

Ascension St. Vincent's East

Opioid Conversion Calculations
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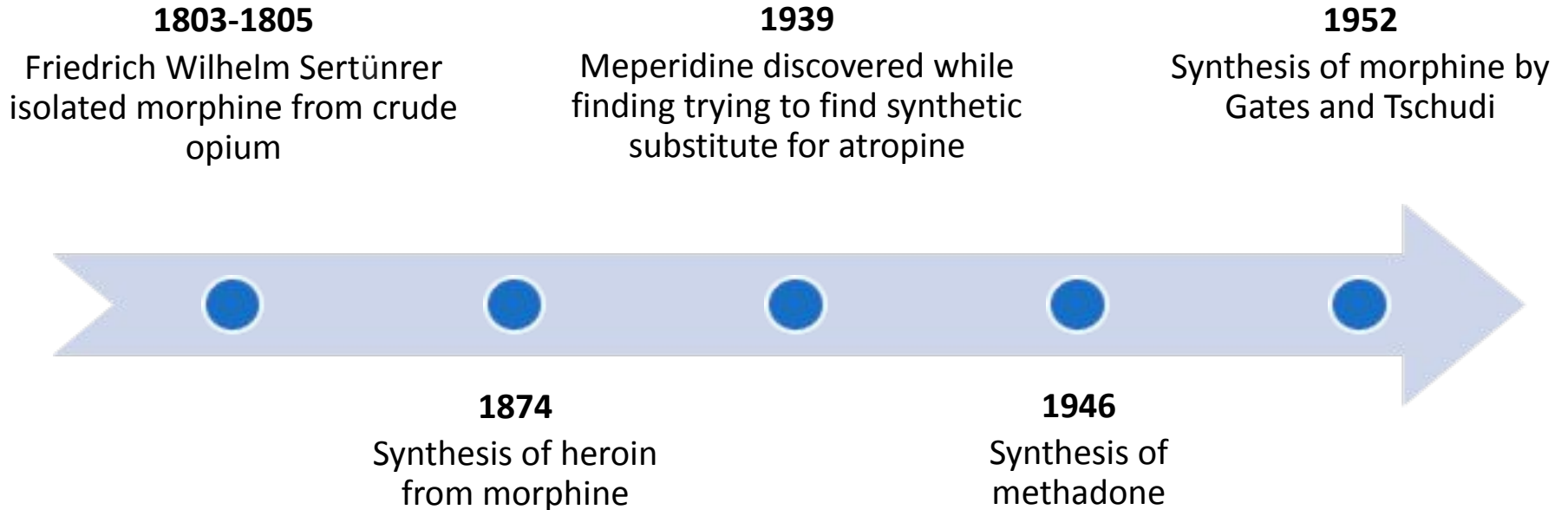
Disclosure

- No conflicts of interest or any financial relationships to disclose

Objectives

- Explain morphine milligram equivalents (MME), equianalgesic tables and their differences
- Apply equianalgesic dosing to different opioid conversion scenarios

Brief Opioid History



Opioids

Mechanism of Action: Act on opioid receptors in the CNS and periphery. Hyperpolarization of neurons and inhibition of transmitter release. Inhibition of pain pathways, altering perception and response to pain.

- Mu, Kappa, Delta main receptor types
- Can act as agonists, partial agonists, and antagonists
- Most clinical effects derived from action on mu receptor
 - Analgesia, euphoria, respiratory depression, physical dependence, etc.

Opioid Clinical Classifications

Natural

- Codeine
- Morphine

Semisynthetic

- Hydrocodone
- Hydromorphone
- Oxycodone
- Oxymorphone

Synthetic

- Buprenorphine
- Fentanyl
- Meperidine
- Methadone
- Tapentadol
- Tramadol

Opioid Chemical Classifications

Phenanthrenes	Phenylpiperidines	Diphenylheptanes	Phenylpropylamines
<ul style="list-style-type: none">● Morphine● Codeine● Hydrocodone● Hydromorphone● Oxycodone● Oxymorphone● Buprenorphine	<ul style="list-style-type: none">● Fentanyl● Meperidine	<ul style="list-style-type: none">● Methadone● Propoxyphene	<ul style="list-style-type: none">● Tapentadol● Tramadol

- True allergy to opioid is rare (< 2%)
- Very low chance of cross-reactivity when using opioid from different class

Effects and Degree of Tolerance

High	Moderate	Minimal or None
Analgesia	Bradycardia	Miosis
Euphoria, dysphoria		Constipation
Mental clouding		Convulsions
Sedation		
Respiration Depression		
Antidiuresis		
Nausea and vomiting		
Cough suppression		

