IV Methadone: When All Else Fails

Annas Aljassem, MD
Levi M. Hall, PharmD, BCPS

Disclosure

- Nothing to disclose

Objectives

- Summarize current evidence based recommendations on indicated uses of parenteral methadone
- Describe the pharmacokinetic and pharmacodynamics properties of methadone
- Identify medical staff and patient/family education needs and implementation strategy
- Evaluate case series and outcomes of opioid-tolerate patients receiving parenteral methadone
- Explore logistics of adding parenteral methadone to your health system formulary, establishing medication prescribing guidelines, development of an order set in electronic health record, and identifying a list of approved prescribers

PAINWEEK

Patient Case: RF 67-Year-Old Man

- CC: Admitted to hospital in with 10/10 pain, dysphagia and 30 pound weight loss
- HPI:
  - Increasing dysphagia resulting in NPO x 3 months
  - Headache in temporal region radiating to left jaw and neck
- PMH: Stage IIIC squamous cell cancer of mid and distal esophagus
- Medication
  - Hydromorphone PCA, 0.6 mg Q 6 minutes + 1 mg/hour
  - Oral morphine equivalent ~700 mg/day
  - Previous failed attempts to transition off the PCA included
    - Fentanyl patch 150 mcg/hr + hydromorphone 2 mg IV (9 doses/day) + morphine 20 mg + methocarbamol Q8H + guaifenesin w/codeine
  - After 4 week of failed pain regimens, you receive the consult to save the day and manage RF's pain

PAINWEEK

The Situation…

- Pharmacologic treatment of acute pain for opioid-tolerant patients requiring high doses of opioids (>300 mg OME per day) can be challenging, suboptimal, and is often based on expert opinions and consensus
- Patients with high OME requirements are uniquely challenging when they are admitted to the hospital due to a pain crisis because increases in traditional opioids, such as hydromorphone and fentanyl, mainly result in increased adverse side effects
- Clinicians who are experienced in pain management may consider a rotation to methadone, but are met with large differences in dosing guidelines when OME requirements reach >300 mg per day

PAINWEEK

Breaking the Pain Cycle

Our Process…

blow up your current plan

PAINWEEK

Breaking the Pain Cycle

- What is the cause of the pain?
  - Did you prescribe the correct class of pain medicine?
- Evaluate complete pain history
  - What medication was tried in past?
  - What worked in the past/now?
- Streamline current opioids
  - One long-acting and one short-acting *plus* IV push opioid for BTP
  - Titrate doses based on monitoring outcome
- Optimize nonopioids/adjuvant agents
  - Schedule APAP
  - Order adjunctive medication ATC with HOLD parameters (aka "RN must offer, patient may refuse")

PAINWEEK

Pain Pearls: Total Pain Syndrome

- If **anxiety, depression or insomnia** is documented in the problem list, is each being addressed with medical management?
  - Anxiety:
    - PRN: buspirone >> BZDs (try to avoid opioids + BZD combo)
    - Constant: SSRI >> SNRI/TCA
  - Depression:
    - First line: SNRI >> TCA
    - Second line: SSRI (no benefit to pain outcomes)
  - Insomnia:
    - First line: melatonin 9 mg (OTC)
    - Second line (w/muscle spasm): tizanidine 4mg QHS
    - Third line: trazodone 50 mg
    - Third line: zolpidem 5 mg or temazepam 15 mg

6/4/18
PAINWEEK

Opioids: Side Effects

Common side effects

- Constipation
- Nausea
- Sedation
- Confusion
- Hallucination
- Sweats
- Dry mouth

Uncommon side effects

- Urinary retention
- Pruritus
- Delirium
- Myoclonus
- Hyperalgesia
- Seizures
- Respiratory depression

