IV Anesthesia

Doctor :

Ashraf Dmour

Done by:

Hala Alzenaty

Mona Alzoubi

Ansam Alzubaidi

Corrected by:

Safaa Matar

Balanced Anesthesia

Use specific drugs for each component

1- Sensory : (no pain)

N20, opioids, ketamine for analgesia

2- Cognitive :Produce amnesia, and preferably unconsciousness, with N2O,

5.-25. MAC of an inhaled agent, or an IV hypnotic (propofol, midazolam, diazepam, thiopental)

3- Motor:Muscle relaxants as needed

4- Autonomic:

If sensory and cognitive components are adequate, usually no additional medication will be needed for autonomic stability.

If some is needed, often a beta blocker +/- vasodilator is used.

- during the surgery there is increased secretion of stress hormones that will cause tachycardia & increase the blood loss intraop.

this will decrease the surgery outcomes & increase its duration which will lead to more complications post op.

Definition

An agents that will induce a state of surgical anaesthesia in one arm brain circulation time

Or ,,, teq of GA based on the concept that administration of a mixture of small amount of several neuronal depressants (narcotics and inhalation) maximize the advantages .

Function of intravenous anaesthetic agents

1- Rapid induction of anaesthesia

2- Maintenance of anaesthesia

3- ICU/theatre sedation

4- Status epilepticus

Pharmacokinetics

- Agent has to cross the BBB
- Speed of action depends upon:
1- Lipid solubility
2- Protein binding
3- Speed of injection
4- Cardiac output

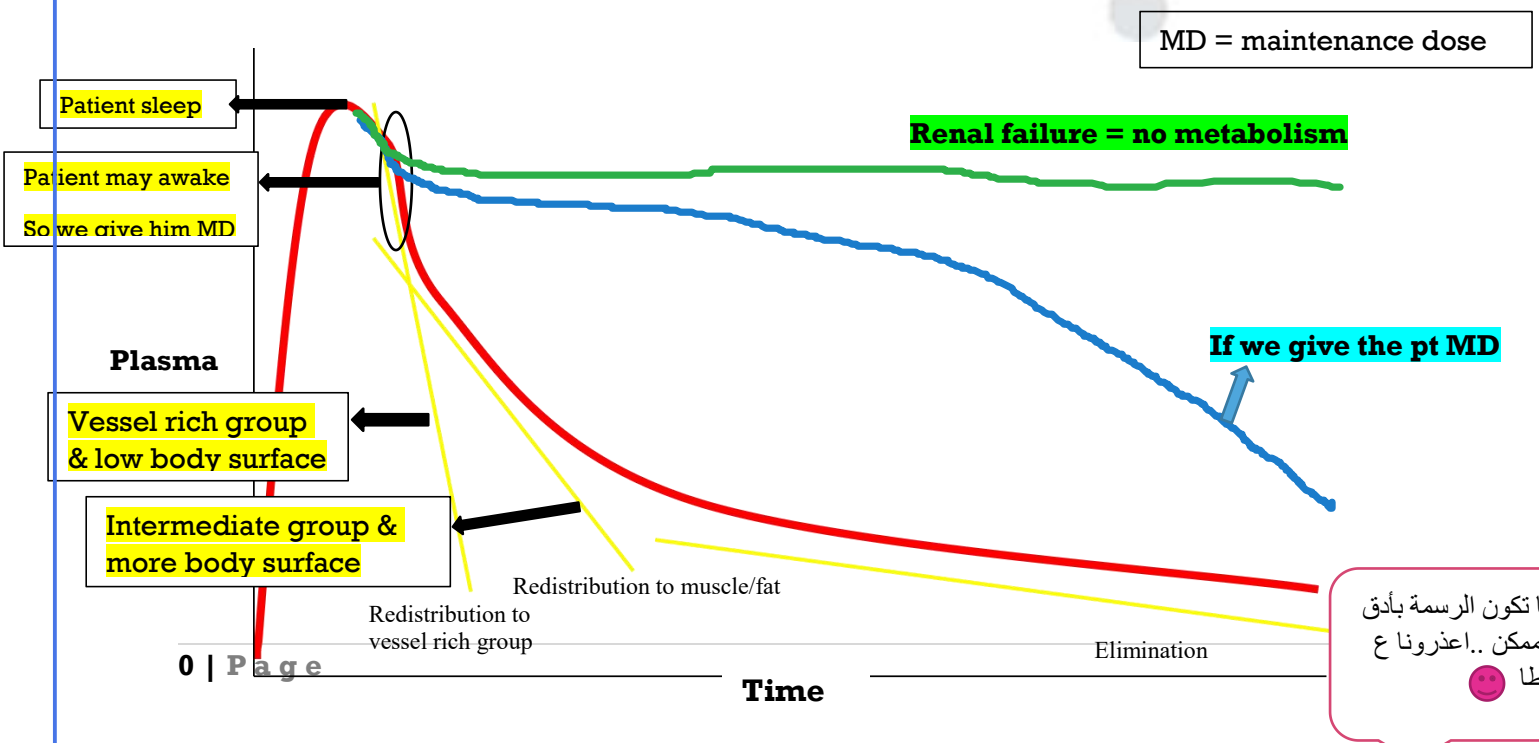
The ideal intravenous agent :

