OPIOIDS

Opioids are the most frequently used analgesics for treatment of moderate to severe pain. Opioids act by attaching to specific proteins called μ-opioid receptors (MOR) which are found in the brain, spinal cord, gastrointestinal tract and other organs in the body. When these drugs attach to their receptors, they reduce the perception of pain. Opioids can also produce drowsiness, mental confusion, nausea, constipation and depending upon the amount of drug taken, also they can depress respiration. Some people experience a euphoric response to opioid medications, since these drugs also affect the brain regions involved in reward. Those who abuse opioids may seek to intensify their experience by taking the drug in ways other than those prescribed.

Doses have to be titrated for each patient, because of considerable inter – patient variation in requirements. In adults, age is a better determinant of dose than weight.

Opium:

Opium comes from the dried latex of unripe capsules of poppy head. Opium contains 25 alkaloids, only morphine, codeine and papaverine of these alkaloids have wide clinical use. Opioids = like opium.

Actions of opioids:

1) On central nervous system:

Depress: awareness, anxiety, pain sensation and respiration.

Stimulate: vomiting centre, secretion of antidiuretic hormone, small pupils, hallucinations (rarely).

2) On smooth muscle:

Depress: vascular tone, peristalsis.

Stimulate: broncho-constriction, bowel sphincters, biliary sphincter, fallopian tube spasm.

3) Other effects:

- Stimulate secretion of catecholamines.
- Depress metabolism.
- Release histamine.
- Induce vagal mediated bradycardia (short acting opioids).

Opioid use disorder:

It is a disorder characterized by an increased strong desire to use and increased tolerance to opioids. Persons using opioids may develop both tolerance (tachyphylaxis) and dependence (addiction).

Opioid tolerance occurs when an opioid drug is used on a regular basis, the brain adjusts so the effects of the same amount of the drug become less over time. A person developing tolerance to opioid drugs needs larger amounts of the drug to get the same effect or "high" experience reduced effects when taking the same amount of a drug. Whyle dependence means that when a person stops using a drug, his/her body goes through "withdrawal": a group of physical and mental symptoms that may be life-threatening.

In addicts, abrupt discontinuation or decrease in the intake results in withdrawal symptoms such as agitation, muscle aches, severe abdominal cramps, diarrhea, trouble sleeping and lacrimation (so called "cold turkey"). relieved by further doses.

Some opioids

1) *Natural:*

Morphine:

The most widely used opioid is morphine, (Morpheus, Greek God of dreams, son of Somnos, God of sleep) has been in use over 2000 years and is still the best available analgesic. It is a good analgesic and a poor relaxer of smooth muscles.

Morphine may be given orally, rectally, topically, parenterally (either I.M or I.V) and via neuroaxial route. The standard parenteral dose for adults is 10 mg (I.M). It has duration of analgesia of 4 – 6 h.

More than 90% of morphine excreted in the urine and the rest in the bile, so, it may accumulate in patients with impaired renal function causing respiratory depression.

Papaverine:

It relieves spasm in arteries. It has almost no central effects and does not suppress intestinal peristalsis. The dose is up to 30 mg intravenously or intra – arterially (very slowly), and 120 – 250 mg orally.

Codeine phosphate:

Codeine is administrated orally (standard analgesic adult dose is 200 mg). Its intravenous administration should be avoided because the significant histamine release. It has marked antitussive effects and also causes significant constipation. It is often combined with paracetamol.

2) *Semi – synthetic:*

Diamorphine hydrochloride (Heroin):

Is the diacetyl ester of morphine, it is a drug of addiction because of the euphoria it creates, in the USA, Australia and many countries its use is proscribed.

Oxycodone:

Is a potent opioid that is very useful for the treatment of even severe pain. It produces predictable and reliable analgesia after oral administration because of its higher and less variable bioavailability than morphine. I.V oxycodone produces similar analgesia to the same doses of morphine.

3) Synthetic:

Tramadol:

It is the analogue of codeine. It has a weak central action on opioid receptors and also acts on descending monoaminergic pathways. The risk of respiratory depression is significantly lower with tramadol than with other opioids given at equivalent analgesic doses. Tramadol causes less constipation. However, nausea and vomiting are common side effects.

Tramadol is contraindicated in patients receiving Monoamine oxidase inhibitors (type of antidepressants). Caution must also be exercised in hepatic impairement.

Tramadol administrated parenteral or oral, the duration of action is 4 – 6 h after 50 – 100 mg.

Pethidine (meperidine):

It is available as parenteral and oral preparations. It's dose is 0.5 mg/kg I.V and 1.5 mg/kg I.M or S.C (but not exceeding maximum of 150 mg as a single dose), the duration of action is 2 – 4 h. Pethedine has other significant effects related to activity at non – opioid receptors, for example: its atropine – like action may cause a tachycardia, in addition to direct myocardial depression at high doses. It was used originally as a bronchodilator. It can also reduce shivering related to hypothermia or epidurals.

Fentanyl:

It is available as parenteral, trans-dermal and trans-mucosal administration. The I.V dose of fentanyl used in acute post-operative pain management is a 10 – 20 mcg bolus (with a 5 – 10 minute lockout interval) up to 50 – 100 mcg, and between 25 up to 100 mcg/h using trans-dermal patch. Fentanyl has duration of action of 1 – 1.5 h and it is 80 – 100 times more potent than morphine in the acute setting, although it is 30 – 40 times as potent when given chronically (e.g. slow-release trans-dermal patches).

Some analogues of fentanyl:

1) **Alfentanil:** an ultra-short-acting (5 to 10 minutes) analgesic.

2) **Sufentanil:** a potent analgesic (5 to 10 times more potent than fentanyl) for use in specific surgeries and surgery in heavily opioid-tolerant/opioid-dependent patients.

3) **Remifentanil:** currently the shortest-acting opioid, has the benefit of rapid offset, even after prolonged infusions.

Opiods antagonists

Naloxone:

Is a short-acting opioid antagonist, it can reverse opioid – induced respiratory depression but repeated administration may be required because of its short duration of action. It can be given by continuous infusion.

Naltrexone:

Is a long-acting opioid antagonist used in the management of opioid dependence. It is available only in oral formulation.

Perioperative uses of intravenous opioids

Intravenous (IV) opioids are commonly used to provide analgesia and supplement sedation during general anesthesia or monitored anesthesia care (a planned procedure during which the patient undergoes local anesthesia together with sedation and analgesia) and are the most widely used agents for treatment of acute pain in the immediate postoperative period.

Perioperative uses of intrathecally and epidurally opioids

Commonly opioids can be administered intrathecally or epidurally to improve the block and provide post-operative pain relief, examples include morphine and fentanyl. Moreover, intrathecal or epidural administration of pethedine can be used to provide analgesia and reduce the incidence and intensity of shivering.

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