Miaskowski C, et al. APS Guideline for the Management of Cancer Pain in Adults and Children, 2005.
Emanuel LL, et al. EPEC-O. Education in Palliative and End-of-Life Care – Oncology, 2005.
Swarm R, et al. NCCN Clinical Practice Guidelines in Oncology™ Adult Cancer Pain, v.1, 2007.
Levy MH. NCCN Clinical Practice Guidelines in Oncology™ Palliative Care, v.1, 2008

PAINWEEK

Opioids in Kidney & Liver Disease

Drug	Renal Failure	Dialysis	Stable Cirrhosis	Severe Liver Disease
Morphine	**Do NOT use**	**Do NOT use**	Caution (reduce dose and frequency)	**Do NOT use**
Oxycodone	Caution (reduce dose and frequency)	Caution	Caution (reduce dose and frequency)	Caution (reduce dose and frequency)
Hydromorphone	Preferred reduce dose and frequency	Preferred not dialyzed but minimal toxicity	Caution (reduce dose and frequency)	Caution (reduce dose and frequency)
Fentanyl	Preferred	Preferred not dialyzed but minimal toxicity	Preferred	Preferred
Methadone	Preferred (with consultation only)	Preferred not dialyzed but minimal toxicity (with consult only)	Preferred (with consult only)	Preferred (with consult only)

Adapted from Meridian Health System, New Jersey

PAINWEEK

Types of Pain

- Physical
- Emotional
- Total pain

- Pseudoaddiction
- Addiction

PainWeek

Assessment

- Recognize patients at **HIGH RISK** for opioid induced respiratory failure:
  - Opioid-naïve patients in acute pain
  - Obese
  - Elderly
  - History of sleep apnea
  - Impaired renal, hepatic, pulmonary, or cardiac function
    - Polypharmacy: benzodiazepines, certain antiemetics, sedatives, hypnotics or other CNS depressants

PainWeek

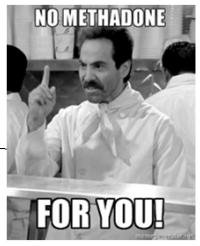
Methadone can be useful…

- Component of neuropathic pain
- Poorly controlled pain despite appropriate use of other opioids (either due to refractory pain or intolerance of side effects)
- Patients requiring high doses of opioids (>300 mg OME)
- Patient with true morphine intolerance/allergy

Mercadante S, Portenoy RK. J Pain and Symptom Manage. 2001 Mar;21(3):255-64.

PAINWEEK

Poor Methadone Candidate



- Risk of respiratory compromise in unmonitored setting
- Paralytic ileus
- History of syncope or arrhythmias
- QTc >500 msec
- Cardiac impairment
- Very limited prognosis (less than week to live)
- Multiple drug interactions
- Poor cognitive function with limited home support
- History of unpredictable adherence or misuse

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing, pp.112.

PAINWEEK

Palliative and Supportive Care (2008), **6**, 165–176. Printed in the USA.

doi:10.1017/S1478951508000254

REVIEW ARTICLES

Consensus guideline on parenteral methadone use in pain and palliative care

LAUREN SHAIOVA, M.D.,[1] ANN BERGER, M.D.,[2] CRAIG D. BLINDERMAN, M.D., M.A.,[3] EDUARDO BRUERA, M.D.,[4] MELLAR P. DAVIS, M.D., F.C.C.P.,[5] SUSAN DERBY, N.P.,[6] CHARLES INTURRISI, PH.D.,[7] JILL KALMAN, M.D.,[8] DAVENDRA MEHTA, M.D., PH.D., F.R.C.P.,[9] MARCO PAPPAGALLO, M.D.,[10] AND EUGENE PERLOV, M.D.[11]

