

Dilemmas in Acute Pain Management

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Objectives

- Apply opioid dosing principles to patient controlled analgesia (PCAs)
- Discuss a management plan for opioid induced respiratory depression
- Describe opioid adjustments in renal/liver failure and the elderly

How should PCA opioids be initiated for acute pain control?

- 52 y/o M opioid naïve
- POD #0 s/p x-lap for SBO with LOA
- Morphine PCA for pain control

What is the best PCA initiation parameter order?

1. Basal rate of 1 mg/hr at night only
2. Basal rate of 0.5 mg/hr
3. Demand dose of 2 mg
4. Demand dose of 1 mg
5. Lockout time of 20 minutes

PCA Management

- FIRST ask yourself...
 - Opioid naïve or not???

PCA
Parameters
Basal
Demand
Lockout

PCA Basal Rate- Opioid Naïve

- Opioid naïve
 - No basal rate
 - Increased rates of respiratory depression
 - No improvement in pain scores

Sidebotham: JPSMx 1997; Macintyre: Br J Anaesth 2001; Krenn: Euro J Pain 2001; Didem: Can J Anesth 2003; Grass: Anesth Analg 2005; Herr: Iowa City Guideline Summary NGC-5382 2006.

PCA Basal Rate- Opioid Tolerant

- Opioid tolerant
 - Convert 24 hour total opioid requirement to hourly rate (by equianalgesic dosing)

Macintyre: Br J Anaesth 2001; Lehmann: J Pain Symptom Manage 2005; Grass: Anesth Analg 2005.

PCA Demand Dose- Opioid Naive

- Morphine 0.5, 1, 2mg
- 0.5 unable to achieve adequate analgesia
- 2 mg higher rates of respiratory depression
- 1 mg optimum starting dose

Owen: Anaesth 1989.

PCA Demand Dose- Opioid Naive

- Demand doses of IV Morphine PCA > 1 mg associated with ↑ rates of respiratory depression

Sidebotham: J Pain Symptom Manage 1997.

PCA Demand Dose- Opioid Tolerant

- Demand dose
 - 50% of the basal rate (50-100%)



Grass: Anesth Analg 2005.

PCA Lockout Time

- Based on time to peak effect



Opioid Time to Peak Effect

Route of Administration	Time to Peak Effect
Oral	60 minutes
IM/SQ	30 minutes
IV	10 minutes

EPEC Module 4 1999; APS 2003.

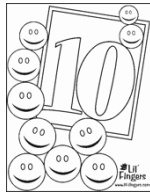
PCA Lockout Time

- Morphine 7 vs 11 minutes
- Fentanyl 5 vs 8 minutes
 - No difference in pain relief, anxiety or side effects

Ginsberg: Pain 1995.

PCA Lockout Time

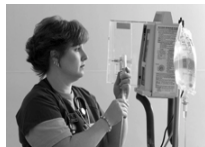
- 10 minutes is a standard interval



Ginsberg: Pain 1995; Macintyre: Br J Anaesth 2001; Walder: Acta Anaesthesiol Scand 2001; Grass: Anesth Analg 2005.

PCA Nurse Initiated Bolus

- Not studied
- Variable
- Twice the demand dose



Grass: Anesth Analg 2005.

PCA Dosing Summary

- Basal Rate
 - Opioid naïve: none
 - Opioid tolerant: Convert 24 hour total opioid requirement to hourly rate (by equianalgesic dosing)
- Demand Dose
 - Opioid naïve: 1 mg IV Morphine equivalent
 - Opioid tolerant: 50% of the basal rate
- Lockout Time
 - 10 minutes
- Nurse Initiated Bolus
 - 2x the demand dose

- 52 y/o M opioid naïve
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What is the best PCA initiation parameter order?

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What is the safest way to titrate opioids for acute pain control?

- 52 y/o M POD #8 s/p x-lap for SBO with LOA
- X-lap found pancreatic adenocarcinoma- causing severe pain
- Morphine PCA basal 4 mg/hr, demand 2 mg, lockout 10 min
- Used total 146 mg IV Morphine in past 24 hours

What is the best next step when titrating the PCA for acute pain control?

1. Increase the basal rate to 6 mg/hr
2. Increase demand dose to 4 mg
3. Decrease lockout time to 6 minutes
4. Change PCA opioid to Hydromorphone
5. Add Oxycodone SR 10 mg PO BID

Opioid Titration

- Recommendations by expert opinion / working groups
- Titrate the demand dose for acute pain

Hanks: British J Cancer 2001; Grass: Anesth Analg 2005.

Opioid Titration

- Acute control: immediate release /prn
 - Demand dose
- Chronic control: sustained release/scheduled
 - Basal rate

Grass: Anesth Analg 2005.

