



**Round :** .....Anesthesia.....

**Group no :** .....A4.....

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# IV anesthetic agents

## Triad of general anesthesia

### Analgesia

- Pain management

### Hypnosis

- Loss of consciousness

### Muscle relaxant

- Suppression of undesired reflexes

- In modern anesthesia techniques IV drugs are used for » induction of general anesthesia .. In contrast inhalation drugs are used for » maintenance of general anesthesia
- Hypnotic agents » barbiturates, propofol, benzodiazepines, ketamines, etomidate
- 2 types of receptors in brain » stimulatory receptors (NMDA), inhibitory receptors (GABA) .. so to induce hypnosis you can either stimulate GABA or inhibit NMDA
- Mechanism of action for these hypnotics » all of them act by stimulating inhibitory receptors GABA except ketamines they act by inhibiting stimulator receptors NMDA
- Main use » induction of GA » rapid onset of action (30 sec-1 min) .. why? Because it's highly lipid soluble » to be able to cross blood brain barrier
- They have short duration of action (10-20 min but they stay in the body for 4-6 h) .. why? Because of redistribution for highly perfused central compartment to low perfused peripheral compartment according to the concentration gradient in that way it's concentration on brain receptors decreases so it's action terminates
- What are the main components of the skull? Brain-meningies, blood, CSF .. skull doesn't have a compensatory mechanism if any of its components increased in size it's rigid » result of increase of any component is increase in intracranial pressure
- These drugs have an effect on ICP by affecting blood volume how? They all decrease ICP » cerebral vasoconstriction, except for ketamines they increase ICP » cerebral vasodilatation
- They undergo metabolism » deactivation (after 10-20 min), turning to hydrophilic to be extracted by kidney
- All of them don't have antidotes except for benzodiazepines » flumazenil
- All of them don't have analgesic properties except for ketamines

## \* Barbiturates

- Mechanism of action » stimulates inhibitory receptors GABA .. Rapid onset of action » high lipid soluble

- Short duration of action » redistribution for central to peripheral components .. Decreases ICP » cerebral vasoconstriction .. no analgesic effect .. no antidote
- It has an alkaline media (ph = 10-10.5) » no bacterial growth, if it's accidentally injected intra-arterial » irritation resulting in spasm that leads to ischemia, first symptom the patient experiences is pain, it could lead to necrosis and gangrene
- It has narrow therapeutic index » effective dose (2 mg) is so close to toxic dose (2.5 mg) » you can only give it as a bolus and not for continuous infusion or maintenance of GA
- The only case you can use inhalation agent for induction and maintenance » pediatrics
- The only case you can use IV drugs for induction and maintenance » malignant hyperthermia
- Uses » 1. Induction of GA 2. Sole anesthesia for short procedures 3. Status epilepticus
- Because these drugs act on CNS they will have effects on RS and CVS, respiratory (respiratory center and airway reflexes » coughing and salivation (protective reflexes that protect from aspiration), cardiovascular » BP, HR)
- Side effects on RS » central apnea, blunt of airway reflexes » need for intubation to secure airway and prevent aspiration with mechanical ventilation
- That's why it's only used in a place where you can do airway instrumentation and mechanical ventilation
- Side effects on CVS » it affects vasomotor center in brainstem by decreasing systemic vascular resistance which results in hypotension and tachycardia resulting from baroreceptors reflex
- It precipitate porphyria » someone who has a genetic predisposition to porphyria, taking barbiturates » attack porphyria .. Porphyria » genetic disease effects children manifest skin and GI symptoms
- One of the side effects it's an enzyme inducer » stimulates different cascades » production of unwanted metabolites » unwanted effects

## \* Propofol

- Mechanism of action » stimulates inhibitory receptors GABA .. Rapid onset of action » high lipid soluble
- Short duration of action » redistribution for central to peripheral components .. Decreases ICP » cerebral vasoconstriction .. no analgesic effect .. no antidote

