

Anesthetics 3

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INTRAVENOUS ANESTHETICS

IV anesthetics cause rapid induction of anesthesia often occurring in 1 minute or less. It is the most common way to induce anesthesia before maintenance of anesthesia with an inhalation agent. IV anesthetics may be used as single agents for short procedures or administered as infusions (TIVA) to help maintain anesthesia during longer surgeries. In lower doses, they may be used solely for sedation.

A. Induction

After entering the blood, a percentage of drug binds to plasma proteins, and the rest remains unbound or “free.” The degree of protein binding depends upon the physical characteristics of the drug, such as the degree of ionization and lipid solubility. The majority of CO flows to the brain, liver, and kidney (“vessel-rich organs”). Thus, a high proportion of initial drug bolus is delivered to the cerebral circulation and then passes along a concentration gradient from blood into the brain. The rate of this transfer is dependent on the arterial concentration of the unbound free drug, the lipid solubility of the drug, and the degree of ionization. Unbound, lipid-soluble, nonionized molecules cross into the brain most quickly. Like inhalational anesthetics, the exact mode of action of IV anesthetics is unknown; however, GABA likely plays a large role.

B. Recovery

The recovery phase is short as these drugs are rapidly redistributed from the CNS into the various compartments of the body. After initial flooding of the CNS and other vessel-rich tissues with nonionized molecules, the drug diffuses into other tissues with less blood supply. With secondary tissue uptake, predominantly skeletal muscle, plasma concentration of the drug falls. This allows the drug to diffuse out of the CNS, down the resulting reverse concentration gradient. This initial redistribution of drug into other tissues leads to the rapid recovery seen after a single IV dose of the induction agent. The final elimination occurs via kidneys or liver. Metabolism and plasma clearance become important only following infusions and repeat doses of a drug. Adipose tissue makes little contribution to the early redistribution of free drug following a bolus, due to its poor blood supply. However, following repeat doses or infusions, equilibration with fat tissue forms a drug reservoir, often leading to delayed recovery.

Propofol

Propofol is an IV sedative/hypnotic used for induction and/or maintenance of anesthesia. It is widely used and has replaced *thiopental* as the first choice for induction of general anesthesia and sedation. Because *propofol* is poorly water soluble, it is supplied as an emulsion containing soybean oil and egg phospholipid, giving it a milk-like appearance.

Onset: Induction is smooth and occurs 30 to 40 seconds after administration. Plasma levels decline rapidly as a result of redistribution, followed by a more prolonged period of hepatic metabolism and renal clearance. The initial redistribution half-life is 2 to 4 minutes. The pharmacokinetics of *propofol* are not altered by moderate hepatic or renal failure.

Actions: Although *propofol* depresses the CNS, it occasionally contributes to excitatory phenomena, such as muscle twitching, spontaneous movement, yawning, and hiccups. Transient pain at the injection site is common. *Propofol* decreases blood pressure without significantly depressing the myocardium. It also reduces intracranial pressure, mainly due to decreased cerebral blood flow and oxygen consumption. It has less of a depressant effect than volatile anesthetics on CNS-evoked potentials, making it useful for surgeries in which spinal cord function is monitored. It does not provide analgesia, so supplementation with narcotics is required. *Propofol* is commonly infused in lower doses to provide sedation. The incidence of postoperative nausea and vomiting is very low secondary to its antiemetic properties.

Barbiturates

Thiopental is an ultra short-acting barbiturate with high lipid solubility. It is a potent anesthetic but a weak analgesic. Barbiturates require supplementary analgesic administration during anesthesia. When given IV, agents such as *thiopental* and *methohexital* quickly enter the CNS and depress function, often in less than 1 minute. However, diffusion out of the brain can also occur very rapidly because of redistribution to other tissues. These drugs may remain in the body for relatively long periods, because only about 15% of a dose entering the circulation is metabolized by the liver per hour. Thus, metabolism of *thiopental* is much slower than its redistribution. Barbiturates tend to decrease blood pressure, which may cause a reflex tachycardia. They decrease intracranial pressure through reductions in cerebral blood flow and oxygen consumption. *Methohexital* is still commonly used for electroconvulsive therapy.

Opioids

- Because of their analgesic property, opioids are commonly combined with other anesthetics. The choice of opioid is based primarily on the duration of action needed. The most commonly used opioids are *fentanyl* and its congeners, *sufentanil* and *remifentanyl*, because they induce analgesia more rapidly than *morphine*. They may be administered intravenously, epidurally, or intrathecally (into the cerebrospinal fluid). Opioids are not good amnestics, and they can all cause hypotension and respiratory depression, as well as nausea and vomiting. Opioid effects can be antagonized by *naloxone*.

Etomidate

Etomidate is a hypnotic agent used to induce anesthesia, but it lacks analgesic activity. Its water solubility is poor, so it is formulated in a propylene glycol solution. Induction is rapid, and the drug is short-acting. Among its benefits are little to no effect on the heart and systemic vascular resistance. *Etomidate* is usually only used for patients with cardiovascular dysfunction or patients who are acutely critically ill. It inhibits 11- β hydroxylase involved in steroidogenesis, and adverse effects may include decreased plasma cortisol and aldosterone levels. *Etomidate* should not be infused for an extended time, because prolonged suppression of these hormones is dangerous. Injection site pain, involuntary skeletal muscle movements, and nausea and vomiting are common

Ketamine

Ketamine a short-acting anti-NMDA receptor anesthetic and analgesic, induces a dissociated state in which the patient is unconscious (but may appear to be awake) with profound analgesia. *Ketamine* stimulates central sympathetic outflow, causing stimulation of the heart with increased blood pressure and CO. It is also a potent bronchodilator. Therefore, it is beneficial in patients with hypovolemic or cardiogenic shock as well as asthmatics. Conversely, it is contraindicated in hypertensive or stroke patients. The drug is lipophilic and enters the brain very quickly. Like the barbiturates, it redistributes to other organs and tissues. *Ketamine* has become popular as an adjunct to reduce opioid consumption during surgery. Of note, it may induce hallucinations, particularly in young adults, but pretreatment with benzodiazepines may help. *Ketamine* may be used illicitly, since it causes a dream-like state and hallucinations similar to *phencyclidine* (PCP).