[1]Pain and Palliative Care Physician, Bethesda, Maryland
[2]Palliative Care Service, Department of Medicine, Massachusetts General Hospital and the Harvard Medical School Center for Palliative Care, Boston, Massachusetts
[3]Department of Palliative Care and Rehabilitation Medicine, University of Texas MD Anderson Cancer Center, Houston, Texas
[4]Harry R. Horvitz Center for Palliative Medicine, Cleveland Clinic Foundation, Cleveland, Ohio
[5]Pain and Palliative Care Service, Memorial Sloan-Kettering Cancer Center, New York, New York
[6]Weill Cornell Medical College, New York, New York
[7]Cardiovascular Institute, Mount Sinai Medical Center, New York, New York
[8]Section of Cardiac Electrophysiology, Mount Sinai Hospital and School of Medicine, New York, New York
[9]Mount Sinai School of Medicine, New York, New York
[10]Visiting Nurse Service of New York Hospice Care, New York, New York
[11]Pain and Palliative Care Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, New York

PAINWEEK

N-methyl-D-aspartate (NMDA) Receptor

- Play a role in opioid tolerance, neuropathic pain, hyperalgesic states
- NMDA receptor blockers
  - **Methadone**
  - Ketamine
- Limited well-controlled trials have restricted their recognition and use
  - Hospice/palliative care teams have extensive use

Bechwith SK, Wellman C. Weiner's Pain Management. ©2007

PAINWEEK

Methadone…

- Racemic mixture of R- and S-methadone
- Synthetic opioid receptor agonists (μ,κ,δ)
- Inhibits reuptake of serotonin and norepinephrine
- Antagonists at NMDA (N-methyl-D-aspartate)
  - Prevent central sensitization
  - Reduce opioid tolerance
  - Increase effectiveness in treating neuropathic pain compared to other opioids

Bechwith SK, Wellman C. Weiner's Pain Management. ©2007

PAINWEEK

Methadone: Reasons for Resurgence

- Useful in different types of pain syndromes
- **No active metabolites**
- Positive pharmacoeconomics
  - **Methadone 10 mg, #120: $12.20**
  - Fentanyl transdermal patch 25 mcg/hr, #5: $31.19
  - Morphine ER 30 mg, #60: $50.80
  - Oxycodone ER 20 mg, #60: $138.43
- Multiple routes and dosage forms
- Oral and rectal absorption
- Favorable dosing schedule with long half-life

GoodRx, Inc. iPhone App: Dec 3, 2015 Version 4.3.10

PAINWEEK

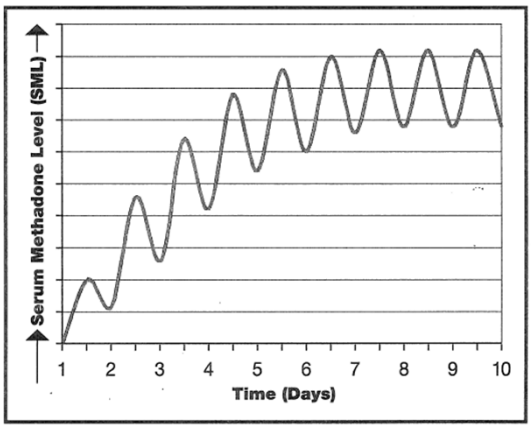
Pharmacokinetics

- Absorption
  - Almost completely absorbed by the GI tract (3x higher than other opioids)
  - Bioavailability approaching 70%-80%
- Distribution
  - Rapid and extensive distribution phase
  - Tissue stores slowly release back into plasma during redistribution → long half-life
  - Binds to alpha 1-acid glycoprotein (free fraction varies 4-fold
  - Competition for protein binding sites → increased free fraction
    - TCA and neuroleptic medications
- Metabolism/elimination
  - N-demethylation to inactive metabolite
  - Slow elimination phase (range 4.2-130 hours)
  - Eliminated mostly by the fecal route

Bruera EB, Sweeney C. J Palliative Med. 2002;5(1):127-138.

PAINWEEK

Don't start methadone and walk away!

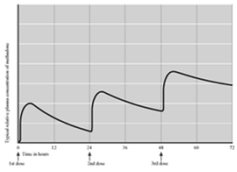


PAINWEEK

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing, pp.114.

