OPIOIDS-
PRACTICE ESSENTIALS

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1

Disclosure Slide

Julie M. Lehn, PharmD, BCGP

- No conflicts of interest to disclose
- No financial conflicts to disclose
- Presentation is educational in nature

2

At the conclusion of this session participants should be able to

- Select the most appropriate opioid agent(s) to treat a patient's pain
- Perform equianalgesic conversions from one opioid entity to another
- Strategically establish an appropriate dosing regimen for Patient Controlled Analgesia (PCA)
- Convert opioids from one dosage form to another

3

Patient Interview

- Details about the patient's pain syndrome (OOPQRST)
  - Opioid Naïve?
  - Onset
  - Precipitating and palliating factors
  - Quality
  - Region and radiation
  - Severity
  - Temporal-constant or intermittent

4

Pain Source	Pain Character	Drug Class Therapy Examples
Somatic Pain	Constant and localized Often worse with movement Aching gnawing	Muscle relaxants APAP NSAIDs
Bone Pain (axial skeleton with thoracic and lumbar spine most common)	Deep, aching, throbbing Punctuated by sharper intense pain Often triggered by movement	NSAIDs Corticosteroids Bisphosphonates Radiation therapy
Visceral pain (injury to sympathetically innervated organs)	Pain is vague in quality Sharp and deep Aching, dull, squeezing, colicky and referred pain	Opioids
Neuropathic pain (injury to some element of the nervous system; plexus or spinal root)	Burning, stinging, tingling, weakness, radiation, numbness or altered sensation	Tricyclic antidepressants Opioids
Nerve damage dysesthesia (may not respond well to opioids)	Dysesthesia, burning, tingling, numbing, shooting electrical pain	Anticonvulsants

5

Major Adverse Effects of Opioids

Effect	Manifestation
Mood Changes	Dysphoria or euphoria
Somnolence	Lethargy, drowsiness, apathy, inability to concentrate
Stimulation of chemoreceptor trigger zone	Nausea, vomiting
Respiratory depression	Decreased respiratory rate
Histamine release	Pruritis, urticaria, asthma exacerbation
Decreased GI motility	Constipation
Tolerance	Larger doses required for same effect
Dependence	Withdrawal symptoms upon abrupt discontinuation

6

A patient with metastatic lung cancer presents with intractable leg pain. The pain is described as deep and throbbing. With movement there is sharp, intense pain that is short-lived. Assuming no contraindications to therapy, what would be the best initial treatment option?

- Prn opioids
- Prn muscle relaxants
- Scheduled tricyclic antidepressants
- Scheduled NSAIDs

7

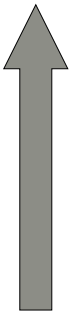
Opioid Characteristics

Opioid	Bioavailability of Oral	Active Metabolite	Metabolism	Primary Route of Elimination
Codeine	~50	Morphine	Hepatic	Urine (3 to 15% unchanged)
Morphine	~20 to 30	Morphine-6-glucuronide Normorphine Morphine-3-glucuronide	Hepatic	Urine (2 to 12% unchanged)
Hydromorphone	~60	Hydromorphone-3-glucuronide	Hepatic	Urine
Fentanyl	NA	None	Hepatic	Urine (10% unchanged)
Oxycodone	100 (IR vs ER)	Negligible	Hepatic	Urine
Methadone	~80	None	Hepatic	Urine (<10% unchanged)

8

Duration of Opioid's Analgesic Effect

- Methadone
- Extended release PO
- Immediate release PO
- Other IV opioids
- Fentanyl IV



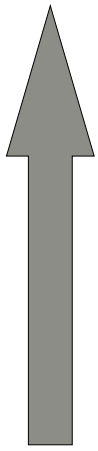
Longest

Shortest

9

Relative Potency

- Fentanyl
- Methadone
- Hydromorphone
- Oxycodone
- Morphine
- Codeine
- Hydrocodone



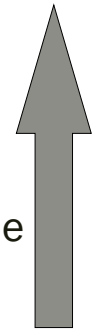
Most Potent

Least Potent

10

Hydrophilicity versus Lipophilicity

- Fentanyl
- Methadone
- Oxycodone
- Hydromorphone
- Morphine



Lipophilic

Hydrophilic

11

Clinical Classification of Opioid

Natural	Semi-Synthetic	Synthetic
Codeine	Hydrocodone	Fentanyl
Morphine	Hydromorphone	Methadone
	Oxycodone	
	Oxymorphone	

You are transitioning a patient from oral morphine to an equianalgesic dose of oral oxycodone. Considering what you know about opioid potency, you would expect the oxycodone dose in milligrams to be less than the morphine dose in milligrams.

