

Perioperative Pain Management and Anesthetic considerations in the opioid tolerant patient

Is it really a “a Riddle
wrapped in a Mystery inside
an Enigma?”

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Opioid Tolerant Patient

- Types of opioid dependent patients
 - Chronic pain
 - Malignant
 - Non-malignant
 - Methadone maintenance
 - Substance abusers



Opioid Tolerant Patient

- Scope of the problem
 - Over the past decade the number of patients who are receiving opioid analgesics for chronic pain problems has increased dramatically.



Opioid Tolerant Patient

■ Factors

- Associated with the increased acceptance for the prescribing of opioids for chronic pain.....

- Physician education
- Concerns of analgesic under-medication.
- Greater variety of opioid analgesics with better side-effect profiles.....
 - Synthetic
 - Semi-synthetic
 - Delivery systems
 - SR
 - CR
 - Transdermal
- Recognition of increased morbidity associated with chronic use of NSAID's



Opioid Tolerant Patient

- Defining Chronic Pain
- ASA
 - “Pain of a duration or intensity that adversely affects the function or well-being of the patient.”



Opioid Tolerant Patient

- Defining Chronic Pain
- IASP
 - “Pain without apparent biological value that has persisted beyond the normal tissue healing time usually taken to be 3 months.”



Opioid Tolerant Patient

- Chronic Pain
 - Malignant
 - Cancer related
 - Non-malignant
 - Chronic LBP
 - CRPS
 - PHN
 - Phantom limb pain



Opioid Tolerant Patient

- Impact of Chronic opioid therapy on postoperative pain!
 - de Leon-Casasola et al
 - Studied 116 patients with cancer related pain who chronically consumed opioids.
 - Daily oral morphine equivalent of **90-360mg**



Opioid Tolerant Patient

- Impact of Chronic opioid therapy on postoperative pain!
 - de Leon-Casasola et al
 - Results (when compared to opioid-naïve patient)
 - Required 3x as much epidural morphine!
 - Required 4x as much systemic morphine!



Opioid Tolerant Patient

- Impact of Chronic opioid therapy on postoperative pain!
 - Rapp et al
 - Case-controlled retrospective study
 - 360 patients who chronically consumed opioids
 - With either malignant or non-malignant pain



Opioid Tolerant Patient

- Impact of Chronic opioid therapy on postoperative pain!
 - Rapp et al
 - Results
 - **3 fold increase** in post-operative opioid requirement in this population of patients.



Opioid Tolerant Patient

Why are chronic pain patients a unique population?

- Unique features

- Tight musculature
- Limited mobility
- Lack of energy
- Changes in appetite
- Depression
- Anger
- Anxiety

- Unique features

- Fear of the unknown
- Fear of re-injury
 - Which hampers return to work or ADLs




Opioid Tolerant Patient

■ Pain

- Disrupts sleep
- Causes
 - Irritability
 - Social withdrawal

■ Associated psychiatric diseases:


- Hypochondriasis
- Depression
- Psychosis



Perioperative management of the chronic pain patient!

■ Clinical Pearls

- Under-medication of post-operative pain can precipitate withdrawal symptoms.
- Patients may under report their use of pain medication.
- Patients may overestimate the effect of painful stimuli.
- Daily epidural and systemic morphine requirement can be increased up to 400%.



Perioperative management of the chronic pain patient!

■ Clinical Pearls

- Expect a prolonged requirement for post operative analgesia.
- Anxiety and poor coping skills may result in poor compliance with post-operative analgesic strategies.
- Expect variations in individual responses to opioid analgesics.
- Opioid dosing will require titration which optimizes analgesia and minimizes side effects.



Opioid Tolerant Patient

■ Definitions

□ Physical dependence

- “A physiologic state of adaptation to a specific psychoactive substance characterized by the emergence of a withdrawal syndrome (specific for that drug) during abstinence, which may be relieved in total or in part by re-administration of the substance.”



Opioid Tolerant Patient

■ Definitions

□ Withdrawal

- “The onset of a predictable constellation of signs and symptoms after the abrupt discontinuation of or a rapid decrease in dosage of a psychoactive substance.”



