	Barbiturates	Etomidate	Alkyl phenols : propofol	Ketamine	Benzodiazepines
	- Derived from barbituric acid - Prepared as sodium salts - Highly alkaline (pH: 10.5) - Available as racemic mixtures	- Contains carboxylated imidazole ring which provides water solubility at physiological pH. -	- Propofol (2, 6-diisopropylphenol) consist of phenol ring with two isopropyl groups attached - Altering the side chain of this alkylphenol influences potency, induction and recovery characteristics. - Formulation can support bacterial growth (soybean oil, glycerol, and egg lecithin). - Not water soluble. - Propofol should be administered within 6 h of opening the ampule.	Has multiple effects through the CNS including: - blocking polysynaptic reflexes in the spinal cord - inhibiting neurotransmitter effects in selected areas of the brain.	- Chemical structure includes a benzene ring and a 7-member diazepine ring - substitution at various positions on these rings affect potency and biotransformation.
Mechanism of action	1. Depress the reticular activating system located in the brain stem that controls several vital functions, consciousness. - Interact with the inhibitory neurotransmitter GABA. - Affect the function of nerve synapses not axons	1. Depresses the reticular activating system 2. mimics the inhibitory effects of GABA. 3. Binds to subunit of GABA type a receptor increasing its affinity to GABA.	-Facilitate inhibitory neurotransmitters mediated by GABA - It can attenuate upper airway reflexes.	1- Ketamine dissociates the thalamus from the limbic cortex (dissociative anesthesia) * Causes the patient to appear conscious but unable to process or respond to sensory input 2- N-methyl-D-aspartate receptor antagonist. 3- Structurally analogue to phencyclidine. - Can cause hallucinogenic effects and nightmares.	- Binding to receptors enhances the inhibitory effects of various neurotransmitters (GABA) in the CNS mainly in the cortex. -
Dose	- Dose 3-5 mg/kg	- Induction dose: 0.2-0.4 mg/kg.	induction IV 1.5-2.5 mg/kg.	- Induction IV 1-2 mg/kg - pre-operative for pediatrics IM 3-5 mg/kg - analgesic dose 0.5-1 mg/kg	Dose Midazolam: - premedication IM 0.07-0.15 mg/kg - sedation IV 0.01-0.1 mg/kg - Induction IV 0.1-0.4 mg/kg.
Absorption		Administered IV only for induction of GA.	-Available only for IV for induction of GA and sedation.	Administered IM or IV with peak plasma level within 10-15 min after IM injection	-Administered orally, IM and IV for sedation or induction of GA.: 1. Diazepam and Lorazepam well absorbed from GI tract, peak plasma level in 1-2 h respectively.
Distribution	- Thiopental is highly protein bound (80%)	-High protein bound and high lipid soluble. -Redistribution is responsible for decreasing the plasma concentration to awakening level.	-High lipid soluble with an onset of action as one-arm-to-brain circulation time. -Very short initial distribution half-life (2-8 min).	-More lipid soluble and less protein bound than thiopental -Distribution half-life is 10-15 min	-Diazepam is lipid soluble and rapidly cross the blood brain barrier -Redistribution is rapid for benzodiazepines (3-10 min). -Highly protein bound (90-98%).
Biotransformation and excretion:		-Hepatic microsomal enzymes and plasma esterases -hydrolyze etomidate to inactive metabolite. -The end product is excreted in the urine.	-Clearance exceeds hepatic blood flow with extra hepatic metabolism. -Conjugation in the liver with inactive metabolites as an end product that are eliminated by the kidney.	1. Biotransformed In the liver to several metabolites (some retain anesthetic properties (nor ketamine)). 2. Short elimination half-life (2 hours). 3. Execrated renally.	- Metabolites are excreted mainly in the urine - Enterohepatic circulation produces a second peak in diazepam plasma concentration 6-12h following administration. -Rely on the liver for transformation into water-soluble glucoronide end products. -Slow hepatic extraction, long half-life for diazepam (30h).
Drug interactions:	- Interact with the inhibitory neurotransmitter GABA.	-etomidate: 1. Fentanyl increases the plasma level and prolongs the elimination half-life of etomidate 2. Opioids decrease the myoclonus characteristic of an etomidate induction	- Fentanyl and alfentanil: concentrations may be increased with concomitant administration of propofol -Midazolam: can reduce the required propofol dose by more than 10%.	- Diazepam and midazolam: attenuate ketamine's cardio stimulatory effects - diazepam: prolongs ketamine's elimination half-life.	- The combination of opioids and benzodiazepines markedly reduces arterial blood pressure and peripheral vascular resistance - Benzodiazepines reduce the minimum alveolar concentration of volatile anesthetics as much as 30%.
Adverse effects	-Hypotension -Respiratory depression -Laryngeal spasm -Bronchospasm -Allergic reactions (1 in 14,000) -Extravasation tissue necrosis -Intra-arterial injection -Thrombophlebitis	-May activate seizure, extrapyramidal activity. -Pain on injection -Adrenocortical suppression. -Allergic reactions.	-Allergic reactions. -Lactic acidosis (Propofol infusion syndrome). -Bacterial growth. -Pain on injection.		
Contraindications	1- Airway obstruction (histamine release) 2- Porphyria (Barbiturates promote aminolevulinic acid synthetase, which stimulates the formation of porphyry (an intermediary in heme synthesis). They may precipitate acute intermittent porphyria or variegate porphyria in susceptible individuals.) 3- Hypersensitivity		Indications: -Induction of anesthesia. -Sedation. -Maintenance of anesthesia. (TIVA) -Antiemetic. -Antipruritic. -Anticonvulsant. -Attenuation of bronchoconstriction.		
Note	Concentrations greater than recommended cause an unacceptable incidence of pain on injection and venous thrombosis.				Flumazenil (antidote) is a specific benzodiazepine-receptor antagonist that effectively reverses most of the CNS effect.

