Chronic Pain Drugs

Drugs	Pharmacokinetics	Pharmacological actions	Tolerance & Dependence	Uses	Side effect	Contraindication
Opioids	T ½ is 2-3h →converts to active morphine 6-glucuronide & an inactive morphine 3-glucuronide metabolite. It is slowly & erratically absorbed orally. Medically given by IM or IV injection. It should be repeated if sustained effect is needed. Non-medically also be inhalation. Undergoes enterohepatic recycling, **crosses** BBB & placenta.	In acute & chronic pain. Euphoria → powerful sense of contentment & well being. **Respiratory depression**→↑pCO_2. **Depression of cough** reflexes. N & V → ↑CRTZ. **Pin point pupil**: due to stimulation of occulomotor center by m, k effects. Diagnostic. Effects on GIT:↑ tone ↓motility →severe **constipation**. ↑pressure in the biliary tract→ contraction of gall bladder & constriction of biliary sphincter. Releases histamine from mast cells. ↓LH, FSH, ACTH, testosterone↑Prolactin, GH, ADH → urine retention.	Develops rapidly. **Withdrawal manifestations**. **Dependence** comprises both: Physical dependence: lasting for a few days in form of ↑ body ache, insomnia, diarrhea, goose flesh, lacrimation Psychological dependence: lasting for months / years → craving.	**Control pain**; cancer pain, severe burns, trauma Severe visceral pain (not renal/biliary colics, acute pancreatitis). **diarrhoea.** **Cough.** Acute pulmonary oedema. Myocardial ischemia. Non painful conditions; HF to relieve distress. preanaesthetic medication.	Sedation. Respiratory depression. Constipation. N & V. Itching → histamine release Tolerance; not to miosis, convulsion or constipation Dependence. Euphoria.	Head injury. **Pregnancy**. **Bronchial asthma** or impaired pulmonary function. Liver & Kidney diseases (including renal& biliary colics). Endocrine diseases (myxedema & adrenal insufficiency). Elderly are more sensitive. Not given infants, neonates or during child birth→ ↓conjugating capacity → accumulate → ↓ respiratory. With MAOI.
Meperidine	Effective κ agonism than morphine	Well absorbed orally [↑oral biovailability] Given also by IMI Half-life (short) 2-4 hours →active metabolite →CNS stimulant effect. Excreted→ **urine**	**Action:** ↓analgesic, ↓constipating, ↓depressant on fetal respiration than morphine. Has **atropine like** action. Smooth muscle relaxant. **No cough** effect.	**Uses:** As in morphine but **not** in **cough** & **diarrhea** Severe visceral pain; renal & **biliary colics** (relaxes sm). Obstetric analgesia (No ↓ resp.) Preanaesthetic medication (better)	**Side effect:** **Tremors**, Convulsions, Hyperthermia, **Hypotension**. Blurred vision, Dry mouth, Urine retention Tolerance & **Addiction**.	
Pentazocine	**Analgesia →κ partial agonist / Dysphoria → σ agonist** **μ weak antagonist →** **withdrawal syndrome** in addicts.	Extensively metabolized in the **liver**	**Used:** moderate to severe pain	**Side effect:** N & V, dizziness, sweating, **hypertension tachycardia**.	**Contraindication:** **MI** →can cause dysphoria (k), psychological & physical dependence (m).	

Tramadol	Synthetic, μ **agonist**, ↓ potent analgesia. ↓uptake of NE & 5HT	Given **orally**, ↑ oral bioavailability. Given by other different other routes. Undergoes extensive metabolism.	**Uses:** Mild - moderate acute & chronic visceral pain **During labor**.	**Side effect:** **Seizures** , Nausea , Dry mouth, Dizziness , **Sedation** **Less** adverse effects on respiratory & C.V.S.	**Contraindication:** History of **epilepsy**	
Methadone	Synthetic, μ- Weaker **Agonist**, t½ 55 h.	Firm occupancy of opioid receptors by methadone **↓ desire for other opioid intake**, because it is producing an ↓effect that stop withdrawal manifestations. With time addicts improve → ↓ craving	**Used** to **treat opioid withdrawal**.	In non addicts, it causes tolerance & dependence but not as severe as that of morphine.		
Naloxone	**Pure opioid antagonist**. It has little effect on pain threshold but can cause hyperalgesia under conditions of stress or inflammation, when endogenous opioids are produced.	Used to treat **respiratory depression** caused by opioid overdose & to reverse the effect of analgesia on the respiration of the new born baby. Effect lasts only for 2-4 hours. **Precipitates withdrawal syndrome in addicts**.				
Naltrexone	Very similar to naloxone but with longer duration of action [t½=10h].		**Heroin**	μ **agonist**. Crosses BBB. Converted to morphine. **No medical use**. Strong addicting drug.	**Codeine**	μ **agonist**. ↓efficacy [1/10 morphine] 10% converted to morphine **Less Dependence**. Large dose causes excitement. **Used** in mild & moderate pain, cough, diarrhea.