1-Rapid onset
2-Rapid recovery
3-Analgesic
4-No CVS/RS depression
5-No emetic effects
6-No excitatory phenomena
7-No pain on injection
8-Safe if injected intra-arterially
9-None toxic to other organs
10- No histamine release
11- No allergic reaction

Compartment Model

- Offers a simple way to characterize the distribution of drugs in the body
- Can be conceptualized as a group of tissues that posses similar pharmacokinetics (Central and peripheral compartments)
- Distribution phase vs. Elimination phase

* Redistribution and elimination of intravenous anaesthetic agents



حاولنا تكون الرسمة بأدق شكل ممكن ..اعذرونا ع أي خطا

- Injected > Blood > Circulation > brain (5-10)min > Redistribution > Elimination

- Vessel rich groups : brain, liver, heart, kidneys, supra-renal glands.

Have low surface area higher plasma concentration

- Intermediate groups: muscles, fat.

- We can keep the patient unconscious through inhalational anesthesia and TIVA

- When the infusion is stopped plasma concentration will decrease rapidly & the patient may awake

Intravenous Anesthetic Agents

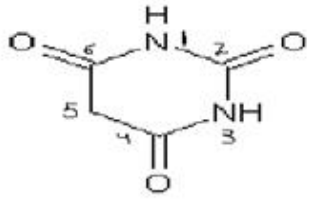
Agonist & antagonist :

That directly change cell function by binding to receptors .

- Another type bind to receptors but do not cause direct effect on the cell.

Competitve and non-competitive antagonist:: reversible and irreversible

Barbiturates

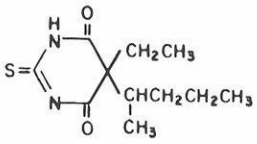


- Derived from barbituric acid

- Prepared as sodium salts

- Highly alkaline (pH : 10.5)

- Available as racemic mixtures



Thiopental

- Oxybarbiturates ➔ methohexital

- Thiobarbiturates ➔ thiopental, thiamylal

- Mechanism of action :

Thiopental :

- Depress the reticular activating system located in the brain stem that controls several vital functions, consciousness

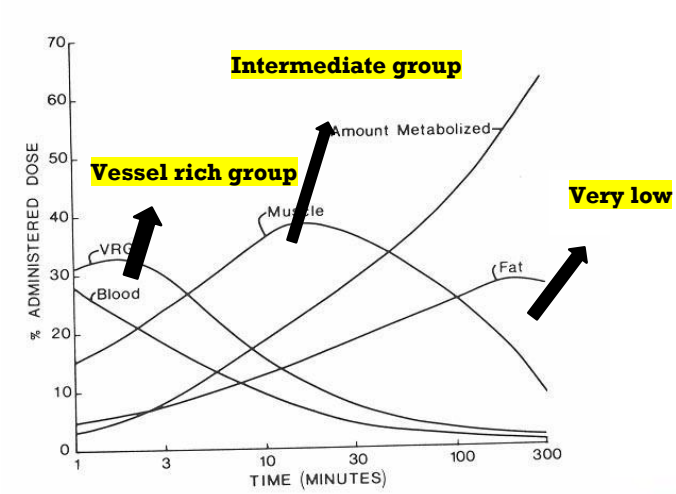
- Affect the function of nerve synapses not axons

- Interact with the inhibitory neurotransmitter GABA.