Opioid Tolerant Patient

- Withdrawal

- Opioid

- Symptoms

- Increase in sympathetic and para-sympathetic response resulting in:
 - **Hypertension,**
 - **Tachycardia,**
 - **Diaphoresis,**
 - **Abdominal cramping and diarrhea.**



Opioid Tolerant Patient

- Definitions

- Tolerance

- Rightward shift of the dose response curve



Opioid Tolerant Patient

- Definitions
 - Tolerance
 - Innate
 - Acquired



Opioid Tolerant Patient

- Definitions

- Tolerance

- Innate

- Preexisting insensitivity to a drug which is genetically determined.



Opioid Tolerant Patient

■ Definitions

□ Tolerance

■ Acquired

- Pharmacokinetic
- Learned
- Pharmacodynamic



Opioid Tolerant Patient

■ Definitions

□ Tolerance

■ **Acquired** (following multiple exposures to a chemical)

□ Pharmacokinetic

- Enzyme induction

□ Learned

- Learned compensatory mechanisms.



Opioid Tolerant Patient

- Definitions

- Tolerance

- Acquired

- Pharmacodynamic

- Neuroadaptive changes such as



Opioid Tolerant Patient

■ Definitions

□ Tolerance

- Evidence suggests that glutamate and the NMDA receptor play a critical role in the development of:
 - Wind-up
 - Tolerance
 - Opioid induce hyperalgesia



Analgesic Adjuncts

- Ketamine

- MOA

- **Non-competitive antagonist** @ the PCP receptor site in the NMDA receptor complex channel.
 - Via a Mg^{++} dependent channel blockade!



Opioid Tolerant Patient

■ Definitions

□ Cross Tolerance

- Tolerance to one opioid is transferred to a newly substituted opioid.

HOWEVER!!!!!!

■ Cross tolerance

- Is very often:
 - Incomplete!
 - Assymmetric!



Opioid Tolerant Patient

- Etiology

- Incomplete Cross tolerance

- The newly administered opioid acts at different opioid receptor subtypes.

- Differences in efficacy of the opioid agonists

- Low versus high efficacy opioids (morphine vs fentanyl)
 - Morphine occupies more receptors than fentanyl.



Opioid Tolerant Patient

- Equianalgesic dosing guidelines
 - **MUST**
 - Account for Incomplete Cross Tolerance

 - When converting from one opioid to another it is recommended that you must decrease the dose of the new opioid by **at least 50%** of the calculated equianalgesic dose!

Opioid Tolerant Patient

- Equianalgesic dosing guidelines
 - When switching the patient over to methadone the decrease in the calculated methadone dose is even **more dramatic!**
- **The potency of methadone relative to morphine is not linear!**





Opioid Tolerant Patient

- Definitions

- Addiction

- “....the aberrant use of a specific psychoactive substance in a manner characterized by loss of control, compulsive use, preoccupation, and continued use despite harm...”



Opioid Tolerant Patient

- Definitions

- Pseudo-Addiction

- “....describes the behavior of seeking more analgesic medication in response to under-treatment of the pain syndrome.”

- Patients are angry and isolated.
 - Health care provider may be frustrated and distrustful.
 - The patients drug seeking behavior disappears once the pain is adequately treated.



Opioid Dependent Patient

- What Happens!!!!
 - In the event we do not provide adequate substitution of opioids in the perioperative period.
- Withdrawal!!!!



Opioid Dependent Patient

- Question?????

- When is a patient, who is on chronic opioid therapy, considered to be at risk for displaying opioid withdrawal symptoms?



Physical Dependence

- Based on clinical experience patients with continuous opioid intake which equates to:

For a period of 2-4 weeks!

- Daily intravenous morphine equivalent exceeding 30mg
or
- Oxycontin[®] 80mg po q 12h
or
- MS Contin[®] 100mg po q 12h
- Opana[®] 20mg po q12h



Opioid Tolerant Patient

- Management Strategies of acute pain??

- **Multimodal Analgesia!**

- Opioids

- Baseline requirement
 - Acute pain requirement

- Neuraxial analgesia

- Peripheral nerve blockade

- Co-analgesics

- NMDA receptor antagonist
 - Ketamine
 - Dextromethorphan
 - Alpha-2-agonists
 - Clonidine and dexmedetomidine
 - NSAIDs
 - Acetaminophen
 - Anti-convulsants
 - Gabapentin
 - Pregabalin



Opioid Tolerant Patient

■ Strategies

- Epidural with bupivacaine plus PCA opioid
- PNB catheter plus PCA opioid
- Epidural bupivacaine with a morphine dose two fold higher than normal
- Epidural bupivacaine with sufentanil instead of fentanyl.