Methadone: Oral

- Oral bioavailability 70%-80% (range 36%-100%)
- Onset 15-45 minutes after oral, peak in 2.5-4 hours
- Duration from single dose 4-8 hours



- How supplied
  - Oral solution:
    - 5 mg/5 mL
    - 10 mg/5 mL
    - 10 mg/1 mL
  - Oral tablet
    - 5 mg
    - 10 mg
- Sublingual
  - Lipophilic
  - 34% absorbed

PAINWEEK

Methadone: Parenteral (IV/SQ)

Intravenous

- Chlorobutanol, preservative increase risk of QT prolongation and Torsades
  - Prefer PF for patients with risk factors for arrhythmia
- Duration of action is 4-8 hours in single dose studies
  - Shorter than its elimination half-life

Subcutaneous

- Racemic mixture available is not always well tolerated
- Local reaction as site of injection
  - Erythema
  - Induration
- May add dexamethasone 1-2 mg per day or hyaluronidase 150 IU injection

Bruera EB, Sweeney C. J Palliative Med. 2002;5(1):127-138.

PAINWEEK

Signs of Methadone Overdose

- Methadone-associated mortality is higher shortly after initiating (3-5 days)
- Acute intoxication
  - Euphoria
  - Slurred speech
- Late signs of accumulation
  - Loud snoring
  - Slow or shallow respirations or apnea
  - Extreme tiredness or sleepiness
  - Inability to think, talk, or walk normally
  - Pinpoint pupils

Chou R, Cruciani RA, Fiellin DA, et al. J Pain. 2014;15(4):321-337.

PAINWEEK

Methadone Drug Interactions

CYP-mediated drug interactions Metabolized by 3A4, 2B6, 2C19		
Interaction Description	CYP 3A4 inhibitors Increased methaDONE levels 1-2 days for inhibition (FAST)	CYP 3A4 inducers Decreased methaDONE levels 1-2 weeks for induction (SLOW)
Examples of interacting medications	• Macrolides • Imidazoles • Fluoroquinolones • Antidepressants (SSRIs, TCAs)	• Antiepileptics • Antipsychotics • Antiretrovirals • Antitubeculars
Therapeutic Recommendations	Decrease dose empirically by 25% or more; encourage rescue medication	Encourage rescue medication and titrate appropriately

	Concurrent CNS depressants	QTc-prolonging medications
Interaction Description	Increased risk of CNS depression	Increased risk of QT-prolongation and Torsade's
Examples of interacting medications	• Alcohol • Neuroleptics • Benzodiazepines • Antidepressants	• Antiarrythmics • Antipsychotics • Antidepressants
Therapeutic Recommendations	Evaluate and recommend discontinuation of interacting medications if clinically appropriate	

PAINWEEK

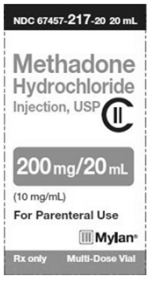
Parenteral Administration

- Intermittent IV administration
  - IV push
  - IV piggyback
- Continuous IV infusion
  - PCA
  - **PCA + CIV ± RN bolus**
  - CIV only
- Continuous SQ infusion

PainWeek

Parenteral Methadone

- Methadone PCA 50 mg/50 mL in 60 mL syringe
- Only compatible in 0.9% sodium chloride
- On formulary of accepted drugs
  - Pharmacist must place initial order
- Alaris Guardrail: methadone PCA



PainWeek

PCA Medication Order Format

- PCA Demand Dose: _____ mg
- Lockout Interval: _____ minutes
- Continuous Infusion: _____ mg/hour
- Max Limit: _____ mg/hour

- RN Bolus: ____ mg (ONCE) Q____H PRN BTP

PAINWEEK

Parenteral Methadone: Dosing

1. Convert opioid to oral methadone dose equivalent
2. TDD of IV methadone is 50% of the TDD of PO methadone
3. Divide by 24 to determine an hourly infusion rate
   or divide into intermittent doses to be administered every 6-8 hours

Shaiova L, Berger A, Blinderman CD. Palliat Support Care. 2008 Jun;6(2):165-176.