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CVS	1. Decrease blood pressure and increase heart rate maintain CO. 2. Depression of the medullary vasomotor center - vasodilates peripheral capacitance vessels - increases peripheral pooling of blood - decreases venous return to right atrium.	1. Minimal effect on CVS. 2. Mild reduction in PVR and arterial BP. 3. Myocardial contractility and cardiac output are unchanged. 4. No histamine release.	1. Decrease BP due to: -drop in systemic vascular resistance -drop in cardiac contractility and preload. 2. Impairs the normal arterial baroreflex response to hypotension.	1. Increases Blood pressure, heart rate, and cardiac output. 2. Increases pulmonary artery pressure and myocardial work. 3. should be administered cautiously in patient with: -coronary artery disease -uncontrolled hypertension -congestive heart failure -arterial aneurysms. 4. indirect stimulatory effects may be benefit to patients with acute shock.	-Minimal CVS depressant effects. -Arterial BP, Cardiac output, and PVR slightly decreased -Heart rate sometimes increased. -Intravenous midazolam tends to reduce blood pressure and peripheral vascular resistance more than diazepam.
RS	1. Depresses the medullary ventilatory center - decreases the ventilatory response to hypercapnia and hypoxia. 2. Tidal volume and respiratory rate are decreased 3. Histamine release and bronchial smooth muscle constriction - bronchospasm.	Ventilation is affected less than barbiturates	1. It is a respiratory depressant causes apnea following induction dose 2. Inhibits hypoxic ventilatory drive and depresses the normal response to hypercarbia 3. Can produce bronchodilation and decrease the incidence of wheezing intraoperatively.	-Minimal effect on the ventilatory drive. -Potent bronchodilator. -Preserve airway reflexes.	-Depresses ventilatory response to CO2. -Ventilation must be monitored.
Cerebral	1. Constrict the cerebral vasculature 2. cause decrease in cerebral blood flow and intracranial pressure. 3. Decreases cerebral oxygen consumption (up to 50%) 4. Cerebral perfusion pressure increases -cause the drop in ICP -exceeds the drop in arterial BP 5. Have anti-analgesic effect by lowering the pain threshold.	1. Decreases cerebral metabolic rate 2. Decreases cerebral blood flow 3. Decreases intracranial pressure. 4. CPP is well maintained (minimal CVS effect). 5. PONV are common but minimized by antiemetic.	1. Decreases cerebral blood flow and intracranial pressure 2. Auto regulation and response to CO2 are not affected. 3. Decreases intraocular pressure. 4. Have predominantly anti-convulsant properties. 5. Has antipruritic effect and antiemetic properties 6. Can cause critical reduction in CPP in patients with elevated intracranial pressure (< 50 mm Hg).	-Increase cerebral oxygen consumption, cerebral blood flow and intracranial pressure. -Myoclonic activity is associated with increased subcortical electrical activity. -Undesirable psychotomimetic effects (illusions, dreams and delirium). -Have analgesic effects.	1. -Reduces cerebral oxygen consumption. 2. -Decreases cerebral blood flow and intracranial pressure 3. -Effective in preventing and controlling grand mal seizures. 4. -Sedative dosages cause antegrade amnesia.
Renal	1. Reduces renal blood flow 2. Reduces glomerular filtration rate in proportion to fall in BP				
Hepatic	1. Decreases hepatic blood flow 2. Induction of hepatic enzymes, increases the rate of metabolism of some drugs (Digitoxin) 3. Combination with the cytochrome p-450 enzyme system interfere with biotransformation of some drugs (TCA)				
Endocrine		1. Inhibit enzymes involved in cortisol and aldosterone synthesis 2. Can lead to adrenocortical suppression in the long run			

Opioids	
	1. Opioids bind to specific receptors located throughout CNS. 2. M1, 2 is responsive for analgesia and res depression. 3. kabba res responsive for sedation and analgesia.
Mechanism	1. Inhibits the presynaptic release and postsynaptic response to excitatory neurotransmitters (acetylcholine) : fentanyl, morphine, remifentanyl, alfentanil, pethidine
	-histamine release. -Chest wall rigidity. -Nausea and vomiting. -Blocks the release of stress hormone after surgical stimulation.

Diazepam	Lorazepam	Midazolam
1. -Often used as premedication or seizure activity, rarely for induction. 2. -Minimal systemic effects-- respirations decreased with narcotic usage. 3. -Not water soluble-- venous irritation (propylene glycol). 4. -Metabolized by liver-- not redistributed.	1. Slower onset of action (10-20 minutes) -- not used for induction 2. Used as adjunct for anxiolytic and sedative properties 3. Not water soluble-- venous irritation	1. -More potent than diazepam or lorazepam. 2. -Induction slow, recovery prolonged. 3. -May depress respirations when used with narcotics. 4. -Minimal cardiac effects. 5. -Water soluble.