Inhalational Anaesthetics

Volatiles exert solute movement throughout the CNS

1. Thalamic and midbrain reticular formation activity occurs during anaesthetic-induced unconsciousness

2. Inhalation agents globally depress cerebral blood flow and glucose metabolism

3. Diffusion hypoxia during emergence from anaesthesia = when the inspired gas mix is changed from N2O/O2 to N2/O2, the resulting in a higher FA/Fi ratio, leading to faster induction of anaesthesia.

4. Isoflurane has a weaker affinity for red cells than serum constituents and vice versa.

5. The second gas effect: Both nitrogen and nitrous are relatively insoluble in blood, N2O is 30 times more soluble than N2. Increased uptake of N2O from the alveoli is high, the associated loss of alveolar volume leads to concentration of and increases in the exhaled partial pressures of simultaneously administered agents (such as volatile anaesthetic agents) resulting in a higher FA/Fi ratio, leading to faster induction of anaesthesia.

6. Diffusion hypoxia during emergence from anaesthesia = when the inspired gas mix is changed from N2O/O2 to N2/O2, the volume of N2 diffusing out from the mixed venous blood into the alveoli is greater than that of nitrogen taken up from the alveoli, meaning less N2 uptake into the venous blood. This, the concentration of N2 in the alveolar air is diluted by N2O, leading to a reduction in Rg = hypoxia...

Volatiles reduce neuronal and synaptic transmission via GABA-A & glycine

Serotoninergic/Nicotinic/ Glutamatergic Inhibition of pre-synaptic excitation

Actions on protein receptors (e.g. ligand gated ion channels) are also important for many of the effects of inhaled anaesthetic agents.

Gross Mechanism

At spinal cord level, they decrease transmission of noxious afferent information ascending the spinal cord to cerebral cortex via the thalamus, thereby decreasing supraspinal arousal.

Inhibition of spinal effluent neuronal activity reducing movement response to pain.

Hypnosis and amnesia, are mediated at the supraspinal level.

- Inhalation agents globally depress cerebral blood flow and glucose metabolism.
- Thalamic and midbrain reticular formation activity occur during anaesthetic-induced unconsciousness.
- EEG changes including generalisation slowing, increased amplitude, and uncoupling of coherent anterio-posterior and interhemispherical activity occur during anaesthetic-induced unconsciousness.

Alveolar Concentration

The concept of alveolar equilibrium of the volatile is key.

Otherwise it cannot reach therapeutic effect in the CNS and exert its effect. It is dependent on 3 things:

1. Inspired concentration of the agent. The higher the conc, the more rapid the onset of anaesthesia due to increased rate of alveolar-venous equilibration. The equilibrium time taken for the drug to reach equilibrium.

2. Blood-gas partition coefficient (BGPC) of the drug.

3. Pulmonary blood flow (cardiac output)

- Pulmonary blood flow (cardiac output) in the absence of a shunt, pulmonary blood flow equals cardiac output. Higher cardiac output results in a greater uptake of the volatiles, as blood (blood tissue coefficient 1:1), but perfusion is much lower than brain tissue equilibrium is much faster, and therefore faster induction of anaesthesia.

Drug Uptake from the Lungs

- Pulmonary alveolar blood flow (cardiac output).

- The highest concentration of the anaesthetic agent is reached in the alveolar compartment.

- Uptake depends on alveolar concentration & pulmonary circulation uptake.

- Getting to alveolar equilibrium is key. Initial high conc, good ventilation and awareness of FVC is important.

- Faster onset & recovery is conferred having LOW BGPC’s = less soluble and so have a higher alveolar partial pressure.

- Increased uptake with high BGPC’s, molecular weight = decrease in the time it takes for the drug to reach equilibrium. Higher fresh gas flow and low volumes in the circuit (less low circuit respiration) aid this.

- The higher the conc, the more rapid the onset of anaesthesia due to increased rate of alveolar-venous equilibration. The equilibrium time taken for the drug to reach equilibrium.

- Cardiac output, and greater delivery of cardiac output to vessel-rich tissues. Lower albumin and cholesterol levels in the blood deliver less fat tissue = longer time to equilibrate after induction and a prolonged emergence time.

- Fat–blood coefficients are significantly >1. Large affinity of fat tissue for anaesthetic and its low perfusion levels = very long equilibration time.

- Both nitrogen and nitrous are relatively insoluble in blood, N2O is 30 times more soluble than N2.

- Initial volume of N2O from the lungs is high, the associated loss of alveolar volume leads to concentration of and increases in the exhaled partial pressures of simultaneously administered agents (such as volatile anaesthetic agents) resulting in a higher FA/Fi ratio, leading to faster induction of anaesthesia.

- Diffusion hypoxia during emergence from anaesthesia = when the inspired gas mix is changed from N2O/O2 to N2/O2, the volume of N2O diffusing out from the mixed venous blood into the alveoli is greater than that of nitrogen taken up from the alveoli, meaning less N2O uptake into the venous blood. This, the concentration of N2 in the alveolar air is diluted by N2O, leading to a reduction in Rg = hypoxia...

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