

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

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Opioids

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

World Health Organization; Geneva, Switzerland: 2000.
DEA@ <http://www.usdoj.gov/dea/index.htm>
Ballantyne, J. *The Clinical Journal of Pain* 24; (6) 2008. pp.469-78.

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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
deLeon-Casasola, O. *Clinical Anaesthesiology*. 16(4):521-5, 2002 Dec.

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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

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Cellular Mechanisms of Tolerance

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

Gintzler, A. et al. *Molecular Neurobiology* 21(1-2):21-33, 2000.
Smith, H.S., *Drugs for Pain*. 2003. pp. 153-155.
Ballantyne, J., *NEJM*. 2003;349: 1943-53

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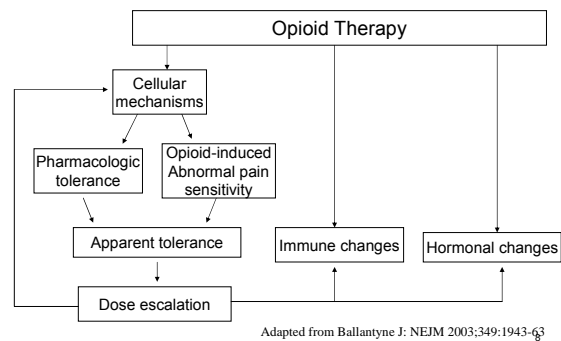
N-methyl-D-aspartate

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

Wong et al. (1996). *European Journal of Pharmacology*, 291:27-33

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Effects of Prolonged Opioid Therapy



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

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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

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Physical Dependence

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

St. Marie, B. Definitions. *Core Curriculum for Pain Management Nursing*. W.B. Saunders Co. 2002; 436-37
deLeon, OA. *Current Review of Pain*. 2000, 4:203-205

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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
Fishbain DA, et al: *Clin J Pain* 1992;8:77-85

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Pseudo-addiction

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

St. Marie, B. Definitions. *Core Curriculum for Pain Management Nursing*, 2002; p.37 13

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

Angst, M. et al. *Anesthesiology* 104(3), March 2006. 570-587
Wilder-Smith, O. et al. *Anesthesiology* 104(3), March 2006. 601-607
Chu, L. et al. *Clin J. Pain* 24 (6); 2008. 479-496.

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Common Myths

- wean off prior to surgery
- large opioid requirements implies addiction
- high dose opioids preoperatively- same dose post-operatively

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Why You Would Not Stop Opioids

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

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Nursing Assessment

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

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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?

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Postoperative Considerations

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

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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
Turan, A. et al. *Anesth Analg*. 2006; 102. 175-181
Reuben, SS. Buvanendran, A. *J Bone Joint Surg Am*. 2007; 88:1343-58.

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Nursing Interventions

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

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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
Rathmell, JP. *Reg Anesth & Pain Med*. 2006; 31(4 Suppl 1): 1-42
Gordon, DB,et al. *Arch Intern Med*. 2005; 165: 1574-1580

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HELP ME!!!!



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Multimodal Agents

- Opioids
- Local Anesthetics
- Acetaminophen, NSAIDS, COX-2
- Benzodiazepines, Muscle relaxers
- Alpha 2-agonists
- Anticonvulsants
- NMDA receptor antagonists

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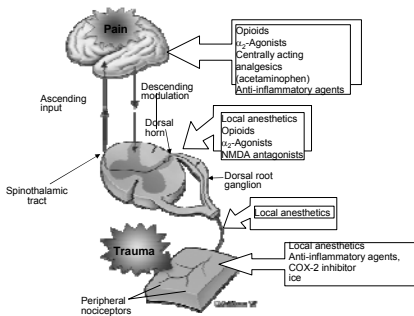
Analgesic Adjuncts in Postop Pain: Which Agents Make a Difference?

- N-methyl-D-aspartate (NMDA) receptor antagonists
 - Ketamine, dextromethorphan, magnesium, amantadine
- α_2 -agonists
 - Clonidine, dexmedetomidine
- Anticonvulsants
 - Gabapentin, pregabalin
- Opioid antagonists (?)
- Neostigmine
- Corticosteroids

Habib AS, Gan TJ. *Anesthesiol Clin North America*. 2005;23:85-107.

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Multimodal Approach



Gottschalk A, Smith DS. *Am Fam Physician* 2001;63:1979-1984.

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Opioids

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



deLeon-Casasola OA, et al: *Anesthesiology* 1992;76:853-6
 deLeon-Casasola OA, et al: *Anesthesiology* 1994;80:303-9
 Inturrisi CE: *Clin J Pain* 2002;18(suppl):S3-13

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Regional Anesthesia/Analgesia

- Spinal
- Epidurals
- Peripheral blocks
- Neuraxial opioids

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NSAIDS, COX-2 inhibitors

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

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Clonidine

- Alpha 2-agonist
- modification of central and peripheral neurotransmitter activity (catecholamines)
- May cause hypotension, bradycardia, dry mouth and sedation

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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

Dahl, J. & Mathiesen, O. (2007) *Advances in Pain Management* 1 (3): pp 82-90.

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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

Sartain, JB., et al: *Anaesth Intensive Care* 2002; 30:487-489
Pasternak, GW: *Trends Pharmacol Sci* 2001; 22:67-70

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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

Schmid, RI, et al; *Pain* 82; 111-25. 1999
Joly, V. et al; *Anesthesiology* 103; 147-55. 2005

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Nursing Reassessment

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

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Discharge


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

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Questions???



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