Intravenous anesthetic agents

Drugs when given intravenously in an appropriate doses cause rapid loss of consciousness.

Rapid onset: Often described as occurring within "ONE ARM-BRAIN CIRCULATION TIME" The time taken for the drug to travel from the site of injection (usually the arm) to the brain, where they have their effect.

USES of Intravenous anesthetics:

1) Induction and maintenance of anesthesia.

2) As a sole anesthetic for short procedures.

3) Intravenous infusion- to maintain anesthesia for longer procedures e.g. TIVA (Total intravenous anesthesia).

4) To provide sedation in places like ICU.

Properties of an ideal induction agent:

Physical properties:

1) Water soluble & stable in solution .
2) Stable on exposure to light.
3) Long shelf life.
4) No pain on intravenous injection.
5) Painful when injected into an artery.
6) Non-irritant when injected subcutaneously.
7) Low incidence of thrombophlebitis.
8) Cheap.

Pharmacokinetic properties:

1) Rapid onset in one arm-brain circulation time.
2) Rapid redistribution to vessel rich tissue.
3) Rapid clearance and metabolism.
4) No active metabolites.

Pharmacodynamics properties:

1) High therapeutic ratio (ratio of toxic dose: minimally effective dose).
2) Minimal cardiovascular and respiratory effects.

3) No histamine release/hypersensitivity reactions.
4) No emetic effects.
5) No involuntary movements.
6) No emergence nightmares.
7) No hang over effect.
8) No adrenocortical suppression.
9) Safe to use in porphyria.

Classification:

The commonest drugs currently in use can be classified according to their chemical structure and include:
1) Barbiturates – THIOPENTAL, METHOHEXITAL
2) Phenols – PROPOFOL
3) Imidazoles - ETOMIDATE
4) Phencyclidines – KETAMINE
5) Benzodiazepines –MIDAZOLAM, DIAZEPAM, LORAZEPAM
They can also be classified based on the onset of their action as:
1) Rapidly acting (within one arm brain circulation time) Thiopentone Propofol Etomidate
2) Slow acting (those that take longer than one arm-brain circulation time) Ketamine Midazolam Classification.

PROPOFOL

Propofol presented as a white liquid in vials or ampoules in concentration of 10 mg/ml, it is the most commonly used induction agent. The dose of propofol is 1 – 3 mg/kg (I.V) for induction. The lower dose should be used in the elderly while an upper children.
Sedation may be produced with a 0.2 mg/kg bolus dose intravenously or in infusion of 1- 3 mg/kg/h.
Propofol is a cerebral vasoconstrictor. It reduces cerebral blood flow and metabolism and intracranial pressure, it can used as anticonvulsant, Central respiratory depression occurs with propofol. Laryngeal tone reduced more than thiopental, making it easier to insert a laryngeal mask airway. There is less risk of coughing and laryngospasm than with thiopental. Nausea and vomiting are very

uncommon after propofol – based anesthesia, in fact, it has an antiemetic properties. Placental transfer of propofol is rapid and causes fetal depression.

Mechanism of action:

Activation of chloride channels of GABA receptors thus enhancing inhibitory synaptic transmission. It also inhibits NMDA subtype of glutamate receptors.

Adverse effects:

1) Unwanted myoclonic movements and fits.
2) Pain on injection.
3) Hypersensitivity.
4) Support of bacterial growth.
5) Propofol infusion syndrome: It is a very rare but potentially lethal syndrome of metabolic acidoses, acute cardiomyopathy and skeletal myopathy associated with prolonged (>48 hours) high – dose (>5 mg/kg/h) infusion.

THIOPENTAL (THIOPENTONE)

Thiopental sodium is a thiobarbiturate, presented as a powder in a multiple dose vials, dissolved in distilled water or normal saline in concentration of 25mg/ml for intravenous use (dose 3 – 6 mg/kg) or in concentration of 50-100 mg/ml for rectal use (dose 50 mg/kg).

The hypnotic action of thiopental is potent but it has no analgesic effect and may be antanalgesic in lower dose, Thiopental is a very potent anticonvulsant, it is also produces sedation, amnesia and depression of the vasomotor centre.

Thiopental produces anesthesia usually at less than 30 seconds after I.V injection, the dose required to produce anesthesia in healthy adults initially is 4 mg/kg administered over 15 – 20 seconds, if loss of the eyelash reflex does not occur within 30 seconds supplementary doses of 50 – 100 mg should be given slowly until consciousness is lost. In young children a dose of 6 mg/kg is usually necessary. Elderly patients often required smaller doses (2.5 – 3 mg/kg) than young adults.

