Preemptive Analgesia: Does it Prevent Chronic Pain?

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History

- **Crile GW. 1916**
  - first described a possible relationship between intraoperative tissue damage and an intensification of acute pain and long-term postoperative pain, which is now referred to as central sensitization.

- **Clifford Woolf 1983**
  - The evidence for a central component of post-injury pain hypersensitivity in experimental studies.

- **Wall P. 1988**
  - Proposed the concept of pre-emptive preoperative analgesia.

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Introduction

- Pain is a complex body reaction to noxious stimuli.
- It is a personal and individualized experience.
- Patients undergoing a surgical procedure are predisposed to pain due to:
  1. Pre-existing pain (acute and chronic)
  2. Psychological fear of recurring additional pain
  3. Neurovascular tissue damage from a prior operation
  4. As well as the extent of the surgery can all contribute to major postoperative discomfort.
Why To Relief Post Operative Pain?
hormones

hypothalamus

- anxiety
- starvation
- heat loss
- acidosis, hypoxia
- haemorrhage
- infection
- afferent stimuli (pain)
- local tissue factors (pain)
Pain & Stress

Pain

Stress Response

Infection

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Friday, October 09, 2015
Pain & Stress

Mechanisms of Stress Response

Afferent Neural Stimuli

Minor → CNS (Pain)

Major → CNS + Other Factors

1. Local Tissue Factors
2. Modifying Factors
Pain & Stress

Stress Response

• Acute (Shock) → Very Short (hrs)

• Hyperdynamic (Flow) → Long (day-week)
  – Catabolic Hormones
  – Anabolic Hormones
Stress response to pain

• Release of:
  – insulin, cortisol, catecholamine, and other hormones

• Resp. Dep → pneumonia

• Hypercoagulability → thrombosis or embolism

• Muscles → spasm or atrophy
  – urinary bladder → urinary retention.

• High sympathetic tone → ischemic H. D

• Sleep deprivation → anxiety and depression.

Pre-emptive analgesia, Jørgen B. Dahl and Steen Møiniche, Department of Anaesthesiology, Glostrup University Hospital, Glostrup, Denmark, Correspondence to: Jørgen B. Dahl, Department of Anaesthesiology, Glostrup University Hospital Ndr. Ringvej, DK-2600 Glostrup, Denmark, Accepted November 3, 2004
Physiology of pain: Pain processing in the brain

- Cerebral cortex
- Thalamus
- Limbic system
- Hypothalamus
- Medulla oblongata
- Reticular formation
- Spinal cord
Physiology

Touch → pain

Touch

Pain

C-fibre

A-β-fibre
Physiology

Peripheral nerve pathways do not react like telephone wires!
Pathophysiology

Nerve pathways are not one-way streets!
Pathophysiology – peripheral and central mechanisms

Massive AP influx on a spinal level
- Intracellular molecular change
- Number of receptors ↑ (AMPA, NMDA, NK1)

Central sensitisation

Peripheral sensitisation

Release of TNF, IL-1 → NGF ↑
- Antero- and retrograde axonal transport
- Expression of bradykinin receptors
- Neuropeptides ↑
- Local effect:
  - Na channels ↑
  - Cytokine ↑
  - Induction of COX-2

Induction of COX-2
Pathophysiology - chronic neuropathy

Central sensitisation: Touch → pain

- C-fibre
- A-β-fibre
- WDR neurone
Pathogenesis of post-herpetic pain

C-fibre degeneration: touch → pain

C-fibre degeneration

"Sprouting"
Pathogenesis of sympathetic pain

Sympathetic nociceptive coupling

Ramer et al., 1998
Chronic postsurgical pain

- Chronic postsurgical pain (CPSP) 3–6 months
- It disrupts their quality of life 10-50%.
- CPSP due to:
  - inflammatory processes
  - initiation of neuropathic pain from peripheral nerve damage
- Several risk factors:
  - psychosocial factors,
  - sex, age,
  - level of pre-existing pain.
  - genetic predisposition
- Multimodal analgesia:
  - *use of surgical techniques that avoid nerve damage are beneficial for preventing long-term postsurgical pain*

Preventive Analgesia (aims and methods)

- To block perioperative pain
- To block neurochemical cascade → chronic pain
- By blockade (NMDA-Rs)
- By arresting glial cells reaction
- By preventing
  - the phenotypic interneurons to become pronociceptive.

Sources of perioperative pain

- **Peripheral sensitization**
  - afferent input arising from nerve injury
  - cut of primary afferents (e.g., retraction)

- **Postoperative inflammation (hours weeks)**

- **Central sensitization**
  - hyperexcitability and ectopic activity in DRG
  - hyperexcitability and ectopic activity in DHN
Factors and phases of perioperative pain

• Preoperative
  – Genetic predisposition,
  – Psychological vulnerability,
  – Non-genetic environmental variables
    • (expectations, cultural, dietary, and more), preoperative noxious inputs, and pain

• Intraoperative
  – Cutting, retraction, manipulation, chemical irritation by sterilizing substances and stress response

• Postoperative
  – regenerating wounded structures fibrosis

Left untreated, acute pain can lead to:

1. Emotional and psychological distress
2. Potential to develop chronic pain state
3. which is much more difficult to manage
The plan for preventive analgesia

• Taking a thorough patient history,

• Including:

1. Factors such as prior responses to pain,
2. Past contact with analgesics,
3. Current medications,
4. Fears or concerns regarding future pain,
5. Any additional relevant information.
Preventive (perioperative) analgesia

• Time of analgesia
  – Before, during and post-operatively
• Type of analgesia (multimodal)
  – Systemic IV → NSAIDs (anti Cox 1,2) & opioids
  – NMDA receptors antagonists → ketamine
  – Anti – convulsants → pregabalin
  – Local analgesics
    • Wound infiltration
    • Peripheral N. block
    • Extended epidural or intrathecal analgesia
      – Pre, intra, and post – operatively
      – Adjuvants (opioids and/or α2 agonists)
• G. anesthesia → no block of stress response

Is There a Link Between Acute Pain and Chronic Pain?

Transition from acute to chronic pain

- N. injury → cascade of reactions
  - leading to the transition from acute to chronic pain
- destruction of → antinociceptive inhibitory Ns
  - In the DHNs
- glial cells → activation
- GABAergic interneurons in the dorsal horn from being normally:
  - antinociceptive → pronociceptive interneurons.

Take home messages

1. Pre-emptive analgesia provides better analgesia postoperatively if applied before incision or surgery.

2. Multimodal analgesia means the use of lower doses of any one medication to be used in combination with less side effects.

3. Preventive analgesia could be used before, during or after incision and surgery.

4. Duration of treatment and effective analgesic regimens are important factors in the administration of preventive analgesia.

5. Preventive analgesia is more effective than peemiptive analgesia to prevent chronic pain.