Morphine Milligram Equivalents

- MME are values that represent the potency of different opioids relative to morphine
 - Hydrocodone/acetaminophen 5/325 mg x 4 tabs/day = 20 MME/day
 - Hydromorphone 3 mg/day = 12 MME/day
 - Oxycodone 60 mg/day = 90 MME/day
- CDC recommends prescribers reassess benefits and risks when MME nearing 50 MME/day and avoid increasing to ≥ 90 MME/day unless absolutely necessary/justified.
 - Dosages 50-99 MME/day 2-5 fold increase risk of overdose compared to dosages 1-19 MME/day
 - Dosages ≥ 100 MME/day up to 9 fold increased risk of overdose compared to dosages 1-19 MME/day

MME Conversion Table

Opioid	Conversion Factor
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone: 1-20 mg/day	4
Methadone: 21-40 mg/day	8
Methadone: 41-60 mg/day	10
Methadone: ≥61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3
Tapentadol*	0.4

*Tapentadol is a mu receptor agonist and norepinephrine reuptake inhibitor. MMEs are based on degree of mu-receptor agonist activity, but is unknown if this drug is associated with overdose in the same dose-dependent manner as observed with medications that are solely mu receptor agonists

Calculating MME

- 1.) Calculate total daily dose (TDD) of current opioid
- 2.) Multiply TDD of current opioid by its conversion factor

Examples:

- Hydrocodone/acetaminophen 5 mg/325 mg x 4 tabs/day (TDD 20 mg hydrocodone) x 1 = 20 MME
- Oxycodone 30 mg ER BID = 60 mg TDD oxycodone x 1.5 = 90 MME

Equianalgesic Table

Drug	Oral Dose (mg)	Parenteral Dose
Morphine	30	10 mg
Codeine	200	100 mg
Fentanyl	NA	100 mcg
Hydrocodone	30-45	NA
Hydromorphone	8	2 mg
Oxycodone	20-30	10-15 mg
Oxymorphone	10	1 mg
Methadone	Variable	
Tapentadol	NA	100

Equianalgesic Table Interpretation

- Horizontal: same drug, different route
 - Morphine 30 mg PO = morphine 10 mg IV
- Vertical: different drug, same route
 - Morphine 30 mg PO = hydromorphone 8 mg PO
- Diagonal: different drug, different route
 - Morphine 30 mg PO = hydromorphone 2 mg IV

Drug	Oral Dose (mg)	Parenteral Dose
Morphine	30	10 mg
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Fentanyl	NA	100 mcg
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Hydromorphone	8	2 mg
Oxycodone	20-30	10-15 mg
Oxymorphone	10	1 mg
Methadone	Variable	
Tapentadol	NA	100

Opioid Conversions

- Different tables/calculators have different equianalgesic recommendations, why?
 - Limited well-designed studies assessing equianalgesic dosing
 - Single dose crossover studies in acute pain versus management of chronic pain and continued dosing (at steady-state)
 - Ranges differ among studies
 - Differences in patient characteristics
 - Bottom-line: Equianalgesic tables are “ballpark” estimates

Methods of Opioid Conversions



Simple Ratio

Cross Multiplication

Proportions

Ratio Conversion

Example 1.)

Oral morphine:parenteral morphine is 3:1

- Patient getting 15 mg oral morphine would be 5 mg morphine IV

Example 2.)

Oral hydromorphone:parenteral hydromorphone is 8:2

- Patient getting 16 mg oral hydromorphone would be 4 mg parenteral hydromorphone

Cross-Multiplication Conversion

$$\frac{(x) \text{ mg TDD new opioid}}{\text{mg TDD current opioid}} = \frac{\text{Equianalgesic factor new opioid}}{\text{Equianalgesic factor current opioid}}$$

$$\frac{(x) \text{ mg TDD new opioid}}{40 \text{ mg TDD oxycodone PO}} = \frac{30 \text{ mg morphine PO}}{20 \text{ mg oxycodone PO}}$$

$$X = 60 \text{ mg morphine PO}$$

Cross-Multiplication Conversion

$(x) \text{ mg TDD new opioid}$	$=$	$\text{mg TDD current opioid}$
_____		_____
Equianalgesic factor new opioid		Equianalgesic factor current opioid

$(x) \text{ mg TDD new opioid}$	$=$	$40 \text{ mg oxycodone PO}$
_____		_____
$30 \text{ mg morphine PO}$		$20 \text{ mg oxycodone PO}$

$X = 60 \text{ mg morphine PO}$

Proportion Conversion

TDD current opioid



equianalgesic factor of new opioid

equianalgesic factor of current opioid

Oxycodone 40 mg PO



Morphine 30 mg PO

Oxycodone 20 mg PO

X = 60 mg morphine PO

Bottom Line With Conversions...

Find what works best for you!