PAINWEEK

Methadone PCA Dosing Pearls

- Patient controlled analgesia (PCA) is preferred method
- Calculate a conservative initial basal rate based on current opioid use
- **Do NOT increase the basal rate for the first 12 hours after starting IV PCA therapy** (with infusion initiation or dose increase)
- PCA demand dose equivalent to the hourly infusion rate during the titration phase, offered every 15-30 minutes **(20 minutes)**
- Clinician-activated boluses at twice the hourly infusion rate may be given every hour

Shaiova L, Berger A, Blinderman CD. Palliat Support Care. 2008 Jun;6(2):165-176.

PAINWEEK

Example: Morphine PO to Methadone IV PCA

Patient JG is taking MS Contin 120 mg PO Q12H + morphINE IR 30 mg every 4 hours PRN (approximately 4 doses/day). He is no longer able to swallow oral medications, and his physician states that he thinks the patient is experiencing significant neuropathic pain not adequately treated with morphine. Therefore, the physician would like to start an IV methaDONE PCA to quickly establish a therapeutic regimen.

1. **Calculate total daily dose of opioids in morphINE equivalents:** long-acting [120 mg x 2] + short-acting [30 mg x 4] = 360 mg per day (TDD in morphINE equivalents)
2. **Utilize conversion chart to determine appropriate morphINE**: methaDONE conversion ratio, and convert to ORAL methaDONE
   a. Patient falls into the 301-600 mg morphINE mg/day category → use 10:1 ratio for morphINE: methaDONE
   b. $360\ mg\ PO\ morphine \times \frac{1\ mg\ PO\ methadone}{5\ mg\ PO\ morphine} = 36\ mg\ per\ day\ PO\ methadone$
3. **Convert PO methaDONE to IV methaDONE (2:1 ratio):** 36 mg divided by 2 = 18 mg IV methaDONE per day
4. **Divide total daily IV methaDONE requirement by 24 hours to obtain hourly infusion rate** = 18 mg/24 hours = 0.75 mg/hour
   a. CIV = 0.75 mg per hour
   b. PCA Demand dose = 0.75 mg
   c. Lockout: 15-30 minutes
   d. RN bolus: 1.5 mg Q3-4 hours PRN

Ayonrinde, 2000						
Morphine dose (mg/day)	<100	101-300	301-600	601-800	801-1000	≥1001
Morphine: methadone	3:1	5:1	10:1	12:1	15:1	20:1

PAINWEEK

Ripamonti, 1998						
Morphine dose (mg/day)	30-90	90-300	Greater than 300			
Morphine: methadone	4:1	6:1	8:1			
Mercadente, 2001						
Morphine dose (mg/day)	30-90	90-300	>300			
Morphine: methadone	4:1	8:1	12:1			
Ayonrinde, 2000						
Morphine dose (mg/day)	<100	101-300	301-600	601-800	801-1000	≥1001
Morphine: methadone	3:1	5:1	10:1	12:1	15:1	20:1
Friedman, 2004						
Morphine dose (mg/day)	<1,000 mg	<1,000 mg	>1,000-<2,000 mg		>2,000 mg	
Age	<65 years	≥65 years	N/A		N/A	
Morphine: methadone	10:1	20:1	20:1		30:1	

PAINWEEK

Loading Dose

- Loading doses are appropriate for patients who meet the following criteria
  - Pain score >5
  - RASS ≥ -1
  - Respiratory rate >10 breaths per minute and no respiratory compromise
- If pain is not controlled when starting PCA, choosing to not give a loading dose will result in treatment failure!

