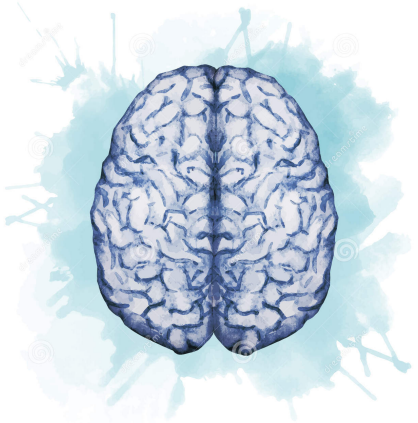
MEDICINE
KING SAUD UNIVERSITY

436 team pharmacology



MCQs | SAQs | summary

drugs used in management of pain

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Summary

Drug	Morphine
Mech. of action	1. Binding to presynaptic opioid receptors coupled to Gi (inhibitory G protein) →↓ AC (adenylate cyclase) & cAMP →↓ N-type voltage-gated Ca2+ channels (inhibit influx of Ca2+,→ reduce release of neurotransmitter) →↓ excitatory transmitter. 2. Binding to postsynaptic receptors → increasing postsynaptic K+ efflux (hyperpolarization) →↓ neuronal excitability
P.K	- T 1⁄2 is 2-3 h - It is slowly and erratically absorbed orally (bioavailability 10-40%) → Given SC, IM, or IV injection. - **Metabolized by conjugation with glucuronic acid** - Undergoes enterohepatic recycling → Crosses BBB. - Crosses Placenta →Infants born of addicted mothers show physical dependence on opiates and exhibit withdrawal symptoms if opioids are not administered
P.D	- Analgesia [in acute & chronic pain] more effective on visceral & skeletal pain. - Euphoria relieves anxiety of patient. → that's why people may addict it. - Respiratory depression → by reduction of the sensitivity of respiratory center neurons to carbon dioxide. - **Depression of cough reflexes** → treatment of non-reproductive cough (antitussive effect). - Nausea & vomiting → ↑ excitation CRTZ (chemoreceptor trigger zoon) - **Pin point pupil (miosis) →Diagnostic feature of opioid addiction**. - Effects on GIT:- - • ↑in tone, ↓motility of intestine →severe **constipation** →) by reducing release of Ach →treat diarrhea. - • **↑biliary tract pressure due to contraction of the gallbladder and constriction of the biliary sphincter→ contraindicated in biliary colic**
TOLERANCE & DEPENDENCE	- Tolerance occurs when the person takes a higher dose of the drug to achieve the same level of response achieved initially. - Occurs rapidly with opioids (e.g. morphine 12–24 hours) - Develops to respiratory depression, analgesia, euphoria and sedation - **No tolerance for miosis so it is good indicator for addict people.**
	- Dependence develops when the neurons adapt to the repeated drug exposure and only function normally in the presence of the drug. - **Physical** dependence →withdrawal manifestations develop upon stoppage. Or giving opioid antagonist. - Lasts for a few days (8-10 days) in form of ↑body ache, insomnia, diarrhea, goose flesh, lacrimation. - **Psychological** dependence lasting for months / years →craving. - Dependence developed mainly with morphine.
Indications	1. **Pain** Control : cancer pain, severe burns, trauma, Severe visceral pain **(not renal colics (because it constricts the ureter) /biliary colics, acute pancreatitis because the gall bladder & pancreas has common sphincter** constricted by morphine) Acute Pulmonary Edema 2. **Myocardial Ischemia** 3. Stress Relief: e.g. heart failure (non painful conditions) 4. **Pre-** anesthetic medication
ADRs	- Itching - Constricted Pupil - Sedation - Nausea /Vomiting - Respiratory Depression - Constipation I Punched Simon's Nose Repeatedly *Crack*
C.I	- Head Injury, due to dilation in cranial blood vessels > intra-cranial Pressure >bleeding - Bronchial asthma or Impaired Pulmonary Function. Due to release of histamine. . - **Biliary colic →it increase the pressure of biliary tract.** - Elderly (more sensitive due to →↓ Metabolism, lean body mass→ Renal function) - Pts take MAOIs (Monoamine oxidase inhibitors). Because depressant actions of morphine are enhanced - **Infants, neonates, or during child birth→ conjugating capacity → accumulate→ respiratory level**