Opioid Titration

Pain Severity	Increase Dose By
Mild	25%
Moderate	50%
Severe	100%

EPEC Module 4 1999; NCCN Palliative Care V.1.2010.

PCA Demand Dose Titration

- Demand dose
 - Can change every 10-15 minutes if needed
 - Practically every 60 minutes and reevaluate



PCA Basal Rate Titration

- Basal rate
 - Minimum of 8-12 hours to achieve steady state (may be 12-24 hours)
 - Avoid changing more frequently than q 8 hrs
 - Every 24 hours reasonable
 - Avoid ↑ by more than 100% at a time



EPEC Module 4 1999; APS 2003.

PCA Basal Rate Titration

- Dose based on 24 hour total opioid usage
- Used total 146 mg Morphine in past 24 hrs
= 6 mg/hr

Opioid Titration

- Titrate up current opioid
 - Don't need to switch
- Opioid rotation may be helpful for refractory pain or signs of toxicity
- Avoid more than one opioid at the same time

Hanks: British J of Cancer 2001; Herr: Iowa City Guideline Summary NGC-5382 2006. Evidence Grade = C

Opioid Titration Summary

- Basal rate
 - Change ~ daily based on 24 hour opioid usage in opioid-tolerant
- Demand dose
 - Titrate for acute pain control
 - ↑ 25-50% mild-moderate pain
 - ↑ 50-100% moderate-severe pain
- Lockout time
 - Keep at 10 min

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How should I manage opioid-induced respiratory depression?

•52 y/o M POD #14 s/p x-lap for SBO with LOA, pancreatic cancer
•Morphine PCA basal 10 mg/hr, demand 5 mg, lockout 10 min
•Cross-cover: RR 7, other vitals/O2 sats stable; lethargic but arousable

What is the best next step?

1. Turn off PCA
2. Turn off PCA and administer Naloxone 0.4 mg IV (1 amp)
3. Discontinue basal rate, lower demand dose to 2.5 mg
4. Discontinue demand dose, administer diluted dose Naloxone 0.04 mg IV
5. Administer diluted dose Naloxone 0.04 mg IV

Respiratory Depression

- Incidence with PCA varies 0.19-5.2%
 - <1% with no basal
- RR or O2 sats alone are limited indicators
- Sedation precedes respiratory depression

EPEC Module 4 1999; APS 2003; Hagle: Orthopaedic Nurs 2004.

Respiratory Depression Risk Factors

- Basal infusions
- Current CNS depressant use
- Older age
- Medical comorbidities
 - Renal or liver dysfunction
 - Cardiac failure
 - Pulmonary disease
 - OSA

Hagle: Orthopaedic Nurs 2004.

Respiratory Depression Management

- Frequently drowsy, arousable, drifts off to sleep during conversation
 - Discontinue other sedatives
 - Hold basal rate
 - Decrease opioid demand dose by $\geq 50\%$

Pasero: Amer J Nurs 1994; EPEC Module 4 1999; Hagle: Orthopaedic Nurs 2004.

Respiratory Depression Management

- Somnolent, minimal or no response to stimuli
 - Discontinue other sedatives
 - Hold opioids
 - Diluted Naloxone 0.04 mg IV q 2 min prn
(0.4 mg amp in 10 mL NS = 0.04 mg/mL)
 - If vitals stable and consistent with goals, consider holding opioids with close monitoring and not administering Naloxone

Pasero: Amer J Nurs 1994; EPEC Module 4 1999; Hagle: Orthopaedic Nurs 2004.

Naloxone Risks

- Acute opioid withdrawal
 - Vomiting → aspiration pneumonia
 - Acute pain crisis → need more opioid
- Catecholamine surge
 - Cardiac arrhythmias
 - Pulmonary edema

Van Dorp: Expert Opin Drug Saf 2007.

Respiratory Depression Management Summary

- Hold/lower opioids
- Avoid Naloxone when possible
 - Diluted dosing

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Which opioid should I use in renal and liver failure?

•52 y/o M POD #14 s/p x-lap for SBO with LOA, pancreatic cancer
•Septic with MOF- ARF, liver failure, delirium; facial grimacing
•PCA Morphine basal 10 mg/hr, demand 5 mg, lockout 10 min

What is the best next step?

