النادي الطبي

Round : Anesthesia-Lecture 5

Group no : B 8

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Inhalational anesthetic agents

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Inhalational anesthetic Agents

- They are synthetic, colorless liquids at room temperature that are non flammable and administered as a vapor from a vaporizer on the anesthetic machine.

- A dose-related depression of cardiorespiratory function is common to each of these inhalational agents.

- Produce smooth muscle relaxation:
  - Decrease in cerebrovascular resistance.(↑ perfusion)
  - Bronchodilation.

Inhalational anesthetic Agents

Modern inhaled anesthetics are halogenated partly or entirely with fluorine. Fluorination provides greater stability and lesser toxicity.

The most commonly used inhaled anesthetics in modern anesthesia include volatile liquids (i.e., halothane, enflurane, isoflurane, desflurane, and sevoflurane) and a single gas (i.e., nitrous oxide). None of these inhaled anesthetics meets all the criteria of an "ideal" inhaled anesthetic.

Inhalational anesthetic Agents

Mechanism of action:

All inhalational anesthetic agents stimulate inhibitory receptors (GABA receptors) except Nitrous oxide which inhibit stimulatory receptors (NMDA receptors)

Inhalational agents are compared to one another according to their minimal alveolar concentration (or **"MAC"**) values.

The MAC value: minimum alveolar concentration of anesthetic required to suppress movement (motor response) to a surgical incision (pain stimulus) in 50% of patients.

Knowledge of the MAC value allows one to compare the potencies of different inhalational agents.

↓ MAC > ↑ Potency & ↑ MAC > ↓ Potency.

Agent	MAC%
Nitrous oxide	105 Lowest potency so we need a very high dose to induce anesthesia
Halothane (Fluothane)	0.75 Highest potency
Isoflurane (Forane)	1.2
Desflurane (Suprane)	6.0
Sevoflurane (Ultane)	2.0

'able 13.1: Factors which alter anaesthetic requirements (MAC).

Increased MAC	No change in MAC	Decreased MAC
Hyperthermia	Gender	Increasing age
Chronic drug abuse: Ethanol	Duration of anaesthesia	Hypothermia
Acute use of amphetamines	Carbon dioxide tensions: $PaCO_2$ 21 - 95 mmHg	Severe hypotension
Hyperthyroidism	Metabolic acid-base status	Other anaesthetic agents: opioids, benzodiazepines
	Hypertension	Acute drug intoxication: Ethanol
		Pregnancy
		Hypothyroidism
		Other drugs: clonidine, reserpine

Amphetamine causes excitation of the CNS, increases heart rate and increases the release of catecholamines

☆ Hyperthyroidism and hypothyroidism both do NOT affect MAC

Onset of action:

The **rapidity** at which the anesthetic state is reached depends on how quickly the anesthetic inhalational agent reaches the brain to exert its effects.

A. Factors determining how quickly the inhalational agent reaches the alveoli :

1. The inspired **concentration** (dose) of anesthetic gas being delivered by the anesthetic machine (concentration effect).
2. The **carrier gas flow rate** through the anesthetic machine.
3. The amount of **alveolar ventilation** (Minute ventilation)

$$V = \text{Respiratory Rate} \times \text{Tidal Volume}$$

4. **Blood solubility** of anesthetic agent.

6L minute ventilation for example so we need to mix inhalational gases to equal 6L in the end.
Oxygen and nitrogen are called carrier gases

Low MAC... High potency... High solubility... slow induction and slow recovery

B. Factors determining how quickly the inhalational agent reaches the brain from the alveoli in order to establish anesthesia:

1. The **rate of blood flow** to the brain. Which is the target organ
2. The **lipid solubility of the inhalational agent** (to cross blood brain barrier).
3. **Concentration gradient:** The **difference in the arterial and venous concentrations** of the inhalational agent.

It moves from high to low down the concentration gradient.

Vaporizers are **color-coded** to prevent filling of vaporizers with the wrong anesthetic (prevent over dose or lower dose).

