

PHARMACOLOGY OF INHALATIONAL ANAESTHETIC AGENTS – PART 2 ANAESTHESIA TUTORIAL OF THE WEEK 80

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Part 2: Specific Inhalational Drugs

Before reading this tutorial think about the following questions;

- (1) What are the effects of the different inhalational anaesthetics on the cardiovascular system?
- (2) Which inhalational anaesthetics would be most appropriate for a patient undergoing a neurosurgical procedure?
- (3) How can I compare the potency of the different inhalational anaesthetics?

Diethyl Ether

This drug was first produced in 1540 but not used as an inhalational anaesthetic drug until the 1840s. It is easy to manufacture and is produced by heating concentrated sulphuric acid with ethanol. It is considered one of the safest inhalational drugs to give because respiratory depression precedes cardiovascular depression. However, giving it is complicated by its slow onset and offset, and airway irritation. Its flammable properties are also a problem if diathermy is being used. Its use in the UK has been superseded by other inhalational drugs, but is still used worldwide, because of its low cost and safety.

Physical Properties

It is a clear, colourless liquid. It decomposes on exposure to air and light. It doesn't contain preservatives, or react with other compounds. Flammable in air and explosive in oxygen. Boiling point 35°C. Sweet smell.

Pharmacokinetic Properties

MAC* 1.92

Blood/gas solubility co-efficient 12

Oil/gas solubility co-efficient 65

85-90 % excreted unchanged.

6 % is metabolised in liver to produce acetaldehyde, alcohol, acetic acid and alcohol.

Pharmacodynamic Properties

CVS

Ether is a direct negative inotrope. However, it also activates the sympathetic nervous system. Cardiac output, heart rate and blood pressure are maintained. It does not sensitise the myocardium to circulating catecholamines and arrhythmias are uncommon. It causes dilatation of coronary arteries.

RS

Initially, ether acts as a respiratory stimulant, increasing respiratory rate. Later on in the induction it acts as a respiratory depressant. Despite causing bronchodilatation and no respiratory secretions, it acts as a respiratory irritant causing coughing and breath holding.

CNS

Ether has mild analgesic as well as anaesthetic properties. It causes cerebral vasodilatation and therefore increases intracranial pressure. It can cause convulsions.

Other

It causes salivation and lacrimation and is normally used in conjunction with an antisialagogue premedication (for example atropine). The incidence of post operative nausea and vomiting is also very common with its use. It reduces gastric motility, splanchnic and renal blood flow, and muscle tone in the pregnant uterus.

Halothane

This inhalational drug was introduced in 1956 and first used in Manchester, UK. It became popular because it was easier to use, safer and non-flammable compared to other drugs available at the time. The fear of halothane-induced hepatitis and introduction of newer drugs led to a decline in its use although it still has a role in gaseous induction in the difficult airway.

Physical Properties

Clear, colourless liquid. Degraded by light. Contains 0.1 % thymol which prevents decomposition on exposure to light. The thymol doesn't evaporate and builds up in the vaporiser, requiring regular emptying and cleaning of it. It is soluble in rubber; it will attack certain metals in the presence of water vapour. It is non-flammable. Boiling point 50.2°C. Characteristic sweet smell.

Pharmacokinetic Properties

MAC* 0.75

Blood/gas solubility co-efficient 2.3

Oil/gas solubility co-efficient 234

20-50% is metabolised in liver to produce acetaldehyde, acetic acid and alcohol.

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Pharmacodynamic Properties

CVS

Halothane causes a dose dependent decrease in cardiac contractility, heart rate and systemic vascular resistance. It sensitises the myocardium to circulating catecholamines and can cause arrhythmias. It does not cause coronary vasodilatation.

RS

Halothane causes a dose dependent reduction in tidal and minute volume. Respiratory rate stays the same and may even increase. It causes bronchodilatation, reduces bronchial secretions and is a non-irritant. May have a role in acute asthma.

CNS

It has no analgesic properties. It causes cerebral vasodilatation and therefore increases intracranial pressure. It is not epileptogenic.

Other

Halothane reduces salivation, gastric motility, splanchnic and renal blood flow, and muscle tone in the pregnant uterus. One of its major disadvantages is that repeated exposure can cause an autoimmune hepatitis. The incidence of this is between 1 in 3000 and 1 in 30,000 exposures. This is caused by halothane metabolites binding to hepatic proteins on the hepatocyte cell membrane and modifying their structure. These modified hepatocyte-specific antigens elicit an antibody response resulting in hepatic necrosis and failure.

Enflurane

Enflurane was introduced in 1966. It is more stable than halothane and undergoes less metabolism. It is less potent, but has a lower blood/gas and oil/gas solubility co-efficient allowing for a more rapid onset and offset of action. It has also been linked with hepatitis, but the incidence is much lower. Like Halothane its use in the UK has been superseded by newer drugs.

Physical Properties

Clear, colourless liquid, degraded by light. Contains no preservatives. It is soluble in rubber but doesn't attack metals. It is non-flammable. Boiling point 56.5°C. Characteristic smell.

Pharmacokinetic Properties

MAC* 1.58

Blood/gas solubility co-efficient 1.9

Oil/gas solubility co-efficient 96

2-8% is metabolised in liver.

Pharmacodynamic Properties

CVS

Enflurane is a negative inotrope and causes dose dependent reduction in contractility and systemic vascular resistance. Heart rate however increases. It sensitises the

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myocardium to circulating catecholamines and occasionally causes arrhythmias. It causes coronary vasodilatation.

