oral oxycodone
3. Switching to 5 ml oral oxycodone/acetaminophen solution (5/325 per 5 ml); dose is 5 ml (5 mg oxycodone/325 mg acetaminophen per 5 ml) q4h
4. Individualization – oxycodone is oxycodone; no need to change dose
5. Monitor response

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 **MSIR 10 mg prn** (takes **six times** per day), plus dexamethasone.
- Admitted to inpatient to switch to IV morphine due to continued pain.
- Oral to IV morphine – divide or multiply by 3?

Case 2

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

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Case 2

TDD current opioid X $\frac{\text{EAF new opioid}}{\text{EAF current opioid}}$ =

120 mg oral morphine X $\frac{10 \text{ mg IV morphine}}{30 \text{ mg oral morphine}}$ =

40 mg TDD IV morphine

25-50% increase - MS 7.5 or 10 IV q4h (TDD 45-60 mg)

EAF – equianalgesic factor

Case 3

- Mrs. Smith is a 92 year old woman with breast cancer, currently receiving **MS Contin 60 mg po q12h**, plus **MSIR 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.
- 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

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

$\frac{\text{"x" mg new opioid}}{180 \text{ mg morphine}} = \frac{20 \text{ mg (oxycodone)}}{30 \text{ mg (morphine)}}$

$(x)(30) = (20)(180)$

X = 120 mg oral oxycodone per day

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Solving the Equation

- Cross multiply, solve for "x"
- Individualize dose for patient
 - Pain controlled; developed adverse effect
 - Reduce 25-50%
 - Calculated oxycodone 120 mg po qd
 - Reduce to 60-90 mg po qd
- Decide how many times per day you're going to dose the new opioid; divided by the appropriate dosing interval, and select a dosage that is available in that strength.
- Oxycodone extended-release 30 mg po q12h with oxycodone IR 10 mg po q2h prn

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 one dose per day).
- Her physician would like to switch her to a parenteral SQ morphine infusion. Recommendation?

Case 4

"x" mg SQ morphine = 10 mg SQ morphine
440 mg oral morphine 30 mg oral morphine

- Cross multiply and solve for "x" as follows:
 - $(30)(x) = (10)(440)$
 - $30x = 4400$
 - $x = 146.7$ mg SQ morphine per day
 - $146.7 / 24$ hours = 6.1 mg/hour
 - Recommend 5 mg/hour
 - What about a bolus? What do you recommend?

Case 4

- Bolus dose?
 - 50-100% of hourly infusion rate
 - 2.5-5 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?

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Case 5

- 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.
- 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 5

- 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 = 120 mg
 - MS Contin 60 mg po q12h
 - MSIR 15 mg po q2h prn

Case 5

- TOTAL daily IV morphine dose = 40 mg
- $\frac{\text{"x" mg po oxycodone}}{40 \text{ mg IV morphine}} = \frac{20 \text{ mg po oxycodone}}{10 \text{ mg SQ morphine}}$
- 80 mg oral oxycodone total daily dose
 - Reduce 25-50% to 40-60 mg oxycodone per day

Case 6

- 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 MSIR 10 mg po q3h prn (taking about 4 doses per day).
- 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?

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Case 6

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

Case 7

- MR is a 91 year old woman with an end-stage malignancy.
- She had been maintained on transdermal fentanyl 50 mcg every 3 days.
- Her pain progressed, and the fentanyl was increased to 75 mcg, and then 100 mcg.
- Unfortunately, the recent dosage increases did not appreciably result in pain relief.
- MR is 5'4", and weighs 78 pounds.
- She is hypotensive and bed-bound.
- She can swallow tablets and capsules, and the physician would like to switch her to oral long-acting oxycodone.
- What do you recommend?

Case 7

- Transdermal fentanyl 100 mcg is approximately equal to 200 mg oral morphine per day.
- HOWEVER, she is very thin, and has not achieved appreciable pain relief with the dosage increase from the 50 mcg patch (equivalent to 100 mg oral morphine per day).
- Total daily dose of morphine = 100 mg
- Total daily dose of oxycodone = 66 mg
- OxyContin 30 mg po q12h with OxyIR 10 mg po q2h prn breakthrough pain.
- Or, oxycodone 10 mg po q4h with an additional 10 mg q2h prn breakthrough pain.

Case 8

- AL is a 62 year old man with a history of prostate cancer admitted to the hospital for a course of palliative radiation.
- Patient on TDF 50 mcg/h; you have been asked to switch him to a continuous IV infusion of fentanyl.
- He has oral morphine 15 mg po q2h prn for breakthrough pain available.
- AL is not in pain at this time.