Summary

Drug	codeine	TRAMADOl	Pethidine (mepridine)	FENTANYL	METHADONE
P. D	- μ Agonist -Dependence < morphine	- Synthetic, μ (mu) agonist - less potent than Morphine. - **inhibits NE and 5HT (serotonin) reuptake.**	- Synthetic, more effective k agonist. - Less analgesic, constipating, depressant on fetal respiration than morphine. - No cough suppressant effect. - Has **atropine-like action (smooth muscle relaxant)** - Does not cause pinpoint pupils but, rather, causes the pupils to dilate because of an anticholinergic action.	- Synthetic, μ (mu) agonist, - more potent than Pethidine and Morphine	- Weaker synthetic μ agonist. - antagonist of the N-methyl- D-aspartate (NMDA) receptor. **-In non-addicts,** it causes tolerance and dependence but not as severe as that of Morphine.
P.K	-	Can be given orally (high bioavailability)	–	• Highly lipophilic. • Short Duration.	T1/2 = 55 hrs
Use	- Used in mild & moderate pain - Dry cough - Diarrhea	Mild to moderate acute and chronic visceral pain. During labor (because it does not inhibit respiration).	• As in Morphine but not in cough and diarrhea. • Better (preanaethetic medication). • **Used in obstetric analgesia (no decrease in respiration)** • **Used in severe visceral pain; renal and biliary colics (smooth muscles relaxant).** - Used for acute pain	• Analgesic supplement during anesthesia (IV or intrathecal = injection into the spinal canal). • **Induce and maintain anesthesia in poor-risk pts (stabilizing heart)** • Used in combination with Droperidol as **NEUROLEPTANALGESIA**. (when we want the patient to cooperate with us during surgery and be conscious) • - In cancer pain and severe postoperative pain; (transdermal patch changed every 72 hrs)	**Used to treat and control opioid withdrawal (in people who have become addicted to opiates such as heroin)** - neurogenic pain (NMDA antagonist.)
ADRs	-	- Seizures (not use with epileptics) - Nausea - Dry mouth - Dizziness - Sedation - Less ADRs on respiratory and CVS	- Tremors, convulsions, hyperthermia, hypotension. - Blurred vision, dry mouth, urine retention (atropine-like effects) - Tolerance and addiction.	- Respiratory depression (most serious) - CV effects are less. - Bradycardia may still occur	

Summary

Opioid antagonists		
Drug	NALOXONE	NALTREXONE
Indications	• Used to treat and **reverse respiratory depression caused by opioid overdose.** • Reverse the effect of analgesia on the respiration **of the new born baby**. • Precipitates withdrawal syndrome in **addicts**. But in normal can relieve the pain without withdrawal symptoms)	
Extra info .	- Pure opioid antagonist - Competitive antagonist to μ, κ, and δ.	Partially antagonist Very similar to Naloxone With Longer duration of action. T1/2 = 10hrs
	(that's why we prefer naloxone because it has short duration so less withdrawal symptoms)	
	Antagonists rapidly reverse the effect of agonists such as (respiratory depression), but precipitate the symptoms of opiate withdrawal	

MCQs

1) Which one of the following drugs is contraindicated in patients take MAOIS such as phenelzine?

a) Aspirin. b) Morphine. c) Naloxone.

2) Which one of the following drugs can not be used as analgesia in new born baby?

a) Pethidine. b) Naloxone. c) Morphine.

3) Which one of the following drugs is used in obstetric analgesia?

a) Pethidine. b) Naloxone. c)Fentanyl.

4) Which one of the following drugs metabolized by conjugation with glucuronic?

a) Thebaine. b) Anticonvulsants. c) Morphine.

5) Patient with biliary colics have severe pain that is treated with one of the analgesic that work on Kappa receptors, Which of the following is the drug with atropine like effect can be used?

a) Pentazocine. b) Pethidine. c) Morphine.

