# **REVIEW ARTICLE**

# Postoperative pain management

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## Background

Pain is a subjective phenomenon that is an unpleasant sensory and emotional experience, associated with actual or potential tissue damage.

Acute pain is a "normal, predicted, physiological response to an adverse chemical, thermal or mechanical stimuli".

Serious suffering that is under managed affects quality of life, recovery, cost of care, morbidity and mortality also. Adequate pain relief is an integral part of anaesthesia. Pain is the fifth vital sign. Pain management should be planned during preoperative assessment.

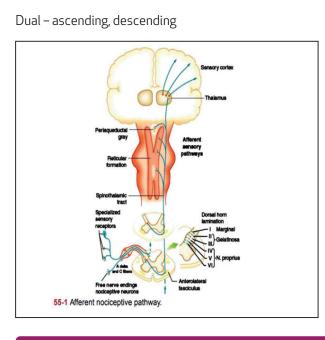
Patient specific approach (surgery, medical condition of patient, patient preferences, age) is required. Acute pain service has to be round the clock.

The two types of pain are Nociceptive and neuropathic.

## Pain pathways

Three neurons

- 1. Nociceptors spinal cord
- 2. Spinal cord thalamus
- 3. Thalamus cortex



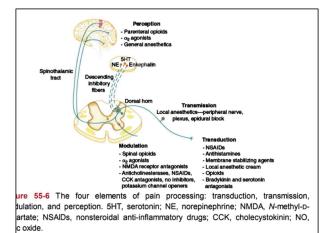
# Pain processing

1. Transduction (algogenic substances)

2. Transmission

3. Modulation (inhibitory - GABA, Glycine, SE, NE, Endorphins, augmentation - sensitization)

4. Perception



# **Chemical Mediators and Receptors**

1. Nociceptors – Substance P, PG, glutamate, histamine, bradykinin, serotonin, adenosine etc

2. Dorsal horn

•Excitatory - glutamate, aspartate, Substance P, neurokinin A

- Inhibitory GABA, glycine
- Receptors NMDA, AMPA, kainite, metabatropic

## Neuroplasticity

1. Central sensitization

- 2. Peripheral sensitization
- 3. Allodynia
- 4. Hyperalgesia

## **Surgical Stress Response**

1. Adverse Neuroendocrine and sympathoadrenal responses

2. Neuroendocrine – hypothalamo-pituitary

3. Increase in catabolic hormones (cortisol, glucagon, GH, CA)

4. Decrease in anabolic hormones (insulin, testosterone)

5. Hypergylemia, negative nitrogen balance

6. Muscle wasting, fatigue, poor wound healing, impaired immunocompetency.

7. Sympatho adrenal response.

# **Chronic effects of Pain**

- Chronic persistent postsurgical pain (CPSP)
- CNS sensitization

## Incidence

- Limb amputation (30%-83%),
- Thoracotomy (22%-67%),
- Sternotomy (27%),
- Breast surgery (11%-57%),
- Gallbladder surgery (up to 56%).

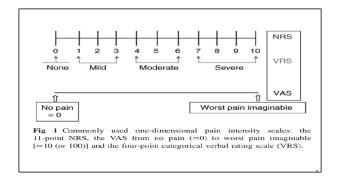
#### **Risk factors**

- Severity of acute postoperative pain
- Area of postoperative hyperalgesia
- Severity of the patient's preoperative pain.

## Assessment of pain

• Unidimensional - VAS, NRS, VRS

• Multidimensional - McGill pain questionnaire, Brief Pain Inventory, Breakthrough pain questionnaire



## Three Classes of Acute Pain

- Background pain
- Breakthrough
- Transitory and intermittent

#### **Strategies of Acute Pain Management**

- 1 Preventive analgesia
- 2) Multimodal techniques to decrease opioids.
- 3) Nociceptive vs neuropathic pain
- 4) Pharmacogenetics

## Preventive analgesia

"Preemptive" analgesia refers to an analgesic intervention that precedes a surgical injury and prevents the establishment of central and peripheral sensitization in entire perioperative period

Essentials of preventive analgesia;

a) Depth of analgesia b) Entire surgical field c) Duration – full perioperative

## Multimodal analgesia

 A complex nature of nociception and mixed mechanisms of generating surgical pain
Multiple strategies and drug classes
Integral part of ERAS protocol

Minimize of opioid use and side effects from opioids by not utilizing opioid analgesics and techniques. They lead to a reduction in hormonal and metabolic stress, preservation of total-body protein, shorter times to tracheal extubation, lower pain scores, and earlier return of bowel function.

Also, earlier fulfilment of intensive care unit discharge criteria when compared to patients receiving traditional pain management.

ERAS pathways integrate the most recent evidence from clinical trials and clinical practice.

