Lecture 3: Opioid or Narcotic Analgesics (Centrally acting analgesics)

- **Opioid analgesics** a group of drugs that cause sleep in conjunction with their analgesic effect, whose name derives from:
- **Opium** "a milky extract from the unripe seeds of the poppy plant"
- Opium was known for thousands of years as an agent which produced euphoria, analgesia, sleep, and to prevent diarrhea.
- **Opioid analgesics** the most effective pain relievers available, used to relieve moderate to severe pain particularly of visceral origin that cannot be controlled with other classes of analgesics.
- Prolong used of opioids can causing CNS depression, physical dependency and abuse liability.
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Opium الأفيون Poppy plant نبات الخشخاش

- **Opioid:** a term applied to natural and synthetic substances which produced morphine-like effect E.g., Morphine – natural .... Meperidine – synthetic
- **Opiate:** a term restricted to natural substances such as morphine and codeine which obtained from the opium poppy
- Opium consists of 9 – 14 % Morphine and 0.8 – 2.5% Codeine.
- **Opioid receptors:** there are three main classes of opioid receptors: **Mu, Kappa,** and **Delta.**
- Opioid analgesics act primarily through activation of **Mu** receptors and weak activation of **Kappa** receptors "do not interact with **Delta** receptors".
- While endogenous opioid peptides (neurotransmitters found in CNS and peripheral tissues) act through activation of all type of opioid receptors.

TABLE 28–1 ▪ Important Responses to Activation of Mu and Kappa Receptors

	Receptor Type	
Response	Mu	Kappa
Analgesia	✓	✓
Respiratory depression	✓	
Sedation	✓	✓
Euphoria	✓	
Physical dependence	✓	
Decreased GI motility	✓	✓

Classification of drugs that act on opioid receptors

- Drugs that act on opioid receptors are classified on the basis of how they affected receptor function.

1. Pure opioid agonists
2. Agonist- antagonist opioids
3. Pure opioid antagonists

Pure opioid agonists		**Mixed Agonist-antagonist opioid**	**Pure opioid antagonist**
Strong High Efficacy	**Moderate** Moderate Efficacy		
Morphine Fentanyl, Methadone Meperidine, Diamorphine Hydromorphone	**Codeine** Hydrocodone Propoxyphene	**Pentazocine** Buprenorphine	**Naloxone**

Morphine

- Morphine is the prototype of the Opioid agonists and considered the standard by which the effectiveness of other opioids is compared.
- **Expected Pharmacological Action and Effects**
- Opioid agonists acting directly on opioid receptors in the spinal cord and brain stem (CNS).
- These drugs act on the Mu receptors, and to a lesser degree on Kappa receptors and produce analgesia, sedation, euphoria, respiratory depression, cough suppression, and suppression of bowel motility.
- **Other actions of opioid:**
- Morphine releases histamine from mast cells by an action not related to opioid receptors. Release of histamine may cause urticaria and itching at the site of injection.
- Bronchoconstriction is also recognized with morphine treatment which is due to histamine release → Morphine is dangerous in asthmatic patient.

- **Therapeutic Uses:** The principal indication for morphine include:
- relieve of moderate to severe pain - constant and dull pain
- relieve of postoperative pain,
- relieve pain of labor and delivery,
- relieve chronic pain caused by cancer
- relieve pain of myocardial infarction
- Morphine may also be administered preoperatively for sedation and reduction of anxiety.
- **Route of administration:** Morphine sulfate – Oral, subcutaneous, IM, rectal, IV, epidural, and intrathecal.

❑ With prolonged opioid use (in high doses), physical dependence develops. Withdrawal syndrome will occur if the opioid is abruptly withdrawn or if give the patient agonist- antagonist opioid. Opioid should be withdrawn gradually.

❑ Opioids are subject to abuse largely because of their ability to cause pleasurable experiences.

- **Adverse Effects**
- **1) Respiratory depression**: The most serious adverse effects, rarely caused by usual therapeutic doses opioid
- All of the pure opioid agonists depress respiration to the same degree. Respiratory depression is caused by reduction of the sensitivity of respiratory center to carbon dioxide.
- Resp. depression is ↑ by concurrent use of other drugs with CNS depressant action. So these drugs should be avoided
- **2) Sedation**: As powerful CNS depression, opioids can cause sedation, drowsiness and some mental clouding, which may be either a therapeutic effects or a side effect, depending on the patient's disease state.