PAINWEEK

Pharmacokinetic Properties

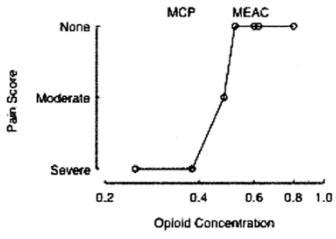
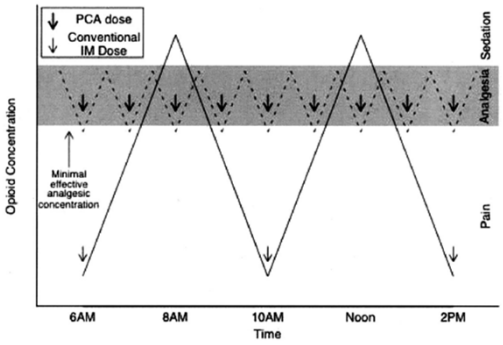


Figure 1. A theoretical representation of the steepness of the concentration/response curve for opioids is shown. The x-axis is plasma opioid concentration; the y-axis is pain rated from severe (bottom) to none (top). Circles represent sequential measurements of opioid concentration and the corresponding pain values during an interval when opioid concentration is increasing. With increasing opioid concentrations, progressive increases in concentration initially produce no change in pain, then over a finite range of concentrations, pain is attenuated, then further increases in opioid concentration produce no additional effect. MCP or "maximum concentration pain" is the maximum concentration of opioid associated with severe pain. MEAC or "minimum effective analgesic concentration" is the smallest opioid concentration at which pain is relieved. Adapted from Austin et al. (9).

Anesth Analg 2005;101:S45



Anesth Analg 2005;101:S46

PAINWEEK

Pitfalls of Opioid Rotation…

- Continuous IV infusion or too rapid oral titration may be dangerous (respiratory depression)—will need frequent dose adjustment (usually downward), if IV continuous infusion given
- Rotation from high dose morphine (eg, 300 mg/24 hrs) should be done with caution using equianalgesic tables
- This makes conversion to methadone (and other opioids) potentially quite dangerous when rotating from high dose opioid therapy
- Such rotations should generally be done in the inpatient setting
- Beware of methadone in equianalgesic; tables can be misleading

Reddy, S, et al. *J Pain Symp Mgt* 2004; 28(4): 301-303
Reddy, S, et al. J. Palliat. Med. 2010; 13 (1): 33-38

PAINWEEK

…Pitfalls of Opioid Rotation

- Be aware of the potential for inducing withdrawal with some rotations (eg, from morphine to fentanyl)
- Account for incomplete cross tolerance and underestimates of actual potency of new opioid due to individual variation when using equianalgesic tables; typically adjust the calculated dose downward by 25%-50%
- Also adjust for individual patient characteristics (psychosocial needs, prior opioid history, substance abuse history, etc)

PainWeek

Parenteral Methadone: IV → PO

- DO NOT use IV dose equal to 50% of the PO dose equivalency
- Methadone bioavailability is 70%-80%
- The 1:2 ratio assumes bioavailability of 50%
  - This low estimate of bioavailability would cause an increase in sedation and confusion
- Study of 8 cancer patients found most accurate conversion oral:parenteral methadone of 1:0.7 with good pain control
- **Multiply TDD of IV methadone by 1.3 to determine TDD of oral methadone**

Gonzalez-Barboteo J, Porta-Sales J, Sanchez D, et al J Pain Palliat Care Pharmacother. 2008;22:200-205.
McPherson ML. Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing, pp.133-134.

