Opioid Free Anesthesia

John P. Maye PhD, CRNA CAPT (Ret) USN
University of South Florida
College of Nursing
Nurse Anesthesia Program
Program Director Advanced Pain Management Fellowship
Objectives

• Discuss the relationship between the neurophysiologic constructs of pain and the mechanism of action of the drugs used to treat pain

• Describe preventative and multimodal approaches as acceptable alternatives to traditional opioid therapy for the treatment of acute and chronic pain
Background and Significance

• Pain is a public health problem affecting at least 100 million American adults at a cost of approximately $560–$635 billion annually (IOM, 2011).

• The financial burden on society has been projected to exceed $600 billion on an annual basis, doubling the cost of heart disease and stroke (Gaskin & Richard, 2012), (IOM, 2011).

• The mounting costs associated with pain may be attributable to multiple factors, including the ongoing opioid epidemic and lost productivity.
Problem

• Only one in four surgical patients receives adequate relief of acute pain.
• Patients who present with high levels of pain, anxiety, and catastrophizing are high risk for experiencing postoperative pain.

Preventative Analgesia

• A method to prevent or attenuate sensitization of nerve fibers and inflammation that develops as a result of a painful insult

• Accomplished through the administration of various analgesic agents primarily before surgery and with consideration to the entire perioperative period

Multimodal Analgesia

- Multimodal analgesia is the administration of two or more analgesics which act through different mechanisms or sites to work synergistically.
- Ultimately, reduces the dosage of each analgesic administered individually and potential side effects.
Regional Anesthesia

- The American Pain Society recommends the use of regional techniques with systemic analgesics for surgeries of the extremities, chest and abdomen
- Kessler et al. found that the inclusion of regional anesthesia reduces postoperative pain, decreases opioid consumption, and increases patient satisfaction

Tornero, C., Rodeiguez, L., & Valls, J. Multimodal analgesia and regional anaesthesia. 2017 Revista Espanola de Anesthesiologia y Reanimacion, 64(7): 401-405
How much do we know about pain?

• What is your understanding of pain and pain treatments?

• Do you understand the complex physiologic and psychological mechanisms that are involved when a patient is experiencing pain?
Why avoid opioids?

- Opioids have many detrimental side effects that we want to avoid in the acute post-op setting to include:
  - Nausea and vomiting
  - Respiratory depression
  - Opioid induced hyperalgesia
  - Pharmacologic tolerance
  - Enhanced pain sensitivity
  - Somnolence
  - Sedation
  - Ileus
  - Urinary retention
  - Addiction
Education Challenges

- Across health care and society there are major gaps in knowledge about pain.
- Educating health professionals about how to better understand pain and what causes pain will help bridge these gaps.
- To improve understanding of pain, federal agencies and other stakeholders should redesign education programs.

The Institute of Medicine of the National Academies: Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. June 2011.
Definitions

Modulation:
Long lasting changes in the electrical potential of a nerve that alter the flow of ions across the cell membrane.
Peripheral Inflammation

- Bradykinin
- Calcitonin Gene Related Peptide
- Glutamate
- Substance P
- Histamine
- IL-1
- NGF
- Prostaglandins
- Thromboxane
- Adenosine
- Serotonin

Trauma / Tissue Disruption

Primary afferent activation

Release
Perception of Pain

To the Limbic System

Descending Inhibitory Pathway
- Neurotransmitters at Dorsal Horn Level:
  - Norepinephrine
  - Serotonin
  - Enkephalins

Spinothalamic Tract

Primary Afferent Neurotransmitter Candidates
- Substance P
- L-Glutamate
- GABA
- VIP
- CCK-8
- Somatostatin

Muscle
- Neurotransmitters Released:
  - Substance P
  - Histamine
  - Serotonin
  - Bradykinin
  - Prostaglandins

Release of Norepinephrine

Trauma

Capillary

Sensory Nerve

Motor of Other Efferent Nerve

Segmental Reflexes:
- Increased Skeletal Muscle Tension
- Decreased Chest Compliance
- More Nociceptive Input
- Increased Sympathetic Tone
- Decreased Gastric Mobility
- Ileus, Nausea, Vomiting
Peripheral Sensitization

- Due to release of inflammatory mediators
- Causes changes in peripheral nerves and receptors making them more sensitive
- Can occur over very short time period after initial injury
- Much harder to manage a patient once it has occurred
- Receptors easier to excite and lowers thresholds (hyperalgesia)
Structural Changes

Leads to Central Sensitization
Central Sensitization

- **Allodynia**: pain to a stimulus that does not normally produce pain
- **Hyperalgesia**: An exaggerated pain response to a normally painful stimulus
- **Receptive Field Expansion**: An expansion of the area of skin innervated by the A-delta and C-fibers
Multimodal Pain Options

