

Recent Inhalant Anaesthetics in Veterinary Practice

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ABSTRACT

Inhalation anaesthesia is widely used in veterinary clinical practice worldwide. Apart from the conventional inhalant anaesthetic agents like halothane, newer and more potent compounds have been identified and used so far. Also various researches are also going pre clinically. New agents like desflurane, sevoflurane and xenon in veterinary medicine is focussed mainly in this article. Prevalent agents like isoflurane, halothane, and nitrous oxide are also revised. Inhalant anaesthetics are either vapour volatile liquids or gases, hence their physical properties having relevance in the concerned topic is also considered. Major advancement in inhalant anaesthetics used in veterinary medicine is the main focus in this article and introduce their characteristics in various veterinary species from the available scientific research data published so far.

Keywords: Anaesthesia, MAC, blood gas partition coefficient, Desflurane, Sevoflurane, Xenon

I. INTRODUCTION

Among the anaesthetic drugs inhalant anaesthetics are unique because, they are administered and in large part removed from the body via lungs. Also their pharmacokinetic characteristics favour predictable and rapid adjustment of anaesthetic depth. To deliver the inhaled agents a special apparatus is used which includes a source of oxygen and a patient breathing circuit, which in turn usually includes an endotracheal tube or face mask, a means of eliminating carbon dioxide, and a compliant gas reservoir. These components facilitate lung ventilation and improved arterial oxygenation, thereby minimizing patient morbidity and mortality. Inhalation anaesthetics in gas

samples can be readily measured continuously and measurement of their concentration improves the precision and safety of anaesthetic management beyond the extend commonly possible with injectable anaesthetic agents. Commonly administered inhalant anaesthetics in veterinary practise include volatile liquids such as isoflurane, halothane, sevoflurane, desflurane and inorganic gases nitrous oxide and xenon. Isoflurane is currently considered the most widely used veterinary inhalation anaesthetics. Sevoflurane comes next to isoflurane. Halothane, once the most popular volatile anaesthetic throughout the world is no longer commercially distributed in countries like north America.

Physical properties of inhalant anaesthetics

	Halothane	Isoflurane	Enflurane	Desflurane	Sevoflurane
Molecular weight	197	184	184	168	200
Saturated vapour pressure at 20° C	243	238	175	669	157
Minimum alveolar concentration(MAC) at 100% oxygen	0.75	1.15	1.8	6	2.05
MAC in 70% nitrous					

oxide	0.29	0.56	0.57	2.5	0.66
Percentage of biotransformation	20	0.2	2	< 0.1	3-5
Blood / gas	2.2	1.36	1.91	0.45	0.6
Oil/gas	224	98	98.5	28	47

Minimum alveolar concentration (MAC)

The MAC of an inhaled anaesthetic is the alveolar concentration at which 50% of patients will not show a motor response to standardized surgical incisions. The standard deviation of MAC ~10%, thus 95% of patients will not respond to 1.2 MAC, and 99% will not respond

to 1.3 MAC. Standard MAC values assume the absence of all other potentially sedative or hypnotic drugs. According to data, MAC values are additive in terms of preventing movements to incision (0.5MAC of nitrous oxide plus 0.5 MAC of isoflurane = 1.0 MAC of any other agent.

Partition coefficients (solvent/gas) of some inhalational anaesthetics at 37° C

Solvent	Desflurane	Enflurane	Halothane	Isoflurane	Nitrous oxide	Sevoflurane
Water	-	0.78	0.82	0.62	0.47	0.60
Blood	0.42	2.00	2.54	1.46	0.47	0.68
Brain	1.30	2.70	1.90	1.60	0.50	1.70
Liver	1.30	3.70	2.10	1.80	0.38	1.80
Kidney	1.00	1.90	1.00	1.20	0.40	1.20
Muscle	2.00	2.20	3.40	2.90	0.54	3.10
Fat	27.00	83.00	51.00	45.00	1.08	48.00

Blood / gas partition coefficient of some inhalant anaesthetics.(SAARES et al; 2012)