- **3) Orthostatic hypotension:** Opioids lower BP by blunting the baroreceptor reflex and by dilating peripheral arterioles and veins. Peripheral vasodilation results primary from morphine-induced release of histamine.
- **4) Emesis:** initial doses of opioids may cause nausea and vomiting. This seems to be due to stimulation of chemoreceptor trigger zone. Tolerance to emesis developed quickly.
- **5) Constipation:** Opioids promote constipation by slowing motility of the GIT and inhibit secretion of fluids into the intestinal lumen. Because of this effect, (slowing motility of the GIT) opioids are highly effective for managing severe diarrhea (anti-diarrheal effects)

- **6) Urinary retention:** by ↑ tone in the sphincter of the bladder and suppress awareness of bladder stimuli. Difficulty with voiding is especially in clients with prostatic hypertrophy.
- **7) Cough suppression:** morphine act at opioid receptors in the medulla to suppress cough lead to accumulation of secretion in the airway.
- **8) Biliary colic:** morphine results in contraction of the gall bladder and induce spasm of the common bile duct, causing↑ pressure within the biliary tract causing severe pain.

❍ ❍This effect is harmful in clients suffering from biliary colic due to gall stones. Therefore, in clients with pre-existing biliary colic, morphine may intensify pain rather than relieve it.

❍ Certain opioids e.g. meperidine causes less smooth muscle spasm than morphine and hence are less likely to exacerbate biliary colic.

- **9) Elevation of intracranial pressure:** by suppression respiration, morphine ↑the CO_2 content of blood, which dilates the cerebral vasculature, causing ICP to rise.
- **10) Euphoria:** it is an exaggerated sense of well-being. Although euphoria can enhance pain relief, it also contributes to the drug's potential for abuse.
- **11) Miosis:** opioids can cause pupillary constriction. In response to toxic doses, the pupils may constrict to pinpoint size.
- Pinpoint pupils are an important diagnostic feature of morphine overdose.

With prolonged opioid use, tolerance develops to analgesia, euphoria, sedation and respiratory depression, but not to constipation and miosis.

- Precautions:

1. Clients who have respiratory impairment (asthma), emphysema, infants, or older adult clients (risk of respiratory depression)
2. Clients taking other drugs that can depress respiration.
3. Pregnancy: use of opioids before and during pregnancy should be discouraged – opioids taken just before or during early pregnancy, increase the risk of spina bifida, and congenital heart defects. The infant whose mother abused opioids during pregnancy may be born drug dependent – observe the infant for signs of withdrawal which usually develop within a few days after birth. Use of morphine during delivery can suppress uterine contractions and cause respiratory depression in the neonate. Following delivery, respiration in the neonate should be monitored closely.
4. Head injury. Why?
5. Clients with hepatic or renal impairment, hypotension, and prostatic hypertrophy (risk of acute urinary retention)

- **Meperidine** (Pethidine). The pharmacologic effect of pethidine is very similar to morphine but there are some differences:

₪ Pethidine is preferred for obstetric analgesia; because it is short acting and does not delay or diminish uterine contraction and cause less neonatal resp. dep.

₪ Pethidine cause less smooth muscle spasm than morphine so it is less likely to cause constipation, urinary retention, and biliary colic.

₪ Pethidine causes restlessness rather than sedation.

₪ Pethidine has antimuscarinic effect which may cause dry mouth.

- **Fentanyl** and Alfentanil: short-acting opioids, used for intra-operative analgesia. These drugs are approximately 100 times more potent than morphine.
- **Codeine:** produce less analgesia, and respiratory depression and have a lower potential for abuse than morphine
- Unlike Morphine it causes little or no euphoria.
- These drugs also produce constipation, urinary retention, cough suppression and miosis.
- Codeine usually administered by mouth and indicated:
  - for relief of mild to moderate pain
  - treatment of persistent cough – codeine is effective cough suppressant and is widely used for this action (the antitussive dose is 10 mg)
  - short-term control of acute diarrhea because long-term use is associated with constipation.