Opioid Conversions

Steps for conversion:

- 1.) Calculate total opioids required in a 24-hour period
 - Long-acting and short-acting/actual amount used for breakthrough pain
 - Do not count doses used for volitional incident pain

- 2.) Use data from equianalgesic table to convert to TDD of new opioid

- 3.) If switching opioids, will *usually* need to decrease dose to account for incomplete cross-tolerance (i.e. decrease new opioid dose by 25-50%)

- 4.) If PRN opioid needed for breakthrough, usually provide 10-20% of TDD

Opioid Conversions

- Different options for conversions

Same opioid, same route, different formulation	Different opioid, same route
Same opioid, different route	Different opioid, different route

- Let's dive into a few examples!

Opioid Conversions

Same opioid, same route, different formulation

- 1.) Patient taking morphine sulfate IR 15 mg q4h around the clock. Decision made to switch to morphine sulfate ER.
 - 15 mg q4h x 6 = 90 mg TDD morphine sulfate IR
 - No conversions necessary since same route (1:1)
 - No need to decrease for cross-tolerance (same opioid)
 - Different morphine sulfate ER products available
 - Can do every 8 or 12 hours (i.e. 30 mg every 8 hours or 45 mg every 12 hours)

Opioid Conversions

Same opioid, different route/formulation

2.) Patient taking hydromorphone 1 mg IV q3 hours PRN. Patient has been consistently receiving about 4 doses in a 24 hour period over the past several days. Decision made to convert to hydromorphone PO.

TDD = hydromorphone 4 mg IV



hydromorphone 8 mg PO

hydromorphone 2 mg IV

- New opioid TDD = hydromorphone 16 mg PO

Opioid Conversions

Same opioid, different route/formulation

- No need to account for incomplete cross-tolerance since same opioid
- Hydromorphone 16 mg/4-6x per day = 2.67 mg q4h PRN - 4 mg q6hr PRN
- Different options (hydromorphone IR oral comes in 2, 4, 8 mg)

Opioid Conversions

Different opioid, Same route

- Patient taking morphine sulfate ER 30 mg PO BID with morphine sulfate IR 10 mg q4h PRN breakthrough pain (takes about 2 doses per day), but renal function has declined and there is concern about active metabolite accumulation. Decision is made to switch to Oxymorphone.
- TDD Morphine PO = 60 mg + 20 mg = 80 mg

Opioid Conversions

Different opioid, Same route

TDD = Morphine 80 mg PO



Oxymorphone 10 mg PO

Morphine 30 mg PO

- TDD Oxymorphone PO = 26.67 mg
- Decrease dose by 25-50% to account for incomplete cross-tolerance
 - $0.25 \times 26.67 = 6.67 \text{ mg} = 26.67 - 6.67 = 20 \text{ mg}$
- One option would be oxymorphone ER 10 mg BID with 10-20% of TDD PRN

Opioid Conversions

Different opioid, different route

3.) Patient has been receiving hydromorphone 0.5 mg IV every 3 hours PRN and has receiving about 4 doses per day consistently over the past several days. Convert to oxycodone PO.

- TDD = Hydromorphone 2 mg

Opioid Conversions

Different opioid, different route

TDD = Hydromorphone 2 mg IV	×	$\frac{\text{Oxycodone 20 mg PO}}{\text{Hydromorphone 2 mg IV}}$
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- TDD Oxycodone PO = 20 mg
- Decrease dose by 25-50% to account for incomplete cross-tolerance
 - $0.25 \times 20 = 5 \text{ mg} = 20 - 5 = 15 \text{ mg}$
- One option would be oxycodone 2.5 mg q4h PRN

Fentanyl

- Fentanyl
 - Many different formulations:
 - Parenteral
 - Transdermal
 - Buccal/transmucosal
 - High lipid solubility
 - Large volume of distribution
 - Metabolized by CYP3A4

Transdermal Fentanyl

- Indicated for **opioid-tolerant** patients with stable chronic pain
 - Not appropriate for acute pain management, uncontrolled chronic pain, or use in opioid naive patients
 - Delivers medication over 3 days (mcg/hr)
 - 47% absorbed at 24 hours
 - 88% absorbed at 48 hours
 - 94% absorbed at 72 hours
 - Comes in many strengths (mcg/hr):
 - 12 (really 12.5), 25, 37.5, 50, 62.5, 75, 87.5, 100

Opioid tolerance

Patients taking, for at least 1 week, 60 mg morphine or equianalgesic dose of another opioid. Some examples:

- Oxycodone 30 PO mg/day
- TDF 25 mcg/hr
- Hydromorphone 8 mg PO/day
- Oxymorphone 25 m PO/day
- Hydrocodone 60 mg PO/day