Ye Olde Apothecary Shoppe



■ Pain Pharmacist is crucial!

- Have them in the loop early!
 - They can create a post-operative plan.
 - Address issues:
 - Equianalgesic dosing of opioids
 - Incomplete cross-tolerance
 - Help manage PCA opioids



Management of perioperative pain in the opioid tolerant patient

■ Pre-operative management

- Continue preoperative opioid regimen
- Regional technique
 - Neuraxial technique
 - Peripheral nerve block
- Pre-medication
 - Consider
 - APAP, COX-II inhibitor, alpha-2-agonist and gabapentin.



Analgesic Adjuncts

- Anti-convulsants

- Gabapentin for Postoperative pain:

- **Movement evoked pain usually responds best!**

- Abdominal hysterectomy.
 - Mastectomy
 - ACL repair
 - ENT surgery
 - Spinal surgery

- Think of it as...

- Opioid sparing co-analgesic



Analgesic Adjuncts

■ Clonidine

- **Selective partial agonist** @ α_2

receptor:

- **Binding ratio:**

- **220:1 (α_2 : α_1)**

- $T_{1/2} = 9-12h$

■ Dexmedetomidine

- **Super selective partial agonist** @ α_2

receptor:

- **Binding ratio:**

- **1620:1 (α_2 : α_1)**

- $T_{1/2} = 2h$



Management of perioperative pain in the opioid tolerant patient

■ Intra-operative management

- Administer opioids to meet baseline needs plus intra-operative surgical requirements.
- Ketamine
 - Bolus plus infusion.
- Regional technique infusion (combined with a dexmedetomidine drip)
 - Epidural
 - Peripheral nerve blockade
 - Single shot
 - Continuous catheter



Analgesic Adjuncts

■ Ketamine:

- Opioid sparing effect.
- Improve analgesia in **opioid resistant pain.**
- May reduce opioid requirements in **opioid tolerant patients.**
- Possible preemptive analgesic effects
 - But the reviews are mixed!



Analgesic Adjuncts

- Ketamine and the patient on **chronic opioids!**
 - Intra-operatively:
 - Bolus
 - 0.25-0.5mg/kg
 - Infusion
 - 2-4mcg/kg/min



Ketamine

- In Summary:

- Ketamine is a non-competitive NMDA receptor antagonist which can potentially:
 - Enhance opioid induced antinociception!
 - Reduce hyperalgesia!
 - Prevent opioid induced tolerance!



Management of perioperative pain in the opioid tolerant patient

■ Post-operative management

- Continue the regional technique.
 - Epidural or peripheral nerve catheter
- Consider
 - Continuing APAP, NSAID, alpha-2-agonist or gabapentin orally if possible.
- Continue opioids!
- Continue an NMDA receptor antagonist.



Analgesic Adjuncts

- Post-operative treatment of morphine resistant pain!
 - 30mcg/kg morphine + saline versus
 - Morphine 15mcg/kg + Ketamine 250mcg/kg
- Results
 - Superior pain control!
 - Improved oxygen saturation!
 - Greater wakefulness!
 - Negligible PONV!



Management of perioperative pain in the opioid tolerant patient

- Pre-operative **“Fentanyl Challenge”**
 - Advantage:
 - **Easily titrated in the OR**
 - Rapid onset
 - No active metabolites
 - Can be used post-operatively as a PCA



Opioid Tolerant Patient

■ Case I

- 50 year old female s/f RCR. Allergy to sulfonamides.
 - History of CLBP
 - Oxycontin 80mg po q 12h x 12 months

■ Anesthetic Plan

- Pre-op
 - APAP, clonidine, neurontin
 - Interscalene block
- Intra-operatively
 - GA
 - Fentanyl IV (rr = 12)
 - Intraarticular bupivacaine plus morphine
- Continue oxycontin post-operatively. Percocet for break-thru pain.