RS

Enflurane causes a dose dependent reduction in tidal and minute volume. It causes bronchodilatation, reduces bronchial secretions and is a non-irritant.

CNS

Minimal analgesic properties. It causes cerebral vasodilatation and therefore increases intracranial pressure. Can cause seizures.

Other

Enflurane reduces splanchnic and renal blood flow, and muscle tone in the pregnant uterus. There have been some reports that repeated exposure can cause hepatitis.

Isoflurane

Isoflurane was introduced in 1980. It rapidly became popular because it had a more rapid onset and offset of action compared to other available drugs at the time, and caused less cerebral vasodilatation making it attractive for use in neuroanaesthesia.. It was also metabolised less and its use did not cause hepatitis. It is still used in the UK today, although its use is declining, being replaced by sevoflurane, desflurane and total intravenous anaesthesia...

Physical Properties

Clear, colourless liquid. Not degraded by light. Doesn't contain preservatives. Soluble in rubber, doesn't attack metals. Non-flammable. Boiling point 48.5°C. Pungent smell.

Pharmacokinetic Properties

MAC* 1.15

Blood/gas solubility co-efficient 1.4

Oil/gas solubility co-efficient 91

0.2 % is metabolised in liver.

Pharmacodynamic Properties

CVS

Isoflurane is a mild negative inotrope. It causes a dose dependent fall in mean arterial blood pressure mainly by decreasing systemic vascular resistance. It causes a reflex tachycardia. It does not sensitise the myocardium to catecholamines or cause arrhythmias. It causes coronary vasodilatation.

RS

Dose dependent decrease in tidal and minute volume. Increase in respiratory rate. It causes bronchodilatation, but also increase bronchial secretions and is a respiratory irritant.

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CNS

No analgesic properties. Low concentrations of Isoflurane (below 1 MAC) do not increase cerebral blood flow and intracranial pressure. Not epileptogenic.

Other

It reduces muscle tone in the pregnant uterus.

Sevoflurane

Sevoflurane is now one of the more popular choices of inhalational drug, particularly in the UK. It is pleasant for the patient to breathe, and has rapid and smooth induction properties. Its low blood/gas solubility co-efficient means that the level of anaesthesia can be rapidly altered.

Physical Properties

Clear, colourless liquid. Not degraded by light. Doesn't contain preservative. Not soluble in rubber, doesn't react with metals. Reacts with soda lime to form compound A. Non-flammable. Boiling point 58.5°C.

Pharmacokinetic Properties

MAC* 2

Blood/gas solubility co-efficient 0.6

Oil/gas solubility co-efficient 53

3-5% is metabolised in liver

Pharmacodynamic Properties

CVS

Sevoflurane causes a dose dependent fall in cardiac output, systemic vascular resistance and mean arterial blood pressure. It does not reduce heart rate. It does not sensitise the myocardium to circulating catecholamines.

RS

Sevoflurane causes less respiratory depression than other drugs. It causes bronchodilatation and is a non-irritant.

CNS

It has no analgesic properties. Studies suggest that it has similar actions on the cerebral circulation as isoflurane.

Other

It reduces muscle tone in the pregnant uterus.

Desflurane

This is the most recent commercially available inhalational drug. Its main advantage is that it has the most rapid onset and offset of action of all the available drugs. Despite this ideal property, it has not gained widespread use. This is mainly because

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of its bronchial irritation, but also because it requires a specialised vaporiser, which is more costly to maintain.

Physical Properties

Clear, colourless liquid. Can be degraded by light. Doesn't contain preservatives. Doesn't react with other compounds. Non-explosive but flammable at concentrations > 17%. Boiling point 23.5°C. Due to its low boiling point and therefore high saturated vapour pressure, it requires a specialised vaporiser, as a conventional vaporiser would be inaccurate. The specialised vaporiser heats the desflurane and keeps it under pressure. It is then injected into the incoming fresh gas which is also heated.

Pharmacokinetic Properties

MAC* 6-9

Blood/gas solubility co-efficient 0.42

Oil/gas solubility co-efficient 19

0.02% is metabolised in liver predominantly to trifluoroacetic acid.

From this data you can see that desflurane is one of the least potent inhalational drugs. It also has quite a high age dependent fluctuation in its potency. Desflurane has the lowest blood/gas and oil/gas solubility co-efficient of all the inhalational drugs. It has a rapid onset and offset. Due to its poor lipid solubility, very little is also metabolised.

Pharmacodynamic Properties

CVS

Desflurane causes a dose dependent decrease in myocardial contractility, systemic vascular resistance and mean arterial blood pressure. Heart rate increases. It does not sensitise the myocardium to circulating catecholamines.

RS

It causes a dose dependent decrease in tidal and minute volume. Respiratory rate can increase. In high concentrations it is a potent irritant. It increases respiratory secretions.

CNS

It has no analgesic properties. Below 0.8 MAC it does not cause an increase in intracranial pressure. It is not epileptogenic.

Other

It decreases renal blood flow.

* **Minimum Alveolar Concentration (MAC)**

This is a term used to describe the potency of an inhalational drug. It is defined as the alveolar concentration of a drug at which only 50 percent of patients will move when exposed to a surgical stimulus. It is measured as a percentage of atmospheric pressure. The lower the value, the more potent the drug.

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