Single bolus of 3-5 mg/Kg used to treat an episode of convulsion, infusion (3-5 mg/Kg/hr.) in status epilepticus refractory to conventional treatment.
Short period of apnea is common and assisted ventilation may be required, ventilatory rate and tidal volume usually lower than normal but they increase in response to surgical stimulation. Increase in bronchial muscle tone, laryngeal spasm may occur by surgical stimulation or the response of secretions, blood or foreign bodies (e.g. oropharyngeal airway). Skeletal muscle tone is reduced at high concentrations. Thiopental crosses the placenta readily. The eye pupil dilates first and then constricted, functions of the liver and kidneys are impaired.

Mechanism of action:

- Mainly through interaction with inhibitory neurotransmitter – GABA in CNS

- GABAA receptor has 5 glycoprotein subunits

- Activation of GABAA receptor Increase in transmembrane Chloride channel conductance Hyperpolarization of post-synaptic neurons

"FUNCTIONAL INHIBITION OF POST-SYNAPTIC NEURONS"

Adverse effects:

1) Hypotension.
2) Respiratory depression.
3) Tissue necrosis.
4) Laryngeal spasm.
5) Bronchospasm (especially in asthmatic patient).
6) Thrombophlebitis.
7) Hypersensitivity.
8) Accidently intra – arterial injection causes emboli and may cause ischemia or gangrene in parts of the forearm, hand and fingers.

METHOHEXITAL (METHOHEXITONE)

Methohexital sodium is an oxybarbiturate, presented as a white powder in vials, dissolved in distilled water or normal saline such as thiopental, the concentration of the solution is 10mg/ml, induction dose is 1-2mg/kg given intravenously.

Methohexital is more potent than thiopental, and has shorter onset and duration of action. Induction is often accompanied by pain on injection but there is less risk of tissue damage than with thiopental, methohexital may induce involuntary myoclonic movements, methohexital is proconvulsant.

Etomidate

Etomidate is an imidazole, it is available as a white liquid in concentration of 2mg/ml, induction dose is 0.3 mg/kg given intravenously.

Etomidate may cause pain on injection, it does not release histamine, cerebral blood flow and metabolism, intracranial and intraocular pressure all fall with etomidate, as with methohexital, excitatory phenomena may be seen on induction, which can be prevented by benzodiazepine premedication or concomitant use of opioids. Central sympathetic outflow is stimulated, which maintains haemodynamics. No effect on mean blood pressure, cardiac output or coronary perfusion. Myocardial oxygen consumption may fall. Respiratory depression is increased in the presence of opioids, but less than with thiopental. Etomidate is adrenocortical suppressive. Etomidate it more likely to associated with nausea and vomiting than other induction agents.

Mechanism of action:

Activation of Chloride channels of GABAA receptors Enhancing inhibitory synaptic transmission.

KETAMINE

Ketamine hydrochloride is phencyclidine, it is presented as a liquid in brown color vials or ampoules in concentration of 10 or 50 mg/ml (50mg/ml is the most common).
It is a powerful analgesic drug and induces anesthesia in 30 – 60 seconds, induction dose is 2 mg / kg (I.V) and it single dose produces unconsciousness for 10 – 15 minutes, larger doses may be required in some patients, and smaller doses in the elderly or shocked patients. Ketamine is also effective within 3 – 4 minutes after I.M injection (10 mg /kg) and has duration of action of 25 – 30 minutes. Dose required to produce analgesia without loss of consciousness is 0.25 – 0.5 mg / kg (I.V) or an infusion of 0.05 mg / kg / minute. A small dose (0.1 mg / kg I.V) provides sedation. Apnea may occur after I.V injection (but ventilation is well maintained thereafter). Pharyngeal and laryngeal reflexes and patent airway are maintained well in comparison with other I.V agents, Bronchial muscles is dilated, skeletal muscle tone is usually increased and spontaneous movement may occur, salivation is increased, ketamine crosses the placenta readily, fetal concentration are approximately equal to those in the mother, intraocular pressure increases, cerebral blood volume and intracranial pressure increase.
Mechanism of action:
a) Inhibits N-Methyl-D-aspartate (NMDA) receptors which have been activated by Glutamate, an excitatory neurotransmitter.
b) Also inhibits serotonin and muscarinic receptors.
c) It is an agonist of μ type of opioid receptors.
Adverse effects:
1) Emergence delirium, nightmares and hallucinations.
2) Hypertension and tachycardia.
3) Prolonged recovery.
4) Salivation.
5) Increased intracranial pressure.
6) Allergic reactions (skin rush have been reported).

Thank you