Opioid Tolerant Patient

■ Case II

□ 65 year old male s/f
THA

■ History of CLBP and
OA schedule for THA

□ Does not tolerate
NSAIDs

□ MS Contin 100mg po
q12h x 3 years

□ Pre-operatively

■ Lumbar plexus and
parasacral sciatic nerve
block

□ Intraoperatively

■ GA

■ Morphine 30mg

■ Fentanyl 750mcg

□ Post-operatively

■ Continue MS Contin

■ PCA for break thru pain



Opioid Tolerant Patient

■ Case III

- 65 year old female scheduled for THA
- PMH significant for
 - CLBP
 - S/P multiple spine surgeries

□ Current meds

- Transdermal fentanyl 75mcg patches #2
- NSAID
- Anti HTN
- BZD



Opioid Tolerant Patient

■ Case III (cont)

- 65 year old female scheduled for THA

- Anesthetic Plan

- Pre operatively

- Not given

- APAP, Clonidine, Neurontin

- Patient refused

- Femoral/Sciatic nerve block

- Anesthetic plan

- Preoperatively

- Fentanyl patch continued

- Intraoperatively

- Lots of morphine

- Post-operatively

- Morphine and dilaudid did not help pain
Respiratory depression but no resolution of pain

- Low dose ketamine in recovery room

- Success!!!!



Opioid Tolerant Patient

- Case IV (Same as last patient)
 - Anterior/Posterior lumbar spine fusion
 - Intercostal nerve block
 - APAP, Clonidine, Neurontin
 - Fentanyl patch continued
 - Fell off
 - Withdrawal sx



Pediatric

■ Case

- The patient is a 7 year old male who had his foot caught in a lawn mower and sustained a de-gloving injury to the foot and amputation of the fifth toe.



Pediatric

■ Case

- The child was admitted to an outside hospital for emergent care:
 - Included irrigation and debridement and placement of a wound VAC.
- Pain control included administration of
 - Multiple opioids and anxiolytics with poor results.



Pediatric

■ Case

- The patient was subsequently transferred to the UC Davis Medical Center:
 - The Chronic Pain Service was consulted and an epidural catheter was placed
 - Became dislodged or migrated.
 - Without significant pain control.



Pediatric

■ Case

- Consultation with the Acute Pain Service
- We recommended placement of a Popliteal catheter.



Pediatric

- Popliteal Catheter

- Ropivacaine infusion 0.2% @ 3-5ml/hr x 7days.

- Additional analgesics included:

- Methadone 3mg po qid.
- Neurontin 100mg po TID
- Roxanol 2.5-5mg po q2-4h prn breakthrough pain.



Elderly

■ Case

- 85 year old gentleman with a rapidly growing right knee sarcoma s/f resection of the malignancy.

- PMH

- CAD

- s/p CABG in 1983 and 1995 and angioplasty and stent placement in 2004

- Severe aortic stenosis (valve area 0.7cm²)

- CHF/cardiomyopathy (EF 23-40%)

- SP CVA 1985 with no residual defects



Elderly

■ Case

- 85 year old gentleman with a rapidly growing right knee sarcoma s/f resection of the malignancy.

- PSH

- CABG 1983 and 1995
- Hemorrhoidectomy 1960's
- Facial cancer removal 1970
- Back surgery 1975



Elderly

■ Case

- 85 year old gentleman with a rapidly growing right knee sarcoma s/f resection of the malignancy.

- Current medications:

- Plavix, Aspirin, Cozaar, Proscar and Lipitor
- Norco (4-6 tablets qd)



Elderly

- Anesthetic Plan

- General anesthesia or neuraxial anesthesia?

- Peripheral Nerve Block

- Lumbar plexus
- Sciatic



Analgesic Adjuncts

■ Case

- 57 year old female with ESRD on HD (tue, thurs and sat) s/f left arm brachial cephalic AV fistula with superficialization.
- PMH significant for:
 - CAD (CABG in 1996)
 - NIDDM
 - HTN
 - Seizure disorder
 - Obesity (BMI 37.1)



Analgesic Adjuncts

- Case:

- Supraclavicular PNB was placed @ 1130.

- Peri-vascular approach:

- 1-2cm above the clavicle with a nerve stimulator.

- 30ml 1.5% mepivacaine with 1:200,000 epinephrine.



Analgesic Adjuncts

- Case:

- Dexmedetomidine drip for sedation begun in the OR.
 - 0.007mcg/kg/min.



Analgesic Adjuncts

- Case

- The patient arrived in the PACU @ 1710
 - Comfortably sedated.
 - Pain free.