- Dose 3-5 mg/kg

- Thiopental is highly protein bound (80%)

- **Redistribution** :



Effects on organ systems:

- **Cardiovascular** :

1- Decrease blood pressure and increase heart rate→ maintain CO (HR x SV)

2- Depression of the medullary vasomotor center

vasodilates periphral capacitance vessels, increases

periphral pooling of blood and decreases venous return

to right atrium

- **Respiratory** :

- Depresses the medullary ventilatory center and

- decreases the ventilatory response to hypercapnia and hypoxia

- Tidal volume and respiratory rate are decreased

- Histamine release and bronchial smooth muscle constriction --→ bronchospasm

So its contraindicated in asthmatic patients

- **cerebral** :

- Constrict the cerebral vasculature and cause decrease in cerebral blood flow and intracranial pressure

- Cerebral perfusion pressure increases cause the drop in

- ICP exceeds the drop in arterial BP

- Decreases cerebral oxygen consumption (up to 50%)

- Have anti-analgesic effect by lowering the pain threshold

- **Renal** :

- Reduces renal blood flow and glomerular filtration rate in proportion to fall in BP

- **Hepatic** :

- Decreases hepatic blood flow

- Induction of hepatic enzymes, increases the rate of metabolism of some drugs (Digitoxin)

- Combination with the cytochrom p-450 enzyme system > interfere with biotransformation of some drugs (TCA)

Adverse effects :

1- Hypotension

2- Respiratory depression

3- Laryngeal spasm

4- Brochospasm

5- Allergic reactions (1 in 14,000)

6- Extravasation tissue necrosis

7- Intraarterial injection

8- Thrombophlebitis

Contraindications :

1- Airway obstruction

2- Porphyria

3- Hypersensitivity

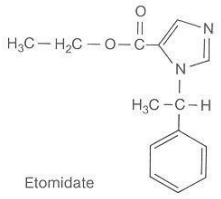
Etomidate

- Contains carboxylated imidazole ring which provides water solubility at physiological pH

Depresses the reticular activating system and mimics the inhibitory effects of GABA

- Binds to subunit of GABA type A receptor increasing its affinity to GABA

- Induction dose: 0.2-0.4 mg/kg



Absorption :

- Administered IV only for induction of GA

Distribution :

- High protein bound and high lipid soluble

- Redistribution is responsible for decreasing the plasma concentration to awakening level

Biotransformation and excretion :

- Hepatic microsomal enzymes and plasma esterases hydrolyze etomidate to inactive metabolite

- The end product is excreted in the urine

Effects on organ systems:

- Cardiovascular :

- Minimal effect on CVS

- Mild reduction in PVR and arterial BP

- Myocardial contractility and cardiac output are unchanged

- No histamine release

- Respiratory :

- Ventilation is affected less than barbiturates

- **Cerebral** :

- Decreases cerebral metabolic rate, cerbral blood flow, & ICP

- CPP is well maintained (minimal CVS effect)

- PONV are common but minimized by antiemetic

- **Endocrine** :

- Inhibit enzymes involved in cortisol and aldosterone synthesis

- Can lead to adrenocortical suppression in the long run

Adverse effects:

- May activate seizure, extrapyramidal activity .

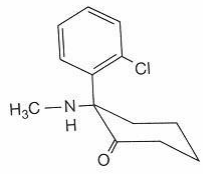
- Pain on injection

- Adrenocortical suppression

- Allergic reactions

Ketamine (hypnotic, analgesics, sedation)

- Has multiple effects through the CNS including blocking polysynaptic reflexes in the spinal cord and inhibiting neurotransmitter effects in selected areas of the brain
- Ketamine dissociates the thalamus from the limbic cortex (dissociative anesthesia) Causes th pt to appear concious but unable to process or respond to sensory input .
- N-methyl-D-aspartae receptor antagonist
- Structurally analogue to phencyclidine
- Can cause hallucinogenic effects and nightmares
- Dose : Induction IV 1-2 mg/kg, IM 3-5 mg/kg



Ketamine

Absorption :

- Administered IM or IV with peak plasma level within 10- 15 min after IM injection

Distribution :

- More lipid soluble and less protein bound than thiopental
- Distribution half-life is 10-15 min

Biotransformation and excretion :

- Biotransformed in the liver to several metabolites some retain anesthetic properties (norketamine)
- Short elimination half-life (2h)
- Excreted renally

