Methadone for Chronic Pain Management

Melanie Simpson, RN,C, MS, OCN, CHPN
Pain Management Resource Team
The University of Kansas Hospital

Methadone – Unique characteristics

- Synthetic mu opioid
- Developed more than 50 years ago
- Lack of known active metabolites
- No dose adjustments in renal insufficiency
- Has a phenylethylamine structure which is similar to propoxyphene

Layson-Wolf, et al 2002

Methadone – Unique characteristics

- Long and unpredictable half-life (12-120 hours)
- Initially short analgesic action (4-6 hours)
- After 3-4 days - terminal half-life can become quite prolonged (90-120) hours
- Half-life does not match the duration of analgesia (6-12 hours)


Methadone – Unique characteristics

- 3-5 half-life elimination periods to obtain steady state – do not increase dose rapidly to avoid accumulation and overdose
- High lipid solubility – excellent absorption and bioavailability (~80%) PO, PR
- Action as a noncompetitive N-methyl-D-aspartic acid (NMDA) receptor antagonist –blocks hypersensitivity to mechanical stimuli in neuropathic pain and may potentiate the analgesic activity of opioids

Manfredi and Houde, 2003

Methadone – Unique characteristics

- Low cost
- Irritation to the tissues when administered SQ
- Produces only mild euphoria
- Withdrawal symptoms less than with other opioids
- “Start low and go slow”
- Use with great caution in elderly
Methadone – Unique characteristics

- Metabolized by cytochrome P450 enzymes
  - Some meds that decrease Methadone levels
    - Rifampin, Phenytoin, Carbamazepine, and many antiretrovirals
  - Some meds that increase Methadone levels
    - Amtriptyline, Ciprofloxin, Diazepam, Fluconazole, Fluoxetine, Erythromycin, Metronidazole, Propoxyphene, Spironolactone, (grapefruit juice)

Precautions

- Clinical evidence for QTc prolongation and torsades de pointes
  - PO – limited to case studies
  - IV – direct correlation (Preserved with Chlorobutanol)
    - Electrocardiograms
    - Monitor serum electrolytes (especially potassium)

Methadone

- Can be dosed q 4, 6, 8, 12, 24 hours
- “Call Pain Resource for dosing guidelines”
- Must write “for pain” on prescription
- Oral preparations
  - Dolophine
  - Solution
  - Tablets, 5, 10, 40 mg

Methadone Distribution, by Formulation, 1998 - 2002 (grams per 100,000 population)

Source: Adapted from DEA ARCOS-2 data provided by June E. Howard
dpt.samsa.gov/reports/methadone_mortality-05.htm

Source: Data from IMS Health, National Prescription Audit Plus, courtesy of Laura A. Governale, PharmD
dpt.samsa.gov/reports/methadone_mortality-05.htm
Dosing Guidelines and Equianalgesia

Methadone Equianalgesia
- Very controversial
- Many, many different methods

Ripamonti Method
- Determine 24-hour oral morphine equivalent dose
- For 24-hour morphine dose of:
  - 0-90 mg use 4:1 morphine:methadone
  - 90-300 mg use 8:1 morphine:methadone
  - 300+ mg use 12:1 morphine:methadone
- Generally use another opioid for breakthrough pain

Ripamonti, et al., 1998

Morley and Makin Method
- Day 1
  - Stop morphine
  - Commence fixed-dose of methadone q 3h pm
  - Methadone dose = 1/10 of daily morphine (max 30 mg/day)
- Day 6
  - Calculate average daily methadone dose for days 4 and 5
  - Administer as BID dosing with breakthrough dose q 3h pm
  - Increase dose as needed q 4-6 days by 30-50%


Ayonrinde Method
- For 24-hour morphine dose of:
  - <100mg use 3:1 morphine:methadone
  - 101-300 mg use 5:1 morphine:methadone
  - 301-600 mg use 10:1 morphine:methadone
  - 601-800 mg use 12:1 morphine:methadone
  - 801-1000 mg use 15:1 morphine:methadone
  - >1000 mg use 20:1 morphine:methadone