- Preoperative/Preventative
  - Neuraxial approaches (opioids?)
  - Regional anesthesia plexus blocks
  - Regional anesthesia from local peripheral blocks
  - Decadron
  - Tylenol/Ofirmev
  - Cox-2 Inhibitors (Celebrex)
  - Gabapentin/Pregabalin (Lyrica)
Multimodal Pain Options

Intraoperative

– Ketamine (continue into post-op?)
– Magnesium (watch for lethargy and muscle flaccidity)
– Lidocaine infusions (calculate toxicity)
– Dexmedetomidine
– Opioids (last choice)
Multimodal Pain Options

Postoperative

– Regional catheters/Infusions (On-Q Pain Pump)
– Scheduled Toradol/Tylenol
– Gabapentin (continue into postoperative period)
– Ice therapy (be careful)
– Elevation
– Physical therapy/Early ambulation
Ketamine

- Blocks central sensitization of glutamate at the NMDA receptor
- Glutamate is the primary excitatory neurotransmitter in the CNS
- Administration at low doses reduces likelihood of side effects
  - Benzodiazepine medications may help reduce emergence excitation/hallucination reactions.
Ketamine

Dosing schedules vary depending on scholarly resource

- Single induction dose: 0.2 – 0.4 mg/kg IV
- Induction/Maintenance: 0.2 mg/kg, followed by infusion 2.0 - 10 ug/kg/min (Range 10-40 mg/hr)
- Induction/Maintenance/Post-op: Same as above. Continue infusion for 24 hours post-op
Magnesium

- Magnesium effect on NMDA receptor
  - NMDA receptor opens when glutamate binds and allows influx of calcium and sodium into the cell.
  - One of the most important controls on the ionic conductance through the NMDA receptor is the voltage sensitive blocking by Magnesium.
Magnesium

• Recommendations are:
  – Magnesium 30 mg/kg IVPB over 30 minutes prior to surgical incision (if case less than 30 min ½ dose)
  – This dose should not potentiate muscle relaxants or cause a decrease in BP
  – Monitor EKG during infusion and monitor the administration of neuromuscular blocking agents

Ketamine in combination with Magnesium more effective than either alone for post-operative pain prevention!
Lidocaine

Lidocaine infusion 1.5 mg/kg/hr
Mechanism of Action Local Anesthetics

Peripheral Mechanisms of Nociceptor Hyperexcitability

- Neuropeptide release
- Ectopic impulses
- $\alpha$ adrenergic receptor expression
- Sympathetic activity
- CNS Plasticity
Dexmedetomidine

• Mechanism of Action:
  - Dexmedetomidine (Precedex) is a highly selective alpha 2 receptor agonist.
  - It works in a negative feedback loop to decrease catecholamine release.
  - The main site of action for the sedative properties of dexmedetomidine is the pontine noradrenergic nucleus and the locus coeruleus.
Dexmedetomidine

• Main side effects are hypotension and bradycardia

• Reduction of myocardial oxygen demand (antianginal effect)

• Slightly diminished airway reflexes

• Decreases airway reactivity in patients with COPD or asthma
Dexmedetomidine Dosing

- Loading Dose: 1mcg/kg over 10 min
- Maintenance Infusion: 0.2-0.7 mcg/kg/hr
- Onset of action: 10-20 min with loading dose
- Duration of action after stopping infusion: 10-30 min
Decadron

• Corticosteroid/glucocorticoid
• Adjuvant analgesic
  - IV, (Preservative free ESI, PNB)
  - Pain reduction to include neuropathic pain
  - Reduced opioid dose
  - Decreases PONV
• Inhibition of prostaglandin synthesis and proinflammatory cytokines
Gabapentin

• Branched chain amino acid and chemical analogue of the neurotransmitter GABA
• Does not display any activity in the GABAergic neurotransmission system
Gabapentin

- Analgesic effect related to calcium influx inhibition as well as inhibition of the release of excitatory neurotransmitters in spinal and supraspinal pathways


Perioperative administration of gabapentin for shoulder arthroscopy: a prospective, randomized, double-blind, placebo-controlled study. Spence, D. Goff, J., Bowen, K., Osborne, L., Maye, J.P.
Take Home Message

• Adequate pain relief is a problem following routine surgical procedures, especially in patients with a history of chronic pain.
• Inadequate pain relief can lead to the development of chronic pain.
• Preventative/Multimodal techniques are effective in reducing postoperative pain, complications, and opioid use, while expediting recovery, reducing hospital stay and improving patient satisfaction.
QUESTIONS?
johnmaye@health.usf.edu


3. Tornero, C., Rodeiguez, L., & Valls, J. Multimodal analgesia and regional anaesthesia. 2017 Revista Espanola de Anesthesiologia y Reanimacion, 64(7): 401-405


5. The Institute of Medicine of the National Academies: Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. June 2011.