- It's the first choice for induction of general anesthesia and sedation
- **Advantages** » 1. Rapid onset 2. Short duration of action 3. Bronchodilator 4. Antiemetic » treats nausea and vomiting (causes » gases, hypoxia, hypercapnia, hypotension) 5. Antipruritic » treats itching 6. Doesn't cause hangover symptoms » nausea, vomiting, headache, dizziness, blurred vision
- Because of point 6 » they developed day case surgery concept (ambulatory surgery) .. before propofol they couldn't discharge the patient in the same day of the surgery because these symptoms could be mistaken as complications of surgery
- **Uses** » 1. Induction of GA 2. Maintenance of GA 3. Short procedures 4. Ambulatory surgeries 5. Sedation of intubated mechanically ventilated ICU patients
- **Side effects** » 1. On RS (central apnea, blunt airway reflexes) 2. On CVS (affects vasomotor center by decreasing systemic vascular resistance which results in hypotension and bradycardia resulting from blunting baroreceptors reflex) 3. Pain if injected IV
- **Main components** » soybean oil, egg lecithin, glycerol » good media for bacterial growth » if it's contaminated » overgrowth of bacteria » if injected into a patient » 4. Septicemia .. It should be administered within 6 hours of opening to avoid contamination
- **Has high lipid content** » 5. Hyperlipidemia is some patients who have abnormal lipid profiles and repeated doses of propofol
- 6. Propofol infusion syndrome » patients who take large doses in long period of time like ICU patients especially pediatrics and those with adrenal insufficiency .. manifestations of syndrome » hyperlipidemia, metabolic acidosis, cardiac arrest, rhabdomyolysis

## ✿ Etomidate

- **Mechanism of action** » stimulates inhibitory receptors GABA .. Rapid onset of action » high lipid soluble
- Short duration of action » redistribution for central to peripheral components .. Decreases ICP » cerebral vasoconstriction .. no analgesic effect .. no antidote
- It's a stabilizer » very minimal effect on RS & CVS
- **Side effects** » 1. Severe nausea and vomiting 2. Adrenal insufficiency (inhibits 11 $\beta$ -hydroxylase enzyme) » it's contraindicated in Addison patients

## ✿ Kitamines

- **Mechanism of action** » inhibits stimulatory receptors NMDA .. Rapid onset of action » high lipid soluble
- Short duration of action » redistribution for central to peripheral components .. Increases ICP » cerebral vasodilatation .. only one who has analgesic effect .. no antidote
- It's a potent sympathetic stimulator » 1. bronchodilatation » the drug of choice for patients with bronchial asthma (if ketamine not available choose propofol) 2. Increases BP and HR 3. Effect on RS is zero
- Side effects and contraindications** » 1. Increases ICP » contraindicated in brain tumor, head trauma or fracture, hemorrhagic stroke (if ischemic stroke not contraindicated) 2. Increases intraocular pressure » contraindicated in glaucoma 3. Hallucinations and illusions » contraindicated in psychiatry 4. Increases HR and afterload » contraindicated in patients who have evidence of limited cardiac reserve like heart failure, ischemic heart diseases (oxygen demand = supply, if you increased the work of their heart it will result with decompensation) 4. Contraindicated in cardiogenic shock (drug of choice for them etomidate)
- Ketamine is indicated for hypovolemic shock » effects on heart are compensatory in case of shock it increases HR and afterload
- It's the drug of choice for warzones » has an acceptable analgesic effect, drug of choice for hypovolemic shock, zero effect on RS no need for intubation or mechanical ventilation
- System with the top priority » CNS then CVS .. A patient came with multiple trauma and hemodynamic unstable (hypotensive) what is the drug of choice etomidate or ketamine? If the trauma is below head drug of choice is ketamine, if the trauma includes head or basilar skull fracture the drug of choice is etomidate

## ✿ Benzodiazepines

- **Mechanism of action** » stimulates inhibitory receptors GABA .. Rapid onset of action » high lipid soluble
- Short duration of action » redistribution for central to peripheral components .. Decreases ICP » cerebral vasoconstriction .. no analgesic effect .. has antidote » flumazenil
- They're classified according to the duration of action » 1. Short acting: medazolam 2. Intermediate acting: lorazepam 3. Long acting: diazepam
- **Uses** » 1. Induction of GA 2. Anticonvulsant 3. Anxiolytic
- **Side effects** » the same as barbiturates on RS and CVS but weaker

## ✿ Opioids

- Antidote » naloxone
- Side effects » chest rigidity
- The appropriate management of chest rigidity naloxone or muscle relaxant? Naloxone