Opioid Conversions - Fentanyl

- Fentanyl stated to be 75-100 times more potent than morphine (mg/mg)
 - 100 mg morphine = 1 mg fentanyl (1,000 mcg)
 - 60 mg morphine = 0.6 mg fentanyl (600 mcg)
 - 600 mcg/24 hours = 25 mcg/hr
 - Duragesic manufacturer states conversion from morphine to TDF is 60-134 mg/day → 25 mcg/hr patch.
 - This is very conservative based on above math
 - Conversion listed as morphine oral 2.4:1 TDF (mg:mcg/hr)
 - Can use conversion of morphine oral ~2 mg:1 mcg/hr fentanyl to make math easier

Conversion To/From TDF

TDD Morphine PO (mg/day)	TDF (mcg/hr)
25	12
50	25
100	50
150	75
200	100
250	125

Opioid Conversions - Fentanyl

Steps for conversion to TDF:

- 1.) Calculate TDD oral morphine
- 2.) Use the conversion ratio of morphine oral:TDF (2:1)
- 3.) Round up or down to nearest patch size based on patch strengths and patient's level of pain control

Opioid Conversions - Fentanyl

Example of Conversion to TDF Patch:

4.) Patient taking oxycodone ER 60 mg PO BID and oxycodone 10 mg PO q4h PRN (usually only needs 1 dose per day)

- TDD oxycodone = 120 mg + 10 mg = 130 mg

Opioid Conversions - Fentanyl

TDD = Oxycodone 130 mg PO



Morphine 30 mg PO

Oxycodone 20 mg PO

- TDD Morphine PO = 195 mg
- $195 \text{ mg}/2 = 97.5 \text{ mcg/hr}$
- No need to decrease dose for incomplete cross-tolerance - tables account for this!
- Closest fentanyl patch size is 100 mcg/hr.
- Don't forget PRN breakthrough pain (10-20% TDD = morphine 20 mg IR q4h PRN or other short-acting equianalgesic opioid)

Titration TDF

- Shouldn't titrate until at least 3 days after initial application (may take 6 days to reach steady-state)
- Since absorption only ~47% complete at 24 hours, do not count PRN doses used during first 24 hours
 - Calculate rescue medication used during day 2 and 3.
- General rule of thumb to increase patch dose if patient requires > 3 doses of rescue medication in a 24-hour period
 - Example: patient from previous case requires 4 doses of morphine 20 mg in 24 hour period (80 mg total)
 - $80 \text{ mg} / 2 = 40 \text{ mcg/hr TDF}$
 - Increase TDF dose from 100 mcg/hr to 125 mcg/hr-150 mcg/hr

TDF - Important Considerations

- Heat increases absorption by ~33%!
 - Heating pads, blankets, hot baths, etc.
- Caution in cachectic/low body weight patients
 - Increasing doses of TDF may have little to no effect on pain
 - May be wise to convert to a different agent if able using *last effective dose* for conversion calculations

Methadone

- Mu-opioid receptor agonist. Also binds to Kappa and Delta receptors
- Serotonin and norepinephrine reuptake inhibitor
- NMDA receptor antagonist
- Quickly and widely distributed throughout the body
- Elimination half-life 5-130 hours (mean 20-35 hours)
 - Can take 4-10 days to reach steady-state!
 - Caution with toxicity given long half-life/accumulation of drug
- Drug interactions!
 - CYP3A4 (and many other CYP enzymes)
 - Big 3: amiodarone, anti-infectives, antidepressants
 - Always check when starting new agents
- QTc prolongation
 - Consider changing or decreasing dose if QTc > 450 ms
 - Change opioids or immediately reduce dose if QTc > 500 ms

Methadone

- Not linear as conversion to/from other opioids is per chart
 - Less cross-tolerance
 - NMDA receptor antagonist → decreased opioid tolerance → more sensitive to methadone
 - Opioids such as morphine or hydromorphone may have active metabolites that are proalgesic
- Switching from other opioids to methadone - doubtful will see this in the inpatient setting
 - Complicated, many different methods
- Switching from methadone to morphine (oral)
 - Various ratios proposed, but some experts propose a ratio of 1:3 when converting methadone:morphine

Buprenorphine

- Mu-opioid partial agonist
- Oral form used for opioid addiction
- Transdermal form used for chronic pain
 - Transdermal patch meant to be worn 7 days
 - Risk of QTc prolongation, thus only FDA approved for up 20 mcg/hr
 - Dosing guidelines for buprenorphine patch per manufacturer:
 - MME < 30 mg/day = 5 mcg/hr patch
 - MME 30-80 mg/day = 10 mcg/hr patch
 - Manufacturer conversion factors conservative
 - Studies have estimated conversion factor from morphine:transdermal buprenorphine probably 70-100:1
 - Bottom line: patient needs analgesic for breakthrough pain

Tapentadol

- Multiple mechanisms of action
 - Mu-opioid receptor agonist
 - Norepinephrine reuptake inhibitor
 - Studies have shown conversion from morphine:tapentadol to be ~1:3.3

Opioid Conversions

- If there are ever any questions, don't hesitate to call pharmacy!

Thank You!

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