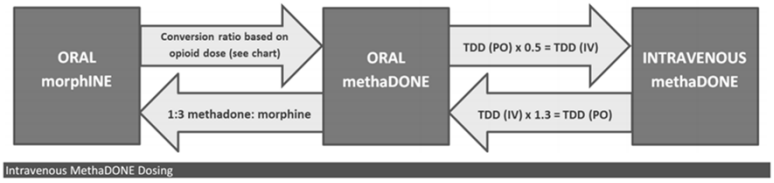
PainWeek

Example: Methadone IV to PO

One week after admission JG's pain is very well controlled on IV PCA methaDONE infusion at 1.5 mg/hour with a 1.5 mg bolus. He has only utilized one bolus dose within the past 12 hours. His physician would like to discharge the patient on oral methaDONE solution. (Note: in the setting of well-controlled pain, would only include continuous infusion dose to convert to oral methaDONE in order to decrease risk of overdose)

1. **Calculate total daily dose of IV methaDONE:** 1.5 mg/hour x 24 hours = 36 mg per day
2. **Convert IV methaDONE to PO methaDONE (IV dose x 1.3 = PO dose**): 36 mg per day x 1.3 = 46.8 mg PO methaDONE per day
3. **Divide total daily PO methaDONE dose to schedule Q8 regimen**: methaDONE 15 mg sol'n PO Q8H, first dose to be given when infusion D/C'd
4. **Calculate breakthrough regimen: 10-15% of total daily dose**
    a. 45 mg x 0.10 - 0.15 = 4.5 – 6.8 mg
    b. Breakthrough regimen: methaDONE 5 mg PO sol'n Q4H PRN

PAINWEEK



Intravenous MethaDONE Dosing

- Preferred route of administration is patient-controlled analgesia (PCA) with continuous infusion + PCA demand dose
- MethaDONE can also be administered by IV injection every 6-8 hours
- **Initial PCA dosing**
    - Calculate patient's total opioid requirement per 24 hours in oral morphINE equivalent. Include all short-acting and long-acting opioids.
    - Use the chart above (Ayonrinde, 2000) to determine the appropriate ratio to use based on the patient's current morphINE equivalents.
    - Once the proper ratio has been determined, use this to find the total daily oral methaDONE dose.
    - Reduce the new oral methaDONE dose by 50% to get the 24-hour amount of IV methaDONE.
    - Divide this total daily amount by 24 to get the hourly infusion rate; the hourly infusion rate will also be the PCA Demand dose, and the optional RN bolus will be 2x the hourly infusion rate.
- **PO to IV and IV to PO (see picture above)**
    - Total daily dose of IV methaDONE is 50% TDD of PO methaDONE; however, you **cannot** double the IV dose to obtain the PO dose due to incomplete bioavailability.
    - The IV methaDONE dose should be multiplied by 1.3 to obtain the equivalent PO methaDONE dose (based on an accepted bioavailability of ~70%)

METHADONE PCA INITIATION GUIDELINES

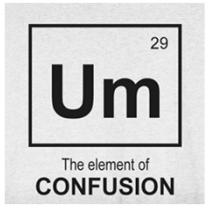
- PCA Demand dose = hourly infusion rate
- Lockout: 15-30 minutes
- CIV: hourly infusion rate
- RN bolus: 2x hourly infusion rate

PAINWEEK

Electrocardiogram Monitoring

QTc Monitoring				
• Each 10 msec increase in QTc associated with a 5-7% ***exponential increase*** in the risk of Torsades • Torsade's primarily occurs in patients with QTc > 500 msec, although risk increases starting around 450 msec.				
Electrocardiograms		QTc thresholds		Risk Factors for QTc prolongation
Baseline	Follow-up	QTc > 500	QTc = 450-500	
• Recommend a baseline EKG in patients with risk factors, prior QTc > 450, or any history suggestive of arrhythmia • Patients on methaDONE PCA need baseline and 48-hour EKGs per guideline	• Recommend if prolonged baseline QTc, or if other risk factors develop • EKG should be obtained once doses reach 30-40 mg/day, and again at 100 mg/day	• Do not start • Recommend switching • ***Immediately reduce dose—may be dose-dependent***	• Consider starting alternative agent • Consider switching to another agent • Reduce dose • Educate patient on risk of continuing therapy	• Electrolyte abnormalities ○ Hypokalemia ○ Hypomagnesemia • Impaired liver function • Structural heart disease ○ Congenital heart defects ○ History of endocarditis ○ Heart failure • Genetic predisposition • QTc-prolonging drugs

PAINWEEK



Misconception:
Ondansetron is a benign antiemetic.