Halothane (red)

Enflurane (orange)

Isoflurane (purple)

Sevoflurane (yellow)

Desflurane (blue)

Nitrous Oxide

- Nitrous oxide ("laughing gas") is a nonirritating potent analgesic but a weak general anesthetic.

- Nitrous oxide undergoes **very little metabolism** and **excreted** by expiration.

- It has a **rapid onset and a quick recovery** of 3 to 10 minutes due to its low solubility in blood.

Nitrous oxide is teratogenic so limited use in pregnant women.

In pediatrics, nitrous oxide can cause pernicious anemia by causing vitamin B12 deficincy

- Its **low potency** (high **MAC = 105%**) limits the amount that can be administered.

- Nitrous oxide is 34 times more soluble than nitrogen which mean that N20 diffusion between compartments is much faster than nitrogen. ➔ This property results in three special anesthetic phenomena.

1- Second gas effect
2- Diffusion hypoxia
3- Closed air spaces

- Nitrous oxide increases the efficacy of other inhalational drugs thats why we administrate it in addition with other drugs

Second gas effect

At the beginning of anaesthesia, N20 leaves the alveoli much faster than other gases can leave.

The result is an increase in the concentration of other gases in the alveoli (oxygen, and other inhalational agents) which leads to increase in their partial pressure.

This increase in partial pressure speeds the onset in inhalational anesthetic effect, and is referred to as **the second gas effect.**

Diffusion hypoxia

- Diffusion hypoxia may result **at the end of the anesthesia.**

- As nitrous oxide is discontinued, the body stores of nitrous oxide are released and flood the alveoli, **diluting the oxygen** present in the alveoli. Fastest to leave the blood to the alveoli, which dilutes the concentration of oxygen in the alveoli and causes hypoxia.

To avoid hypoxia, we turn off nitrous oxide 10 minutes before the end of the surgery and give 100% oxygen

- When only room air is administered at the end of the anesthetic, the dilution of oxygen may be sufficient to create a hypoxic mixture, and result in hypoxemia.

- The administration of **high flow 100% oxygen** at the end of an aesthetic may avoid hypoxemia.

Closed air space

Closed air spaces will expand in the presence of nitrous oxide due to the differences in solubility of nitrogen and nitrous oxide.

With the administration of 66% N2O, a closed air space will expand 2 times in volume over a period of approximately 15 minutes.

=> For this reason N2O is contraindicated in patients with **a pneumothorax, eye bubble, tympanic membrane graft, closed loop bowel obstruction, air embolism,** or any other closed air space in the body

☆ nitrous oxide diffuses faster than nitrogen as it has a higher solubility, this causes closed spaces and organs to become distended as nitrous oxide enters the closed space faster than nitrogen leaves. This increases the risk of rapture.

Halothane

Slowest induction and recovery in comparison to other drugs

- Most potent inhalational anaesthetic (MAC of 0.75%)

  Clearance by the liver is 20%

  It is the best for asthmatic patients since it results in the most bronchodilation.

- Very soluble in blood and low soluble in adipose (prolonged emergence).

  Longer time to leave the body

  + doesnt have a pungent smell

- Halothane's popularity in adult anaesthesia has declined because of its implication in causing **Arrhythmias**. It causes severe bradycardia since it increases the sensetivity of the heart to catecholamines, which results in hypotension and arrhythmias.

- **Halothane hepatitis:** is believed to occur in approximately 1 in 10,000 halothane anaesthetics. (NOT hepatotoxic in children)

- Presents as postoperative fever, jaundice, eosinophilia, and occasionally extensive hepatic necrosis and death.

- Hepatitis following isoflurane and enflurane exposure is very rare.

- The main route of excretion is through the lungs, but approximately 20% of halothane is metabolized by the liver.

Halothane Side Effects

1. Trigger Malignant Hyperthermia.
2. Hypotension.
3. ↑ ICP.

In all inhalational drugs

4. Postoperative Hepatitis.
5. Arrhythmias
6. Bradycardia.

Enflurane

- Stable, nonflammable liquid (at room temp.).
- MAC 1.68%.
- Enflurane lowers the threshold for **seizures**.