- For analgesic use, codeine is dispensed alone or in combination with non-opioid analgesics (aspirin or acetaminophen into a single tablet or capsule) this combination produces greater pain relieve than either drug alone and the dose of opioid can be kept small to avoid dependence and opioid-related adverse effects.

- **Diphenoxylate:** This is a widely used drug for treatment of diarrhea. It is present in combination with a small dose of atropine (Lomotil, or Enterostop).

• Opioid with mixed agonist- antagonist

- **Pentazocine:** These drugs act as agonist at Kappa receptors and antagonist at Mu receptors (produces little or no euphoria).
- Pentazocine produce analgesia when administered alone.
- These drugs produce less analgesia than morphine against severe pain, have a lower potential for abuse and limited respiratory depression.
- Pentazocine when given to a patient who is taking pure opioid agonists these drugs can antagonize analgesia caused by these drugs.
- If administered to a patient that is physical dependence on a pure opioid agonist, pentazocine can precipitate withdrawal syndrome.

Pure opioid antagonist

- **Naloxone**: drug that block the effects of opioid agonists. It is structural analog of morphine; it acts as antagonist at Mu and Kappa receptors.
- This drug does not produce analgesia or any of the other effects caused by opioid agonists.
- Used primarily to reversal of postoperative opioid effects, neonatal respiratory depression and overdose with pure opioid agonists.
- Reverse respiratory depression, coma, analgesia and most other effects of pure opioid agonist.
- Naloxone cannot be used orally because of rapid first pass metabolism in the liver. It administered IV, IM, SC.

- **Nursing Interventions/Client Education to minimizing adverse effects**

– Provide patient teaching about the drug, dosage, drug effects, and symptoms of serious reactions to report for accurate administration.

– Dosage should be adjusted to meet individual needs. For all patients, dosage should be reduced as the pain subsides.

– Double check opioid doses with another nurse prior to administration.

– Keep resuscitative equipment and opioid antagonist – naloxone available.

– Warn clients not to increase dosage without consulting the provider.

– Vital signs especially respiratory rate should be determined prior to opioid administration.

- Monitor respiratory rate in all patients. Stop opioids if the client's respiratory rate is less than 12/ min, and then notify the physician.
- Inform patients that opioids may cause sedation, drowsiness, lightheadedness and advise them to sit or lie down if these symptoms occur and should avoid hazardous activities such as driving or operating heavy machinery
- Inform patients to avoid sudden changes in position –slowly moving from a lying to a sitting or standing position to minimize hypotension.
- Perform IV injection slowly (over 4 –5 min) with patient lying down. Rapid inj. may produce severe adverse effects and should be avoided.

- Emesis can be minimizing by pretreatment antiemetic and by having patient remain still.
- The risk of constipation can be reduced by advise the patients to maintaining physical activity, taking an adequate fluid and fiber, and prophylactic treatment with a stimulant laxative.
- To evaluate urinary retention, continuously monitor intake and urine output, and palpate the lower abdomen for bladder distention every 4 –6 hrs.
- Advise clients to cough at regular intervals to prevent accumulation of secretions in the airway. Auscultate the client's lungs for crackles, and instruct clients to increase intake of fluid to liquefy secretions.
- Advise clients with physical dependence not to discontinue opioids abruptly. Opioids should be withdrawn slowly, and the dosage should be tapered over a period of 3 days.

- **To minimizing the abuse of opioids**

– Exercise good clinical judgment.

– Opioids should be administered in the lowest effective dosages for shortest time required.

– Reserve opioids for patients with moderate to severe pain.

– Switch to a non opioid analgesic when the intensity of pain is reduced.

- **Non-opioids analgesics – Centrally acting**
- **Tramadol**: It is a centrally acting moderately strong analgesic. The recommended daily dose is 50–100 mg/4 – 6 hrs
- Tramadol is analog of codeine with relatively weak mu receptor activity, it also inhibits neuronal reuptake of NE and enhances serotonin release.
- Tramadol has lower potential for dependence, abuse, or respiratory depression. Tramadol has a lower incidence of constipation compared with opioids, but has a high incidence of nausea, dizziness, sedation, headache and dry mouth.
- Tramadol is less effective than morphine and no more than codeine combined with aspirin or acetaminophen.
- Analgesia begins 1hr after oral administration and continues for 6 hrs. Tramadol is rapidly absorbed from the GIT. Elimination by hepatic metabolism.