Gazelle, G and Fine, P. Methadone for pain: #75, Journal of Palliative Medicine, vol.7(2), 2004
**MD Anderson Method**
- Determine 24-hour oral morphine equivalent daily dose (MEDD)
- For 24-hour morphine dose of:
  - <30 mg  Use 2:1 morphine:methadone
  - 30-99 mg Use 4:1 morphine:methadone
  - 100-299 mg Use 8:1 morphine:methadone
  - 300-499 mg Use 12:1 morphine:methadone
  - 500-999 mg Use 15:1 morphine:methadone
  - >1000 mg Use 20:1 morphine:methadone

**Edmonton Method**
- 10:1 at any dose morphine:methadone


**KUMed Method**
- For 24-hour morphine dose of:
  - <90 mg  Use 4:1 morphine:methadone
  - 90-300 mg Use 8:1 morphine:methadone
  - 300-600 mg Use 12:1 morphine:methadone
  - 600-1000 mg Use 15:1 morphine:methadone
  - >1000 mg Use 20:1 morphine:methadone

**Dosing Methadone**
- Divide the starting dose of methadone by 3 to determine the q 8 hours dose
- Stop the current opioid and begin methadone
- Use patient's current breakthrough med as needed, and record doses and times
- If pain persists, titrate methadone q 3-4 days by converting all of breakthrough and add to methadone dose

**Case study - JB**
- JB has long history of chronic pain and illness, arthritis, spinal stenosis, HTN, CHF
- Her pain management physician has her on OxyContin 240 mg q 8 h and MSIR 15 mg (1) po q 3 h prn and she averages 5 daily but feels they are not helpful – continues to have mod-severe pain
- Her total po Morphine equivalent (3 X 240) + (15 X 5) = 795 mg

**795 mg**
- 600-1000 mg Use 15:1 morphine:methadone
  - 795 ÷ 15 = 53 mg in 24 h
  - 53 ÷ 3 = 17.6
  - Start patient on 15 mg po methadone q 8 h
  - Rescue (10-20% of total opioid in 24 h)
    - 79.5-159
    - MSIR 30 mg tabs – 3-4 tabs (90-120mg) q 2 h prn
Case study - MW

- MW has sickle cell disease, his doses of MS Contin have risen steadily for the last couple of years.
- There is some concern about his opioid use so he does not receive rescue meds.
- He is now on 200 mg of MS Contin q 12 h for a total of 400 mg morphine in 24 h.
- He no longer has a payor source so he must be switched to methadone for cost issues.

Case study - TS

- MW was just admitted for sickle cell crisis. The resident writes to continue home meds:
  - Methadone 10 mg TID
  - MSIR 30 mg – one po q 4 h pm
  - And add Morphine 2-4 mg IV q 4 h pm
  - How many things can you find wrong with these orders?

Case study - KD

- KD is going home on hospice for metastatic colon cancer.
- He is now on a Dilaudid PCA – and has used 92 mg in the last 24 h (he used 86 mg the day before)
- IV Dilaudid to PO Morphine is 20:1 so 92 X 20 =1840

400mg

- 300-600 mg Use 12:1 morphine:methadone
  - 400 ÷ 12 = 33.3
  - 33.3 ÷ 3 = 11.1
  - Start patient on Methadone 10 mg po q 8 h
  - Rescue dose
    - 10-20% of 400 mg = 40-80 mg po morphine
    - MSIR 30 mg tabs – 2 tabs po q 2 h pm

60 mg

- <90 mg Use 4:1 morphine:methadone
  - 60 ÷ 4 = 15
  - 15 ÷ 3 = 5
  - Methadone 5 mg po q 8 h
1840 mg

- >1000 mg Use 20:1 morphine:methadone
- 1840 ÷ 20 = 92
- 92 ÷ 3 = 30.6
- Start Methadone 30 mg po q 8 h
- Rescue
  - 1840 ÷ 4 for po dilaudid = 460
  - 46-92 mg (Call around for 8 mg tabs or use elixir)
  - Dilaudid 8 mg - 6-10 tabs po q 2 h prn

References


Web Sites/Articles