Dissociative anesthesia : cause the patient to appear conscious (eyes opening , swallowing muscle contracture) but unable to respond to any sensory input

Effects on organ systems:

- **Cardiovascular** :

- Increases Blood pressure, heart rate, and cardiac output (best choice for patients with hypovolemic shock)
- Increases pulmonary artery pressure and myocardial work
- Avoid in patient with coronary artery disease

- **Respiratory** :

-Minimal effect on the ventilatory drive
- Potent bronchodilator (good choice for asthmatic patients)
- Preserve airway reflexes

- **Cerebral** :

- Increase cerebral oxygen consumption, cerebral blood flow and intracranial pressure (contraindicated in patients with increased ICP)
- Myoclonic activity is associated increased subcortical electrical activity
- Undesirable psychotomimetic effects (illusions, dreams and delirium)
- Have analgesic effects (because is acts on opioid receptors)

Alkylphenols

- Facilitate inhibitory neurotransmitters mediated by GABA
- 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
- It can attenuate upper airway reflexes.
- Formulation can support bacterial growth (soybean oil, glycerol, and egg lecithin)
- Dose : induction IV 1.5-2.5 mg/kg
- Not water soluble

Indications :

- Induction of anesthesia
- Sedation
- Maintenance of anesthesia
- Antiemetic
- Antipruritic
- Anticonvulsant
- Attenuation of bronchoconstriction (used for asthmatic patients)

Absorption :

- Available only for IV for induction of GA and sedation

Distribution :

- High lipid soluble with an onset of action as one-arm-to brain circulation time
- Very short initial distribution half-life (2-8 min)

Biotransformation and excretion :

- Clearance exceeds hepatic blood flow with extrahepatic metabolism
- Conjugation in the liver with inactive metabolites as an end product that are eliminated by the kidney

Effects on organ systems:

- **Cardiovascular** :

- Decrease BP due to drop in systemic vascular resistance, cardiac contractility and preload
- Impairs the normal arterial baroreflex response to hypotension

- **Respiratory** :

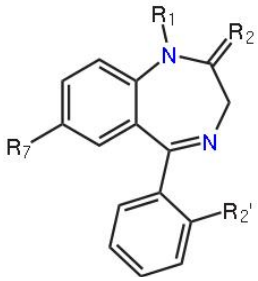
-It is a respiratory depressant causes apnea following induction dose
- Inhibits hypoxic ventilatory drive and depresses the normal response to hypercarbia
- Can produce bronchodilation and decrease the incidence of wheezing intraoperatively

- **Cerebral** :

- Decreases cerebral blood flow and intracranial pressure
- Autoregulation and response to CO_2 are not affected
- Can cause critical reduction in CPP in patients with elevated intracranial pressure (< 50 mm Hg)
- Has antipruritic effect and antiemetic properties
- Have predominantly anti-convulsant properties
- Decreases intraocular pressure

Adverse effects:

- Allergic reactions
- Lactic acidosis (Propofol infusion syndrome)
- Bacterial growth
- Pain on injection



Benzodiazepines

- Binding to receptors enhances the inhibitory effects of various neurotransmitters (GABA) in the CNS mainly in the cortex
- Chemical structure includes a benzene ring and a 7-member diazepine ring, substitution at various positions on these rings affect potency and biotransformation
- **Flumazenil** is a specific benzodiazepine-receptor antagonist that effectively reverses most of the CNS effect

Absorption :

- Administered orally, IM and IV for sedation or induction of GA
- Diazepam and Lorazepam well absorbed from GI tract, peak plasma level in 1-2 h respectively
- 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

Distribution :

- 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 :

- Rely on the liver for transformation into water soluble glucoronide end products
- Slow hepatic extraction, long half-life for diazepam (30h)

Excretion :

- Metabolites are excreted mainly in the urine
- Enterohepatic circulation produces a second peak in diazepam plasma concentration 6-12h following administration

Effects on organ systems:

- **Cardiovascular** :

- Minimal CVS depressant effects Arterial BP, Cardiac output, and PVR slightly decreased
- Heart rate sometimes increased

- **Respiratory** :

-Depresses ventilatory response to CO_2
- Ventilation must be monitored

- **Cerebral** :

- Reduces cerebral oxygen consumption
- Decreases cerebral blood flow and intracranial pressure
- Effective in preventing and controlling grand mal seizures
- Sedative dosages cause antegrade amnesia