6) Patient coming to the ER complaining of sever pain in the middle to right upper abdomen. Investigations shows presence of gallstones. The patient was diagnosed with biliary colic. Which one of the following drugs you should not give it to the patient?

a) Morphine. b) Methadone. c) Naloxone.

7)Which one of the following drugs can be used to relieve the pain in patient with acute pancreatitis due to its atropine-like action?

a) codeine. b) Pethidine. c) Naloxone.

8) Which one of the following opioids receptors is responsible for miosis in addicted person ?

a) Delta. b) Mu1. c) Mu2.

1) B
2) C
3) A
4) C
5) B
6) A
7) B
8) C

MCQs

9) Which one of the following receptors may inhibit the synthesis of dopamine ?

a) Kappa. b) Mu. c) OLR - 1.

10) A young woman is brought into the emergency room. She is unconscious, and she has pupillary constriction and depressed respiration. Based on reports, an opioid overdose of morphine, Which of the listed drugs can be used as antidote in her case ?

a) codeine. b) Fentanyl . c) Naloxone.

11) Which of the following statements about fentanyl is correct?

a) It is 100 times more potent than morphine.
b) It can be used with patient with myocardium infarction or heart failure.
c) It can be used during surgery when we need the patient to cooperate with doctors and be conscious.
D) All of them.

12) Which one of the following drugs inhibit NE & 5HT reuptake?

a) Pentazocine. b)Fentanyl. c) Tramadol.

13) A 27-year-old male came to the ER department, he was suffering from Nausea, vomiting and constipation. The doctor did the examination and he noticed that his pupil was constricted. Which of the following drugs was he mostly take?

a) Naltrexone. b) Pethidine. c) Morphine.

14) Which one of the following is diagnostic feature and good indicator for addict people?

a) Constricted pupil. b) respiratory depression. c) euphoria.

15) Which one of the following opioids can be used to treat or control the withdrawal symptoms with person who has became addicted to Heroin?

a) Pentazocine. b)Fentanyl. c) Methadone.

9) C
10) C
11) D
12) C
13) C
14) A
15) C

SAQs

Q1: Huda a 27-year-old female came to the ER department, she was complaining of sever pain in the middle to right upper abdomen. Investigations shows presence of gallstones. The patient was diagnosed with biliary colic.

1-Which drug you should not give it to Huda?

Morphine

2-What is the mechanism of action of this drug?

1. Binding to presynaptic opioid receptors coupled to Gi (inhibitory G protein) →↓ AC (adenylate cyclase) & cAMP →↓ N-type voltage-gated Ca2+ channels (inhibit influx of Ca2+,→ reduce release of neurotransmitter) →↓ excitatory transmitter.
2. Binding to postsynaptic receptors → increasing postsynaptic K+ efflux (hyperpolarization) →↓ neuronal excitability.

3-Why this drug should given IV repeatedly?

Morphine has very short half life about 2-3 hours.

4-How does it metabolize ?

Metabolized by conjugation with glucuronic acid.

5-Why this drug is contraindication in elderly patients?

They be more sensitive due to 1- decrease in the liver metabolism. 2-impairment of Renal function

6- What is the diagnostic feature of this drug can be easily diagnosed?

Miosis (constructed pupil), there is no tolerance for it.

7- What is the drug of choice to relieve her pain, and why?

Pethidine, due to its atropine like action with smooth muscle relaxant.

Q2: New born baby suffer from sever abdominal pain. And he had given an opioid drug to relieve his pain. Suddenly he developed respiratory depression.

1-What is most likely analgesic drug was used in his case?

Morphine

2-Why this drug is contraindicated with new born baby?

Because they have limited conjugating capacity → which lead to accumulate of morphine → respiratory depression

3- Which drug can be used to reverse respiratory depression?

Opioid Antagonist such as Naloxone & Naltrexone. But we prefer Naloxone due to its short half life.

4-Is there any drug which recommended to be used in obstetric analgesia?

Yes, Pethidine (meperidine)