Acute Pain Management in the Opioid Tolerant Patient

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Objectives

- The participant will be able to define opioid tolerance
- The participant will be able to identify multimodal strategies to be used in the treatment of the opioid tolerant patient

Opioids

- Most widely used and effective analgesics
- Greater awareness of pain
- More opioids being prescribed
- As exposure increases, incidence of tolerance will increase

Opioid Tolerance

- Develops with repeated use of opioids
- Need to increase dose to maintain equipotent analgesic effects
- Expected physiologic occurrence
- Does not imply or cause addiction

Ballantyne, J. NEJM 2003; 349:1943-1963

Types of Opioid Tolerance

- Associative (learned) tolerance - Related to environmental and psychological factors
  - Seen in opioid abusers
  - Seen in methadone clinics
- Non-Associative (adaptive) tolerance - Occurs at the cellular level

Ballantyne, J. NEJM 2003; 349:1943-1963

Cellular Mechanisms of Tolerance

- Uncoupling of G-proteins from opioid receptors
- Down regulation of opioid receptors
- Activation of N-methyl-D-aspartate (NMDA) receptor

Ballantyne, J., NEJM. 2003;349: 1943-53
**N-methyl-D-aspartate**

- receptors for endogenous excitatory amino acid transmitters
- NMDA receptor antagonists may prevent morphine tolerance


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**Effects of Prolonged Opioid Therapy**

- Cellular mechanisms
- Pharmacologic tolerance
- Abnormal pain sensitivity
- Apparent tolerance
- Immune changes
- Hormonal changes
- Dose escalation

Adapted from Ballantyne J: NEJM. 2003;349:1943-63

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**Immune changes**

- Opioid receptors on T-cells
- Immune cells play a role in endogenous opioid secretion
- May suppress B lymphocyte antibody production
- May suppress natural killer cell activity

Ballantyne, J., Opioid Therapy for Chronic Pain. NEJM. 2003;349:1943-53
Hormonal Changes

- Opioids influence two major systems
  - Hypothalamic-pituitary-adrenal axis: ↓ cortisol levels
  - Hypothalamic-pituitary-gonadal axis: ↓ LH, ↓ FSH, ↓ testosterone, ↓ estrogen- with subsequent ↓ libido, amenorrhea, irregular menses, hypogonadism

Ballantyne, J., Opioid Therapy for Chronic Pain. NEJM. 2003;349: 1943-53

Physical Dependence

- Development of withdrawal syndrome
- Expected physiologic occurrence
- Does not imply or cause addiction


Addiction

- Primary, chronic, neuro-biologic disease
- Loss of control
- Compulsive use despite harm
- Preoccupation with obtaining opioids despite adequate analgesia

Smith, H.S., Drugs for Pain. 2003. pp.139-149
Pseudo-addiction

- Behaviors exhibited when dose inadequate
- Correct opioid dose typically eliminates these behaviors


Opioid Induced Hyperalgesia

- Abnormal sensitivity to pain
- May be associated with long term use of opioids
- Pro-nociceptive process
- Along with tolerance can lead to escalating doses of opioids

Wilder-Smith, O. et al. Anesthesiology 104(3). March 2006. 601-607

Common Myths

- wean off prior to surgery
- large opioid requirements implies addiction
- high dose opioids preoperatively- same dose post-operatively
Why You Would Not Stop Opioids

- Most likely will result in withdrawal
- Pain will increase
- Does not decrease opioid requirement

Nursing Assessment

- Determine baseline pain and character
- Use validated pain assessment tool
- Set goals
- Identify medical conditions

Nursing Assessment cont.

- Determine what opioid and non-opioid analgesics pt. was on at home (and dose)
- Duration of opioid and non-opioid therapy
- Is pt. receiving methadone for addiction?
Postoperative Considerations

- Expect higher doses of opioids
- Patient may require monitored bed
- Do NOT administer antagonists

Important Principles

- Always use analgesic drugs in synergistic combinations of two or more
- Avoid analgesic gaps

Bushnell, L.S. Drugs for Pain. 2003; p. 303.

Nursing Interventions

- Ensure baseline analgesics are ordered
- Individualize care
- Determine timing of administration
- Advocate for proper order placement
- Ensure multi-modal approach
Multimodal Approach

- Combine classes to target different pathways
- Can use lower doses of individual agents
- Emerging standard (ASA, ASRA, APS)

Kehlet, H. & Dahl, J.B. Anesthesia & Analgesia. 1993; 77: 1048-1056
ASA Task Force on Acute Pain Management. Anesthesiology. 2004;100:1573-1581

HELP ME!!!!

Multimodal Agents

- Opioids
- Local Anesthetics
- Acetaminophen, NSAIDS, COX-2
- Benzodiazepines, Muscle relaxers
- Alpha 2-agonists
- Anticonvulsants
- NMDA receptor antagonists
Analgesic Adjuncts in Postop Pain: Which Agents Make a Difference?

- N-methyl-D-aspartate (NMDA) receptor antagonists
  - Ketamine, dextromethorphan, magnesium, amantadine
- α2-agonists
  - Clonidine, dexmedetomidine
- Anticonvulsants
  - Gabapentin, pregabalin
- Opioid antagonists (?)
- Neostigmine
- Corticosteroids


Multimodal Approach


Opioids

- Use more effective opioids
- IV PCA- add basal as last resort
- Avoid active metabolites
- Higher doses

Regional Anesthesia/Analgesia

- Spinal
- Epidurals
- Peripheral blocks
- Neuraxial opioids

NSAIDS, COX-2 inhibitors

- Inhibit prostaglandins
- Interact with endogenous opioid systems
- Inhibition of neutrophil activation
- Activity at spinal level
- Monitor for side effects

Clonidine

- Alpha 2-agonist
- Modification of central and peripheral neurotransmitter activity (catecholemines)
- May cause hypotension, bradycardia, dry mouth and sedation
**Gabapentin (Neurontin™)**
**Pregabalin (Lyrica™)**
- Exact analgesic mechanisms unknown
- Approved for neuropathic pain syndromes
- Pregabalin first line choice in treatment of fibromyalgia
- Reduced dose in renal disease
- May cause sedation, dizziness, ataxia


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**Celecoxib, Pregabalin, Acetaminophen**
- Multimodal combination
- Based on Celecoxib/Pregabalin study
- Improved analgesia
- Less nausea, sedation

Reuben, SS. et al. Anesthesia & Analgesia. 2006;103(5): 1271-1277

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**Methadone**
- Powerful synthetic opioid and NMDA receptor antagonist
- Very effective analgesic
- Long half life, excellent bioavailability, low cost
- Multiple sites of action may enhance efficacy

Ketamine

- NMDA receptor antagonist
- May reduce long term tolerance
- Used in treatment of neuropathic pain
- May reduce hyperalgesia
- May cause unpleasant dreams, delirium or hallucinations in higher doses

Joly, V. et al; Anesthesiology 103: 147-55. 2005

Nursing Reassessment

- Reassess after interventions
- Evaluate effectiveness
- Monitor for side effects
  - Sedation/Resp. depression
- Acute Pain Consult

Discharge

- Taper vs. long term
- Arrange for follow up care
  - Pain specialist
  - Addiction specialist