#### Multimodal analgesia Example

- 1) Opioid
- 2) NSAIDs, paracetomol
- 3) Ketamine
- 4) Gabapentin
- 5) Clonidine, dexmedetomidine
- 6) Lignocaine, Mgso4
- 7) Epidural analgesia
- 8) Continuous peripheral nerve blocks
- 9) Plane blocks

# 1. Opioids

1) MOR, KOR, DOR-receptors in the CNS, dorsal horns and peripheral opioid receptors.

2) No analgesic ceiling.

3) Tolerance or side effects – limits its use

4) Wide intersubjective and intrasubject variability in the relationship of opioid dose, serum concentration and analgesic response

Morphine	Fentanyl	Buprenorphine	Tramadol
Prototype	Short acting	MOR agonist, KOR	MOR agonist,
		antagonist	inhibits reuptake of
			MAO
Renal and liver		Ceiling effect on	Serotonin syndrome
failure OSA		respiratory	
		depression	
		prevents	
		sensitization	
1-2mg/hr IV	0.5 to 2µg/kg/min IV	Every 6hrs dose	50 mg IV 6 <sup>th</sup> hourly
Duration: 4-5 hr	Patches	$300\mu g = 10mg$ of	Metabolism prone to
		morphine	genetic
			polymorphism

Tramadol	Tapentadol	
Mild to moderate pain	Moderate to severe pain	
Seizures	Less seizures	
Serotonin syndrome	Less serotonin syndrome	
GI side effects	Less GI side effects	
Genetic polymorphism	No genetic polymorphism	

# **Opioid Side effects**

- 1) Sedation, dysphoria, delirium
- 2) Constipation, urinary retention
- 3) Postoperative nausea and vomiting
- 4) Respiratory depression, airway obstruction
- 5) Early cancer recurrence
- 6) Dependence and abuse

# 2. NSAIDs

• Anti-inflammatory, analgesic, antipyretic

• Inhibition of cyclooxygenase (COX) and synthesis of prostaglandins.

• PG Peripheral – sensitizes nociceptors to pain mediators

• Spinal – release substance P, Glutamate/ sensitivity of neurons

a) COX-1 is constitutive and COX-2 is inducible b) COX-1 - platelet aggregation, hemostasis, and gastric mucosa protection c) COX-2 - pain, inflammation, and fever

# **Ceiling Effect on Analgesia**

Mild to moderate pain – sole analgesic Moderate to severe pain – as adjuvant to opioids

# Nonselective NSAIDs

Platelet dysfunction - bleeding

Gastrointestinal ulcers

Renal dysfunction – hypovolemia, abnormal renal function or abnormal serum electrolytes.

a) Ketorolac – IV 30mg per dose upto 120mg/day b) Diclofenac – upto 1.5mg/kg 12 th hourly.

# COX 2 selective inhibitors

Renal dysfunction

Bone fusion

Hypersensitivity

a) Potent COX 2 inhibitors – Valdecoxib, Rofecoxib (Cardiovascular events in high risk patients).

b) Less selective COX 2 inhibitors – celecoxib.

c) Etoricoxib – upto 120mg/day oral tablets.

## 3. Paracetamol

Antipyretic and analgesic

Activation of descending serotonergic pathways in the CNS, Central COX 3 inhibition

No side effects of NSAIDS

Mild to moderate pain

Adjuvant to opioids

Dose: 4gm/day

#### 4. NMDA antagonist – Ketamine

NMDA;

a) Persistent postoperative pain

b) Sensitization

c) Opioid induced hyperalgesia/tolerance Opioid sparing effect

**Dose:** 1mg/kg bolus or 1.2 mg/kg/hr infusion

**Concerns:** Tachycardia, hypertension, delirium

#### 5. Gabapentinoids

Gabapentin, pregabalin

Seizures, Chronic pain, neuropathic pain, Postoperative pain also Prevents central sensitization

Concerns: Dizziness/light-headedness or visual disturbances

Dose: Pregabalin – 75mg po - BD

#### 6. Clonidine and Dexmedetomidine

Centrally acting alpha 2 agonists

Sedation, hypnosis, anxiolysis, sympatholysis, and analgesia. Very good opioid sparing effect

Preserves airway patency and the normal sleep architecture. Bronchodilator properties.

Lacks any of the common side effects of opioids.

**Dose:** Clonidine 3µg/kg bolus, 0.3µg/kg/hr maintenance

Dexmedetomidine 0.5 to 1µg/kg bolus, 0.2 to 0.7µg/kg/min

#### 7. Continuous epidural analgesia

1. Epidural catheter

2. Spinal nerve roots, dorsal root ganglia, spinal cord itself

3. Bupivacaine 0.125%/ropivacaine 0.2%

4. Adjuvant drugs with LA; Opioids,clonidine, dexmed, tramadol, midazolam

a) Catheter incision site congruencyb) Choice of analgesic drugsc) Rate of infusion

#### Side effects

Hypotension, paraesthesia, motor block (LA related)

Haematoma, abscess, nerve damage, catheter migration (procedure related) – rare

Nausea, vomiting, pruritus, ileus, sedation (opioid related).