Dexmedetomidine

Dexmedetomidine is a sedative used in intensive care settings and surgery. Like *clonidine*, it is an α_2 receptor agonist in certain parts of the brain. *Dexmedetomidine* has sedative, analgesic, sympatholytic, and anxiolytic effects that blunt many cardiovascular responses. It reduces volatile anesthetic, sedative, and analgesic requirements without causing significant respiratory depression. It has gained popularity for its ability to blunt emergence delirium in the pediatric population.

Therapeutic Disadvantages

- Must be delivered using a special vaporizer

- Incomplete anesthesia
- No muscle relaxation
- Must be used with other anesthetics for surgical anesthesia

- Potential renal toxicity at low flows

- Poor analgesia
- Causes significant nausea
- Little muscle relaxation
- Laryngospasm

- Poor analgesia

Inhalation anesthetics

Desflurane

Nitrous oxide

Isoflurane

Sevoflurane

Intravenous anesthetics

Thiopental

Ketamine

Fentanyl

Propofol

Dexmedetomidine

Therapeutic Advantages

- Good analgesia
- Rapid onset/recovery
- Safe, nonirritating

- Good muscle relaxation
- Rapid recovery
- Stability of cardiac output
- Does not raise intracranial pressure
- No sensitization of heart to epinephrine

- Bronchial smooth muscle relaxation good for patients with asthma
- Rapid onset/recovery
- Not irritating; useful in children

- Rapid onset of action
- Potent anesthesia

- Good analgesia

- Not likely to cause nausea
- Rapid onset
- Lowers intracranial pressure

- No respiratory depression
- Blunts undesirable cardiovascular reflexes

DRUG	INDUCTION/RECOVERY	ADVERSE EFFECTS	SALIENT POINTS
<i>Ether</i>	Slow	Nausea, vomiting, respiratory irritation	Risk of explosion, no longer used
<i>Nitrous oxide</i>	Fast	Anemia with prolonged or repeated use	Good analgesia, safe, nonirritating, and mainly used along with other inhalational agents as it causes incomplete anesthesia and no muscle relaxation
<i>Halothane</i>	Medium	Malignant hyperthermia, hepatotoxicity, arrhythmias, hypotension; sensitizes myocardium to actions of catecholamines; reduces hepatic and renal blood flow	Fair analgesic, skeletal muscle and uterine relaxant properties, and excellent hypnotic properties; use is declining as better newer anesthetics are available
<i>Enflurane</i>	Medium	Increased seizure potential, malignant hyperthermia; pungent may result in breath holding or coughing; contraindicated in patients with renal failure	Good analgesic, skeletal muscle, and excellent hypnotic properties Widely used as less risk of toxicity than <i>halothane</i>
<i>Sevoflurane</i>	Fast	No respiratory irritation and fewer side effects such as nausea and vomiting in some cases; potential renal toxicity at low flow as it produces fluoride ions during its liver metabolism	Nonirritating; mainly used for daycare surgeries and in children Causes bronchodilatation, useful in bronchial asthma patients
<i>Desoflurane</i>	Fast (faster than <i>isoflurane</i>)	Cough, bronchospasm, respiratory tract irritation, salivation; must be delivered using a special vaporizer	Mainly used for daycare surgeries; minimal metabolism, rarely produces organ toxicity
<i>Isoflurane</i>	Medium	Can cause coronary ischemia (coronary steal phenomenon), pungent odor	Widely used as an alternative to <i>halothane</i> ; good analgesic, sedative-hypnotic and muscle relaxation effect, stability of cardiac output; does not raise intracranial pressure, no sensitization of heart to catecholamines; minimal metabolism

Intravenous anesthetics:

<i>Thiopentone</i>	Fast	Significant nausea, laryngospasm	Potent anesthetic but poor analgesia; little muscle relaxation; short duration of action; contraindicated in patient with acute intermittent porphyria
<i>Propofol</i>	Fast	Postoperative nausea and vomiting though lesser pain on injection and that it is prepared in a lipid emulsion	Poor analgesia; lowers intracranial pressure; has displaced barbiturates in many anesthesia practices
<i>Fentanyl</i>	Fast	Hypotension, postoperative nausea, and vomiting	Good analgesia; useful drug in patients with renal failure; used as an adjunct to inhalation and IV anesthetic agents; used in high doses to achieve general anesthesia during cardiac surgery when circulatory stability is important
<i>Ketamine</i>	Fast	Pleasant dream-like states to vivid imagery, hallucinations, delirium, confusion, excitement, irrational behavior (less in children), hypertension, tachycardia, severe respiratory depression following rapid intravenous administration, tonic-clonic movements resembling seizures	Produces dissociative anesthesia, an effect in which the patient feels dissociated from the surroundings; produces good analgesia with or without loss of consciousness; used as an induction agent for diagnostic, surgical procedures; used in low doses in infants and children in case of trauma, minor surgical, and diagnostic procedures