- True
- False

13

Equianalgesic Dosing

Opioid	IM/IV (mg)	PO (mg)	Duration (hrs)
Codeine	120	200	4 to 6
Morphine	10	30	3 to 6
Hydromorphone	1.5	7.5	4 to 6
Fentanyl	0.1 (100 mcg)	NA	1 to 2
Oxycodone	NA	20	4 to 6
Tramadol	100	120	9
Methadone	consult a provider with expertise in dosing		

14

Calculating the Equianalgesic Dose

$$\frac{\text{x mg of new opioid (PO morphine)}}{\text{10 mg PO oxycodone}} = \frac{\text{30 mg PO morphine}}{\text{20 mg PO oxycodone}}$$

Cross multiple: 30mg x 10mg = 300mg

300 = 20 x

300 ÷ 20 = x

X = 15 mg PO morphine as new drug/dose

Double check based on your knowledge of potency.

Morphine is LESS potent than oxycodone so we would expect the morphine dose to be GREATER than the oxycodone dose

15

Selecting a Starting Dose and Interval

- *Opioid naïve or tolerant?*
- *PRN or scheduled?*
- *Immediate or extended release?*

16

Opioid Naïve or Tolerant

- Naïve
  - Start low-go slow
  - Consider outpatient dosing
- Tolerant
  - Moderate pain 25-50% increase from baseline
  - Severe pain 50-100% increase from baseline

17

As Needed or Scheduled

- As needed (prn)
  - Mild to moderate pain
  - Opioid Naïve
  - Impaired organ function
- Scheduled
  - Poor control despite adequate prn
  - Moderate to severe pain

18

Immediate or Extended Release

- Immediate Release
  - Short duration anticipated (e.g. post-op)
  - Opioid Naïve
  - Symptoms less than 50% of day
  - Mild to moderate pain
  - Opioid Naïve
  - Impaired organ function
- Extended Release
  - Extended duration expected (e.g. cancer pain)
  - Poor control despite adequate prn
  - Pain greater than 50% of the day
  - Moderate to severe pain
  - Normal organ function

19

A 40yo patient presents with acute renal failure and altered mental status. Patient has chronic back pain for which he takes Morphine ER 30mg orally twice daily and Percocet 5/325 mg orally every 4hrs as needed as an outpatient. Patient generally takes 2 to 3 Percocet in 24 hours. Given no formulary constraints, what would be the best option for controlling the pain as an inpatient?

1. Discontinue the morphine ER and start a fentanyl PCA with 12.5 mcg on demand every 20 minutes
2. Continue the outpatient pain regimen
3. Schedule morphine immediate release 15mg orally every 6 hours
4. Change morphine ER to oxycodone ER 20mg orally every 12 hours with Percocet (5/325mg) 1 tab orally every 8hrs as needed for breakthrough pain

20

IV to Oral Conversion

- Acute versus chronic pain syndromes
- Oral dose is generally higher than IV dose
- Add total amount of IV drug (whether by IV prn or via PCA) used over 24 hours for past 24 to 72 hours
- Sublingual doses forms may need to be titrated based on effect versus mathematical conversions

21

Patient Controlled Analgesia (PCA)

- Unsure of requirement?
  - Start reasonable demand dose for patient-specific characteristics
  - Re-evaluate requirements periodically and consider dose changes based on previous requirements
- Basal rate or not?
  - Opioid naïve patients must generally “earn it”
  - Chronic opioids with history of extended release use

PCA Initial Doses

	Morphine 1 mg/mL	Hydromorphone 0.2 mg/mL	Fentanyl 20 mcg/mL
Infusion (continuous):	0 to 2 mg/hr	0 to 0.3 mg/hr	0 to 25 mcg/hr
If opioid naïve:	1 mg/hr	0.2 mg/hr	10 mcg/hr
Loading Dose:	4 to 8 mg	0.5 to 1 mg	50 mcg
If opioid naïve:	2 to 4 mg	0.5 mg	12.5 to 25 mcg
PCA Demand Dose:	1 to 2.5 mg	0.2 to 0.4 mg	10 to 25 mcg
If opioid naïve:	1 mg	0.2 mg	10 mcg
Lockout Interval	12 to 20 minutes	8 to 20 minutes	6 to 15 minutes
If opioid naïve:	12 to 20 minutes	8 to 20 minutes	6 to 15 minutes
4-Hour Limit (Optional)	Total of maximum demand doses in 4 hrs +/- basal dose for 4 hrs	Total of maximum demand doses in 4 hrs +/- basal dose for 4 hrs	Total of maximum demand doses in 4 hrs +/- basal dose for 4 hrs

23

Evaluation of Therapeutic Outcomes

- Consistently monitor effectiveness versus side effects
- Functional status versus numerical rating scale
- Titrate treatment as warranted by prn use
- If intubated or sedated, monitor agitation, vital signs and general appearance

24

Take Home Points

- Use characteristics and description of pain to guide initial therapy
- Be consistent in the conversion ratios used
- Double check your math
- Remember incomplete cross-tolerance
- Consider all angles

Resources and References

- Demystifying Opioid Conversion Calculations by Mary Lynn McPherson
- Methadone Safety: A Clinical Practice Guideline From the American Pain Society and College on Problems of Drug Dependence, in Collaboration With the Heart Rhythm Society by Chou R, Cruiani RA, Fiellin DA et al. J Pain. 2014 Apr;15(4):321-37.
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