Desflurane

Clearance by the liver is 0.02%

- Provides very rapid onset and recovery.

- Desflurane is unique in that it boils at room temperature (requiring administration via a special heated vaporizer).

Heated until its tempreture is 39c electrically by the special vaporizer, since at 22-23.5c it changes from liquid to gas

- Desflurane has a MAC value of 6%.

☆Desoflurane produces carbon monoxide (CO) thats why we need an absorber under the ventilator when using it

☆It doesnt cause renal toxicity and it is the safest in patients with liver problems

- Cardiovascular, respiratory, neurological and neuromuscular effects are similar to those of isoflurane.

Isoflurane

It has a pungent odor

- MAC value of **1.2%**

Clearance by the liver is 0.2%

- Not as well tolerated as halothane because of its <u>pungent odour</u> and tendency **to irritate the airways**. (coughing and breath-holding if administered too quickly).

It decreases the tidal volume and increases the respiratory rate by irritating the respiratory system with its smell. IV drugs do the opposite (increases the tidal volume and decreases the respiratory rate

- <u>The preferred agent for **neurosurgical procedures** as it causes the least increase in cerebral blood flow and intracranial pressure.</u>

Cranial vasodilation

Sevoflurane

Clearance by the liver is 2%

- Is metabolized in the liver. Approximately 3% of sevoflurane is broken down in this fashion.
- Has a MAC value of 2%.
- Is more **pleasant smelling** and is well suited for inhalational induction of anaesthesia.
- Production of a renal toxin called **"compound A"** at low fresh gas flows has lead to the recommendation that sevoflurane be administered <u>with a minimum of two liters of fresh gas flow.</u>

Which is nephrotoxic

It was discovered in animals but still applied theoretically to human

- Anaesthesia sufficient for laryngeal mask placement and intubation can be achieved after three to five minutes of breathing a high concentration of Sevoflurane.

Contraindications

- ✓ Trigger Malignant hyperthermia.
- ✓ Hypotension .
- ✓ Elevated ICP.
- ✓ Renal toxicity .

Desflurane & Sevoflurane

- While structurally **similar** to their parents Halothane and Isoflurane, the **substitution** of a couple of key chlorine atoms with fluorine atoms results in their lower observed solubility. (Low blood soluble agents => rapid actions)
- This translates clinically into a more rapid induction and recovery from anaesthesia.

Gases from fastest to slowest:

Desoflurane > Sevoflurane > Isoflurane > Halothane

	Halothane	Isoflurane	Desflurane	Sevoflurane
Arrhythmias	Increased	—	—	—
Sensitivity to catecholamines (Dopamine + Norepinephrine + Epinephrine)	Increased	—	—	—
Cardiac output	Decreased	Decreased to a lesser extent than *halothane*	Decreased to a lesser extent than *halothane*	Decreased to a lesser extent than *halothane*
Blood pressure	Dose dependent decreased	Dose dependent decreased	Dose dependent decreased	Dose dependent decreased

Respiratory reflexes	Inhibited	Initial stimulation	Initial stimulation	Inhibited
Hepatic toxicity	Some risk	Low risk	Low risk	Low risk
Renal toxicity	Low risk	Low risk	Low risk	Some risk

Trigger Malignant Hyperthermia

- Is a life-threatening condition, which creates a hypermetabolic state in patients with a hereditary skeletal muscle defect. It is most commonly caused by administering **halogenated anaesthetic agents (not Nitrous oxide)** or depolarizing neuro-muscular agents such as **Succinylcholine**. There is no way to pre-identify patients who may develop MH, but if the signs and symptoms develop, you should interfere.

- Duchenne dystrophy, myotonia, osteogenesis imperfecta, and central-core disease, are **susceptible to malignant hyperthermia**.

- **Treatment**: IV **dantrolene** (2.5 mg/kg), stop anaesthesia adminesteration and supportive treatment for each manifestation.

- Mortality rate is 50% .

We can test for it with two tests:
1. Genetic testing
2. Leg muscle biopsy (live muscle sample) then examine it by exposing it to halothane and caffeine. Known as halothane caffeine contracture test