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Case 8

- At time zero, remove TDF patch, establish IV access
- Provide bolus dose option, fentanyl 25 mcg every 20 minutes for the first 6 hours
- At 6 hours, the continuous infusion of fentanyl should begin at 25 mcg/h, keep bolus option
- At 12 hours increase IV infusion of fentanyl to 50 mcg/h and bolus option remains in place. Adjust as needed.

Case 9

- AL, our 62 year old man with prostate cancer admitted for palliative radiation has completed his course and is ready for discharge home.
- His current fentanyl infusion is 70 mcg/h, and he has only used his 35 mcg bolus once in the past 24 hours.
- He would like to resume TDF therapy.
- What do you suggest and how?

Case 9

- 70 mcg/h infusion – round to closest TDF strength – 75 mcg/h
- 8 am – apply 75 mcg/hr TDF patch, continue infusion and bolus option
- 2 pm (6 hours later) – reduce continuous infusion to 35 mcg/h and maintain bolus option
- 8 pm (12 hours later) – discontinue continuous infusion, maintain bolus option or switch to oral rescue analgesia at this time
- 8 am – discontinue infusion and discharge

Fentanyl Tidbits

- Converting from oral LA opioid to TDF
 - If patient not taking oral morphine, convert to oral morphine
 - Using the 2 mg oral morphine/day ~ 1 mcg/h TDF, calculate TDF patch strength
 - Advise patient to take one last dose of the oral long-acting opioid at the same time the first TDF patch is applied
 - Increase TDF if necessary in 3 days, and every 6 days thereafter

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010.

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Fentanyl Tidbits

- Converting from ATC SA opioid to TDF
 - If patient not taking oral morphine, convert to oral morphine
 - Using the 2 mg oral morphine/day ~ 1 mcg/h TDF, calculate TDF patch strength
 - Advise patient to take two or three scheduled doses of their oral SA opioid after TDF patch application: one at the time of patch application, another 4 hours later, and another 4 hours later if needed
 - Increase TDF in 3 days if necessary, then every 6

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010.

Fentanyl Tidbits

- Titrating TDF upward
 - After initiation of TDF therapy, evaluate use of rescue opioid on days 2 and 3. If patient using > doses of rescue opioid, calculate TDD of rescue opioid and increase TDF patch in equivalent amount
 - Increase by 25-50 mcg/h, but not to exceed a 100% increase. No dosage increase should exceed 50 mcg/h
 - Increase from 25 to 50 mcg/h
 - For patients on ≥ 50 mcg/h, increase by 50 mcg/h

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010.

Fentanyl Tidbits

- Converting from TDF to an oral opioid
 - Based on the TDF patch strength, calculate oral morphine evaluate (2 mg oral morphine/day ~ 1 mcg/h TDF)
 - Once the new opioid product is in the patient's home, remove TDF patch
 - For the first 12 hours after patch removal, use only the previously prescribed rescue opioid
 - 12 hours after patch removal begin with 50% calculated scheduled opioid regimen; rescue available
 - 24 hours after patch removal, increase to 100% calculated opioid regimen; rescue available

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010.

Fentanyl Tidbits

- Converting from TDF to IV fentanyl
 - Establish IV access, remove TDF patch
 - Allow "as needed" bolus dose of fentanyl
 - Six hours after TDF patch removal, begin 50% of IV fentanyl infusion (which should be 50% of the patch strength); bolus option remains in place
 - Twelve hours after TDF patch removal, increase IV fentanyl infusion to 100% of prescribed amount (which should be equal to the TDF patch strength); bolus option remains in place

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010.

Opioids and Opioid Rotation

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Fentanyl Tidbits

- Converting from IV fentanyl to TDF
 - Apply TDF patch in same strength as IV fentanyl infusion
 - Six hours after application of TDF, reduce IV fentanyl infusion by 50%; bolus option remains in place
 - Twelve hours after application of TDF, discontinue IV fentanyl infusion; bolus option remains in place
 - Twenty-four hours after application of TDF, discontinue IV fentanyl bolus

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010.


Case 10

- JT is a 53 year old male hospitalized for management of severe pain related to metastatic lung cancer.
- He had been maintained on **hydromorphone IV 4mg per hour** with prn boluses of **2 mg q 30min** and required 4 boluses per day for the past 2 days prior to discharge.
- He is able to swallow and tolerate oral meds without difficulty.
- How would you recommend his conversion to oral meds?

Case 10

- TDD IV hydromorphone
 - 4 mg/hour x 24 hours = 96 mg
 - 2 boluses x 2 mg = 8 mg
 - TDD = 104 mg
- Oral hydromorphone = 208-520 mg
- Oral morphine = 2080
- What do you recommend?

Opioid Conversion Calculations



Mary Lynn McPherson, Pharm.D., BCPS
Professor, University of Maryland School of Pharmacy
mmcphers@rx.umaryland.edu
