

### Introduction to pain

**Definition of pain** An unpleasant sensory & emotional experience associated with actual/potential tissue damage

**Purpose of pain**

1. As a protective mechanism
2. Cause individual to react to remove pain stimulus

### Nociceptive pain mechanism

Wide spread in superficial layers of skin & certain internal tissues

Excited by 3 different stimuli : mechanical, thermal, chemical

Pain is related to degree of receptor stimulation by processes causing tissue injury (more receptor stimulated=more pain)

**2 nociceptor systems**

1. A delta fibres (faster)

2. C fibres (slower)

**Chemicals that stimulate nociceptors**

Histamine

Bradykinins

5-HT (serotonin)

### Nociceptive pain mechanism (cont)

some metabolic substances released from damaged cells (lactic acid,ATP)

**Sources of nociceptive pain**

**Visceral pain** Pain from internal structures, poorly localised, often radiates or referred to other areas

### Neuropathic pain

Pain resulting from pathophysiologic changes in peripheral or CNS

A state of chronic pain is sustained

### Idiopathic pain

**Patient's state contribute to pain** May be due to anxiety,depression, other psychological disorders

### Pharmacotherapy in management of pain

1. Opioid analgesics

2. NSAIDs

3. Local anaesthetics

4. Alpha 2 agonists

### Opioids

**MOA** Binds to opioid receptors and inhibit action on neurons

### Opioids (cont)

**Type of opioid receptors**

1. Mu receptors effects: analgesia,respiratory&physical depression,miosis,reduced GI motility
2. Kappa receptors effects: sedation,-miosis
3. Delta receptors effects: dysphoria,hallucinations

### Classification of opioids

**Strong agonists** Morphine, Pethidine, Methadone, Fentanyl, Sufentanil/Alfentanil

**Mild to moderate agonists** Codeine

**Mixed agonist-anatagonists** Pentazocine, Buprenorphine

### Strong agonist opioid's desirable effects

**Analgesia** Centrally mediated, Alters emotional perception of pain

**Sedation**

**Sense of well being**

**Cough suppression**

**Reduce GI motility** Can help with diarrhoea

### Strong agonist opioid's adverse effects

**Respiratory depression** Dose related, Most important side effect which limits clinical use

**Miosis** Constriction of pupil, Decreases ability to see in dim light

### Strong agonist opioid's adverse effects (cont)

**Orthostatic hypotension**

**Nausea & vomiting**

**Constipation**

**Anorexia**

**Sedation**

**Development of dependence** Cause addiction

Caution:

\*Eldery are more prone to adverse effects of narcotic analgescis, thus lower dose is required

### Tolerance of strong agonist opioids

**Due to regular/intermittent use** Regular administration of fixed dose of drug give rise to progressively decreasing effect

Progressively higher dose has to be administered to achieve the same effect

### Develops gradually

**Cross tolerance between opioids** Will develop tolerance to drugs of similar pharmacological action

### Clinical uses of strong agonists opioids

**Severe pain**

**Pre-medication for anaesthesia**

**Methadone** Substitution therapy in drug dependence clinics

Chronic use: long term treatment in terminal cancer patients

### Mild-moderate agonists (CODEINE)

**Indications** Mild-moderate pain Usually in combination with non-opioid analgesics

Cough suppression At lower dose than that for analgesia

### Mixed agonist-antagonist opioids

Opioids with full agonist activity at one receptor subtype but behaves like an antagonist or partial agonist at another receptor subtype

Examples: Pentazocine  
Buprenorphine

**Clinical uses** Chronic severe pain  
Drug abusers

### Advantages of mixed agonist-antagonist

**Less adverse effects mediated by specific receptors**

**Less prone to cause dependence and abuse**

Caution:

\*Should not be given to patients that are already on treatment with pure strong agonist as it may precipitate severe withdrawal syndrome

### Tramadol

Chemically unrelated to other opioid drugs

**MOA** Partial mu agonist Less affinity than morphine

Inhibition of serotonin and noradrenaline reuptake Levels of serotonin&noradrenaline increase

Block nociceptor impulse at spinal level

**Clinical use** Mild to moderate pain

**Adverse effects** Less constipation,less respiratory depression,less dependence than opioids

Dizziness,sedation,nausea,vomiting

Constipation,headache

### Counselling points for opioids

**Drug may cause drowsiness,dizziness,blurring of vision** Do not drive or operate heavy machinery

**Avoid alcohol**

**If patient experience GI effects** Drug can be taken with food

**Seek medical attention if** Experience severe nausea,vomiting,constipation

