Intravenous Anesthetic Agents

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1- barbiturates

2- NON BARBITURATES: propofol & ketamine

3- BENZODIAZEPINES: Midazolam & diazepam

4- narcotics
Propofol is an intravenous sedative agent used in the induction and maintenance of anesthesia, it is non-analgesic.

Mechanism of action: facilitation of inhibitory neurotransmission mediated by GABAa receptor binding

Physical & chemical properties:
- highly lipid soluble oil
- combined with glycerol, egg, and soya bean oil (1% propofol 10mg/ml, 10% soya bean oil, 2.25% glycerol, 1.2% purified egg phosphatide)
- It has a pH of 7
- Has no effects on muscle relaxants
- low incidence of nausea & vomiting
- Neither precipitates histamine release nor triggers malignant hyperthermia
- Propofol formulations can support the growth of bacteria, so sterile technique must be observed in preparation and handling
Dosage:

<table>
<thead>
<tr>
<th>Propofol</th>
<th>Route</th>
<th>Indication</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV</td>
<td>Induction</td>
<td>1–2.5 mg/kg</td>
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<tr>
<td></td>
<td>IV</td>
<td>Maintenance infusion</td>
<td>50–200 mcg/kg/min</td>
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<tr>
<td></td>
<td>IV</td>
<td>Sedation infusion</td>
<td>25–100 mcg/kg/min</td>
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</tbody>
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Elderly patients <= 1 mg/kg
Effects on different organ systems:

- **Cerebral:**
  1. decreases cerebral blood flow and intracranial pressure.
  2. has antiemetic, antipruritic, and anticonvulsant properties.

- **Cardiovascular:**
  1. decrease systemic vascular resistance \(\rightarrow\) decrease BP (Hypotension is more pronounced than with thiopental)
  2. decrease contractility and preload
  3. impairs the normal arterial baroreflex response to hypotension

- **Respiratory:**
  1. profound respiratory depression
  2. depression of upper airway reflexes exceeds that of thiopental

- **Venous irritation:**
  Pain on injection (more than thiopental)
Indications:
1-Initiation and maintenance of Monitored Anesthesia Care sedation → adults only
2-Combined sedation and regional anesthesia → adults only
3-Induction of General Anesthesia → Patients ≥ 3 years of age
4-Maintenance of General Anesthesia → Patients ≥ 2 months of age
5-ICU sedation of intubated, mechanically ventilated patients → adults only

Contraindications:
1-egg allergy
2-Lack of resuscitation equipment or knowledge of the drug
3-Inability to maintain a patent airway
4-Conditions in which reduction in blood pressure can’t be tolerated (such as aortic or mitral stenosis, tamponade & shock)
KETAMINE

It’s a dissociative anesthetic agent (the patient is unconscious but appears awake and doesn’t feel pain). It has anesthetic and analgesic effect.

Physical & chemical Properties:
-chemically related to the psychotropic drug
-Water soluble, and 10x more lipid soluble than thiopental.
-pH=3.5 - 5.5
-potent analgesic at sub-anesthetic plasma concentrations
-has a wide margin of safety ( up to 10x the usual dose )
Pharmacokinetics:
- Route of administration & dosage:
  1-IV \( \rightarrow \) 1 – 2 mg/kg - dissociated stage is noted in 15 seconds, subsequent IV doses of 1/3 – ½ of the initial dose maybe required
  2-IM \( \rightarrow \) 5 – 10 mg/kg - peak plasma level reach approximately in 15 minutes
  3-oral
  4-rectal: needs higher dose due to extensive first pass metabolism and decreased absorption
- Metabolism & excretion:
  . rapid absorption and distribution
  . Hepatic metabolism is required for elimination
  . <5% excreted unchanged in urine
Mechanism of action:

There are 3 theories:

1- N-methyl aspartate receptor theory:
NMA receptors may represent a subgroup of the sigma opiate receptors that blocks spinal pain reflexes

2- Opiate receptor theory:
Ketamine may have some affinity for opiate receptors

3- Miscellaneous receptor theory:
It reacts with muscarinic, cholinergic and serotonergic receptors
Effects on different organ systems:

-CNS:
1. Increases cerebral oxygen consumption, cerebral blood flow, and ICP
2. Generalized increase in the muscle tone & increases the effects of muscle relaxants
3. Unpleasant dreams, hallucinations or delirium esp. in females

-Respiratory:
1. Preserves laryngeal & pharyngeal airway reflexes
2. A potent bronchodilator
3. FRC, ventilation, TV \( \rightarrow \) unchanged
4. Causes increased secretions but this can be limited by anti-cholinergic drugs
-Cardiovascular:
1-central sympathetic stimulation, which increases BP, CO, HR, pulmonary artery pressure, coronary blood flow & myocardial oxygen uptake
2-It may cause myocardial depression if the sympathetic nervous system is exhausted or blocked

-GI:
Minimal anorexia, nausea & vomiting

-GU:
Placental transfer does occur, but neonatal depression hasn’t been observed if the dose is limited to < 1 mg/kg

-Endocrine:
Increased sympathetic stimulation → increased blood glucose, increased plasma cortisol
Indications:
1- anesthetic for diagnosis and surgical procedures
2- induction of anesthesia
3- supplement regional or local anesthetic techniques
4- for anesthetic induction in severe asthmatic pts. Or patients with cardiovascular collapse requiring emergency surgery

Contraindications:
1- lack of resuscitative equipment
2- inability to maintain a patent airways
3- allergy to ketamine
4- history of psychosis
5- cerebro-vascular disease
6- Patients for whom hypertension is hazardous
Benzodiazepines

Features:
1- amnesia
2- minimal cardiorespiratory depressant effect
3- anticonvulsant activity
4- low incidence of tolerance and dependence
5- highly lipid soluble
6- highly protein bound (albumin)
Mechanism of action:
1-inhibit the actions of glycine by increasing the conc. of a glycine inhibitory neurotransmitter which will lead to antianxiety and muscle relaxant effects
2-facilitate the actions of the inhibitory neurotransmitter GABA which results in the sedative and anticonvulsant effects

Pharmacokinetics:
They are metabolized by the liver through conjugation with glucuronic acid and excreted by the kidneys
Midazolam and diazepam:
The differences between them:

1- Midazolam is 2-3 times more potent than diazepam

2- The dose for IV conscious sedation: 0.5 – 3 mg up to 0.1 mg/kg for midazolam, and 1-10 mg for diazepam

3- The dose for inducing anesthesia: 0.2 – 0.4 mg/kg for midazolam, and 0.15-1.5 mg/kg for diazepam.

4- Midazolam has a more rapid onset, greater amnestic effect, less postoperative sedative effects than diazepam.

5- Pain on injection and subsequent thrombophlebitis is less likely with midazolam

6- Midazolam is more costly than diazepam

7- Midazolam duration of action is less than diazepam but almost 3 times that of thiopental

8- Half life for midazolam range from 1-4 hours, and for diazepam from 21-37 hours
Benzodiazepine antagonist (Flumazenil):
- antagonizes benzodiazepine’s central effects by competitive inhibition
- half life is one hour (less than Benzodiazepines) therefore we will need repeated administrations
- The usual initial dose is 0.2 mg over 15 seconds, if the desired level of consciousness is not obtained within one minute of administration we can give repeated doses of 0.1 mg every minute up to the maximum of 2 mg, and if sedation recurs we can use infusions of 0.1-0.4 mg/hour
- The most common side is nausea (4% of patients)
THANK YOU