Pharmacology - Dr. Safa - Lecture 1

Opioids

General anesthesia: is a state characterized by unconsciousness ,analgesia, amnesia,skeletal muscle relaxation and loss of reflexes.

The opioid analgesics are drugs which act on a variety of specific receptors both centrally in the C.N.S. and peripherally. Drugs such as morphine which bind to opioid receptors and produce dose-dependent agonist effects are termed opioid agonist. Naloxone binds to opioid receptors also antagonizing the effects of morphine and is an opioid antagonist.

The term opioid agonist-antagonist is applied to drugs such as nalbuphine which possess agonist effects at one receptor type and antagonist effect at another.

Endogenous opioids:
These are a series of endogenous polypeptides(the endorphins and enkephalins).
Possessing analgesic properties similar to those of exogenous opioids.

The enkephalins: are found in high concentrations in the central grey matter of the brain stem and the substantia gelatinosa of the spinal cord.
B-endorphin: is present in high concentrations in the hypothalamic-pituitary axis and regulates endocrine function.

There is evidence that endogenous opioids are an important element in the immune system.

Opioid receptors:
Opioids act on specific receptors which are distributed throughout the C.N.S. and are the site of action of all opioids.

There are three classes of receptors:
Mu,kappa,and delta. The sigma receptor is associated with dysphoria and is not a true opioid receptor because its effects are not reversed by high concentrations of naloxone.

Morphine:
It is a tertiary amine and a weak base.
It is more water soluble than most other opioids used in anesthetic practice.
It is excellent analgesic.

Summary of actions and side effects of morphine:
Central:
Depressant:

- Analgesia.
- Sedation.
- Depression of cough reflex.
- Depression of respiratory centre.
- Depression of metabolic rate(hypothermia).
- Depression of vasomotor centre.

Excitatory:

- Euphoria,hallucinations.
- Convulsions (in very high doses).
- Miosis(stimulation of oculomotor centre).
- Nausea,vomiting(stimulation of chemoreceptor trigger zone).
- Bradycardia(vagal stimulation).
- Release of A.D.H. and other pituitary hormones.

Peripheral:

- Increase in smooth muscle tone.
- Histamine release.
- Bronchospasm.
- Hypotension.
- Erythema.
- Sensation of warmth,flushing.

Distribution and elimination:
After I.V. injection 35% of morphine is bound to protein,the remainder is distributed with a half-life of 20-25 min.
Metabolism occurs in the liver.
Elimination occurs through the kidney.
Morphine crosses the placental barrier and may depress neonatal respiration.

The duration of action after either I.V.or I.M. injection is 3-4 hr.
Oral morphine is used in the treatment of chronic pain in the form of morphine sulphate tablet(MST).

Pethidine:
It is a synthetic opioid with an analgesic potency approximately one-tenth that of morphine.

Actions and side effects of pethidine:
Mild cholinergic effects.
Smooth muscle relaxation.
Sedation.
Little euphoria.
Respiratory depression.
No specific action on the cough reflex.
Reduce myocardial excitability and ventricular arrhythmias.

Hypotension may occur in the hypovolemic patient as a result of venous and arterial dilatation.
Smooth muscle relaxation of the gastrointestinal and renal tracts.
Nausea and vomiting.
Histamine release.

Its duration of action is 2-3hr.after i.v.or i.m. injection.
It crosses the placenta,and may cause respiratory depression in the fetus.
Its metabolites cause hyperexcitability and convulsions.

Fentanyl:
It is synthetic opioid related structurally to pethidine.
Its analgesic potency is approximately 100 times that of morphine.
It is lipid soluble.its onset of action occurs in 1-2 min.
Its duration of action is 20-30 min.

Actions and side effects of fentanyl:
Depression of respiration.
A small reduction in arterial blood pressure.
Heart rate may decrease because of vagal stimulation.
Sedation.
Nausea,vomiting.
Histamine release.
Spasm of sphincter of oddi

Fentanyl is used as an analgesic during anesthesia.
Transdermal fentanyl has been used with some success for post-operative analgesia and the control of cancer pain.

Alfentanil:
It is synthetic derivative of fentanyl,with high lipid solubility,and short duration of action.

Actions and side effects:
Depression of respiration.
Depression of cardiovascular system.

The duration of action is 5-10 min.

Sufentanil:
It is related to fentanyl and is 600-700 times more potent than morphine.
It is highly lipid soluble and has rapid onset and short duration of action.

Naloxone:
It is opioid antagonist.
It acts within one minute of I.V.injection and has duration of action of approximately 30 min.

Actions:
All the C.N.S. effects of opioids administered systemically are antagonized by naloxone.
Naloxone antagonizes opioid induced respiratory depression.
Arterial pressure may increase after administration of naloxone,due to reduction of sedation and emergence of pain.naloxone is effective in relieving opioid induced spasm of sphincter of oddi.