1. Discontinue opioids
2. Continue current opioid and PCA settings
3. Decrease Morphine PCA to basal rate 5 mg/hr, demand dose 2.5 mg, lockout time 10 minutes
4. Change PCA to Fentanyl IV basal rate 60 mcg/hr, demand dose 30 mcg, lockout time 10 minutes
5. Change PCA to Hydromorphone basal rate 3 mg/hr, demand dose 1.5 mg, lockout time 10 minutes

Renal Failure (RF)

- Majority of opioids renally cleared
- Limited studies
- No consistent GFR studied to define RF dose reductions
- Recommendations based on presence of active metabolites

Dean: J Pain Symptom Manage 2004; King: Palliat Med 2011.

Renal Failure

- Morphine, Codeine
 - potent metabolites cleared renally
 - NOT recommended in RF
- Hydromorphone, Oxycodone, Tramadol
 - Poorly studied
 - Cautious dosing
- Fentanyl
 - Limited studies
 - No known active renal metabolites
 - No dose adjustment short term
 - consider decreasing dose long term

Dean: J Pain Symptom Manage 2004; King: Palliat Med 2011.

Liver Failure

- Impaired oxidation and glucuronidation
- Limited studies- most extrapolated from RF
- High prevalence and increased risk of RF in cirrhosis
- Avoid Morphine and Tramadol
- Avoid transdermal preparations

Davis: Clin Pharmacokinetics 2007; Rhee: J Palliat Med 2007; Chandok: Mayo Clin Proc 2010.

Renal and Liver Failure Summary

- Cautious opioid dosing
- Consider short acting preparations
- Consider longer dosing intervals
- Avoid Morphine, Codeine, Tramadol
- Fentanyl safer choice

•52 y/o M POD #14 s/p x-lap for SBO with LOA, pancreatic cancer
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How should I dose adjust opioids in the elderly patient?

•78 y/o M with mild dementia, mechanical fall → hip fracture
•POD #0 L hip ORIF receiving multimodal pain therapy

What is the best next step when ordering opioids in the elderly?

1. Adjust opioids with a 50% dose reduction.
2. Avoid postop opioids to reduce risk of delirium.
3. Administer opioids via PCA for optimal acute pain control and reduced risk of delirium.
4. Use Tramadol instead of opioids for optimal acute pain control.

Opioid Reduction

- Advanced age is the best predictor of postop Morphine requirements

Macintyre: Pain 1995.

Opioid Reduction

- Opioid sensitivity increased by 50%
- Pain intensity decreased by 10-20% each decade after 60 years of age
- Require less opioid than younger patients to achieve same relief

Herr: Iowa City Guideline Summary NGC-5382 2006.

Opioid Reduction

- Initiate opioids at 25-50% lower dose than recommended for younger adults



Herr: Iowa City Guideline Summary NGC-5382 2006. Evidence Grade = B

Opioid of Choice

- Mu opioid agonists first line for moderate-severe acute pain in older adults
- Morphine opioid of choice for most
 - Caution with renal dysfunction

Herr: Iowa City Guideline Summary NGC-5382 2006. Evidence Grade = B

Opioid of Choice

- Tramadol has limited use for acute pain
 - slow titration (over weeks-months)

APS 2003. Evidence Grade = D

Opioids PO vs PCA

- N= 110, 60-85 y/o s/p THA, non-blinded
- Oxycodone PO vs IV Morphine PCA
- No difference in pain at rest or movement
- Oxycodone non-inferior to IV Morphine PCA

Rothwell: Br J Anaesth 2011.

Delirium

- N= 333, interviews, ≥ 65 y/o, noncardiac surgery, majority ortho
- 46% postop delirium
- Increased risk for postop delirium
 - Undertreated pain
 - Opioids via IV PCA (vs oral opioids)

Linnea: Anesth Analg 2006.

Delirium

- N = 541, prospective cohort
- Majority ≥ 80 y/o, all had hip fracture
- 14% postop delirium
- Increased risk for postop delirium
 - Undertreated pain
 - < 10 mg IV Morphine equivalents/day

Morrison: J Geront 2003.

Delirium

- N=100, retrospective
- Mean age 86 yrs, baseline cognitive impairment, majority fracture-related pain
- 27% postop delirium
- No association with amount of opioid

Mehta: Pain Med 2010.

Elderly and Opioids Summary

- 25-50% opioid dose reduction
- Postop opioids PO or IV PCA
- Treat pain → decrease delirium risk

•78 y/o M with mild dementia, mechanical fall → hip fracture
•POD #0 L hip ORIF receiving multimodal pain therapy

What is the best next step when ordering opioids in the elderly?

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Acute Pain Mx Summary

- Manage PCA based on opioid naïve vs tolerant
- Titrate PCA demand dose for acute control
- Hold/lower opioids for oversedation
 - Avoid naloxone when possible
- Avoid Morphine in RF/cirrhosis
- ~ 50% opioid dose reduction for moderate-severe pain in elderly