PAINWEEK

Medication Prescribing Guidelines

- List of approved prescribers
- List of units approved for medication administration
- Dosing guidelines—multiple methods creates a challenge for your clinical pharmacists for order verification
- Pharmacist verification process
- Limitation on dose escalations/timing
- Pharmacy compounding/dispensing

PainWeek

Development of Methadone Order Set Within your EMR

- Developing a standardized order set for IV methadone is preferred to ensure the following:
  - Uniform dosing for all patients following EBM guidelines
  - Preparation of one medication concentration
  - Limiting prescribing ability to those credentialed to use IV methadone

PainWeek

Patient Case: Conclusion

- He was requiring: 720 mg oral morphine equivalent (via hydromorphone PCA + CIV)
- Was started on the following methadone IV PCA
  - PCA demand: 1.25 mg → 2.5 mg
  - LO: 20 minutes
  - CIV: 1.25 mg/hr → 2.25 mg/hr
  - RN Bolus: 1.25 mg per PCA pump Q4H PRN BTP → 2.5
- Final oral methadone 20 mg PO Q8H
- Outpatient follow-up regimen: methadone 5 mg PO TID PRN pain (no longer requiring scheduled methadone regimen)

PAINWEEK

Challenges

- PCA interrogation & documentation
  - PCA demands
  - PCA delivered
- Pain reassessment
- Delay in pump programming and medication procurement
- Patients chasing euphoria as experienced with previous ineffective opioid regimens
- Nursing compliance with policy and fear of patient harm

PAINWEEK

Lack of Robust EBM

- Several conversions have been published for rotating to methadone create false or misleading dose design for prescribers that are less familiar with methadone
- Numerous studies suggest that equianalgesic dose depends on the previous opioid treatment but there are few studies on the use of IV methadone for management of severe or refractory pain
- Essentially no dosing recommendations for oral morphine equivalents >2,000 mg oral morphine/day
- Must of this has been based on clinical experience (or a lack there of)
- More research is needed on dose recommendations for patients with high OME (>1,000-5,000 OME)

PAINWEEK

When all else fails…

…Call the Bearded Bandits

PAINWEEK

References

- Manfredi PL, Borsook D, Chandler SW, Payne R. Intravenous methadone for cancer pain unrelieved by morphine and hydromorphone: clinical observations. Pain 70 (1997): 99-101.
- Shaiova L, Berger A, Blinderman C, et al. Consensus guidelines on parenteral methadone use in pain and palliative care. Palliat Support Care. 208;6:165-176.
- Lossignol D, Libert I, Michel B, et al. Intravenous methadone for severe cancer pain: A presentation of 10 cases. ISRN Pain. 2012 Nov 28;2013:452957.
- Ayonrinde OT, Bridge DT. Med J Aust. 2000 Nov 20;173(10):536-40.
- Ripamonti, L. Groff, C. Brunelli, D. Polastri, A. Stavrakis, and F. De Conno, “Switching from morphine to oral methadone in treating cancer pain: what is the equianalgesic dose ratio?” Journal of Clinical Oncology, vol. 16, no. 10, pp. 3216–3221, 1998.
- Walker PW, Palla S, Pei B, et al. Switching from methadone to a different opioid: what is the equianalgesic dose ratio? J Palliat Med. 2008;11:1103-1108
- Weschules DJ, Bain KT. A systematic review of opioid conversion ratios used with methadone for the treatment of pain. Pain Med. 2008;9:595-612.
- Gonzales-Barboteo J, Porta-Sales J, Sanchez D, et al. Conversion from parenteral to oral methadone. J Pain Palliat Care Pharmacother. 2008;22:200-205.

PaiNweek

PaiNweek®

IV Methadone: When All Else Fails

Annas Aljassem, MD