Diazepam

- Often used as premedication or seizure activity, rarely for induction
- Minimal systemic effects-- respirations decreased with narcotic usage
- Not water soluble-- venous irritation(propylene glycol)
- Metabolized by liver-- not redistributed

Lorazepam

- Slower onset of action (10-20 minutes)-- not used for induction
- Used as adjunct for anxiolytic and sedative properties
- Not water soluble-- venous irritation

Midazolam

- More potent than diazepam or lorazepam
- Induction slow, recovery prolonged
- May depress respirations when used with narcotics
- Minimal cardiac effects
- Water soluble

Agent	Cardiovascular		Respiratory		Cerebral		
	HR	MAP	Vent	B'dil	CBF	$CMRO_2$	ICP
Barbiturates							
Thiopental	↑↑	↓↓	↓↓↓	↓	↓↓↓	↓↓↓	↓↓↓
Thiamylal	↑↑	↓↓	↓↓↓	↓	↓↓↓	↓↓↓	↓↓↓
Methohexital	↑↑	↓↓	↓↓↓	0	↓↓↓	↓↓↓	↓↓↓
Benzodiazepines							
Diazepam	0/↑	↓	↓↓	0	↓↓	↓↓	↓↓
Lorazepam	0/↑	↓	↓↓	0	↓↓	↓↓	↓↓
Midazolam	↑	↓↓	↓↓	0	↓↓	↓↓	↓↓
Ketamine	↑↑	↑↑	↓	↑↑↑	↑↑↑	↑	↑↑↑
Etomidate	0	↓	↓	0	↓↓↓	↓↓↓	↓↓↓
Propofol	0	↓↓↓	↓↓↓	0	↓↓↓	↓↓↓	↓↓↓

Properties of Intravenous Anesthetic Agents

Drug	Induction and Recovery	Main Unwanted Effects	Notes
thiopental	Fast onset (accumulation occurs, giving slow recovery) Hangover	Cardiovascular and respiratory depression	Used as induction agent declining. Decreases cerebral blood flow and O2 consumption. Injection pain
etomidate	Fast onset, fairly fast recovery	Excitatory effects during induction and recovery, **Adrenocortical suppression**	Less cardiovascular and respiratory depression than with thiopental, Injection site pain
propofol	Fast onset, very fast recovery	Cardiovascular and respiratory depression. Pain at injection site.	Most common induction agent. Rapidly metabolized; possible to use as continuous infusion. Injection pain. Antiemetic
ketamine	Slow onset, after-effects common during recovery	**Psychotomimetic effects** following recovery, Postoperative nausea, vomiting and salivation	Produces good **analgesia** and amnesia. No injection site pain
midazolam	Slower onset than other agents	Minimal CV and respiratory effects.	Little respiratory or cardiovascular depression. No injection pain. Good amnesia.

Opioids

- Opoids bind to specific receptors located throughout CNS

Table 1

OPIOID RECEPTORS	
Opioid Receptor Class	Effects
Mu_1	Euphoria, supraspinal analgesia, confusion, dizziness, nausea, low addiction potential
Mu_2	Respiratory depression, cardiovascular and gastrointestinal effects, miosis, urinary retention
Delta	Spinal analgesia, cardiovascular depression, decreased brain and myocardial oxygen demand
Kappa	Spinal analgesia, dysphoria, psychomimetic effects, feedback inhibition of endorphin system

Adapted from references 2 and 3.

- M 1,2 is responsive for analgesia and res depression
- kabba res responsive for sedation and analgesia

Mechanism :

- 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

Remifentanyl

- Ultra-short acting

- no side effects

- best choice for continuous TIVA

Archive Questions :

1-Wrong about benzodiazepines ? decrese the mac

2- Wrong regarding ketamine: it is NMDA receptor agonist (actually it is antagonist)

3- IV anesthetic agent which Increase intracranial pressure: Ketamine

4- All of the following have an antiemetic action except?

a. Promethazine

b. Propofol

c. Etomidate

d. Haloperidol

e. Sevoflurane

Ans:c

5-The followings are related to benzodiazepine use in anesthesia except one:

a. Increases hallucinations after ketamine

b. As premedicant

c. As IV. Inductive agent

d. As Anticonvulsant

e. Sympatholytic agent

Ans : b

{ وَأَنْ لَيْسَ لِلْإِنْسَانِ إِلَّا مَا سَعَى }