Species	Desflurane	Halothane	Isoflurane	Sevoflurane	Nitrous oxide
Cat	0.58	-	1.40	0.59	-
Cow	0.44	2.40	1.22	0.52	-
Dog	0.63	3.51	1.40	0.66	0.43
Goat	0.52	-	1.37	0.56	-
Horse	0.54	1.77	1.13	0.65	-
Pig	0.50	-	1.37	0.56	-
Rat	0.61	6.56	1.41	0.74	-
Rabbit	0.72	4.36	1.37	0.70	-
Sheep	0.50	-	1.24	0.56	-
Human	0.50	2.54	1.32	0.64	0.41

The following table shows the comparison or the list of inhalant anaesthetics used for clinical purpose in various periods

Agents in clinical use	New agents	Agents of historical interest
Halothane (1956) Isoflurane (1981) Enflurane (1973) Methoxyflurane (1960) Nitrous oxide (1844)	Desflurane (1992) Sevoflurane (1994) Xenon (1997)	Chloroform (1847) Cyclopropane (1925) Diethyl ether (1846) Fluroxene (1951) Trichloroethylene (1930)

Desflurane

Desflurane differs from isoflurane only by substitution of a fluorine atom for the chlorine atom. Thus it is a fluorinated methyl ethyl ether. Fluorination increases vapour pressure, decreases intermolecular attraction, enhances molecular stability and decreases potency. The presence of measurable concentration of serum and urinary trifluoroacetate is the only evidence of desflurane metabolism and these are one fifth to one tenth those produced by the metabolism of isoflurane. The potency of desflurane is fivefold less than isoflurane and is reflected by MAC.

Desflurane is pungent. The pungency produces airway irritation and as appreciable incidence of salivation, breath holding, coughing or laryngospasm when >6% inspired desflurane is administered to an awake patient. Desflurane produces the highest carbon monoxide concentration resulting from its degradation.

Desflurane in veterinary practice

Ovine

Doses above 1.5 MAC causes significant hypotension. Increasing desflurane concentration do not alter heart rate. Mask induction with 18% desflurane is rapid and smooth with recumbency occurring in less than 5 minutes but in human beings it irritates laryngeal mucosa. Excess salivation or regurgitation struggling does not occur. When desflurane alone is given time to stand after discontinuing anaesthesia is with 5 minutes.

Equine

MAC in adult horses is 7.6%. Mask induction with 18% desflurane produce recumbency in 6 minutes. After

100 minutes of anaesthesia with 1 MAC, time required for sterna recumbency is 6.6 minutes and time to standing is 14.3 minutes. When desflurane is given alone without other drugs recovery is uneventful (Tendillo *et al.*, 1997). Mean time to stand for ponies after cessation of desflurane is 13.3 minutes with minimum ataxia (Clarke *et al.*, 1996).

Canine

After a mask induction with 18V% desflurane, the MAC for adult beagles is 10.3 V% (HAMMOND *et al.*, 1994). When 1:1 nitrous oxide and oxygen is used as carrier gas, the desflurane MAC for adult beagles is 7.99 V% (Doolery *et al.* 1998). Mask induction is rapid. Doses up to 1.5 MAC produce significant increase in systemic vascular resistance and decrease in cardiac output and no significant change in arterial blood pressure (Clarke *et al.*, 1996).

Feline

When cats induced in a 20 plexiglass chamber with 18 V%. Desflurane, mean time from the start of anaesthetic induction until the cat is removed from the chamber is 3.5 minutes and 6.2 minutes from the start of induction until intubation. In adult cats MAC of desflurane is 9.79V% at 1.7MAC desflurane significantly decreases systolic and mean arterial blood pressures, the resulting hypercapnia significantly increases pulmonary artery pressures (MC, Murphy and Hodgson, 1996).

Swine

In pigs the MAC for desflurane is 8.28 V% (tail clamp) and 10 V% (coronary band clamp). When desflurane concentrations increase mean blood pressure, stroke

volume and cardiac output decreases progressively. It is comparable to halothane as a dose related respiratory depressant (Steffey., 1992).

Sevoflurane

Sevoflurane is chemically fluorinated methyl isopropyl ether. Its vapour pressure is similar to enflurane, hence a conventional unheated vaporizer can be used for the delivery of this anaesthetic. Sevoflurane has minimal odour and is non pungent. It produces bronchodilation similar in degree to isoflurane and causes the least degree of airway irritation among the currently available volatile anaesthesia. So it is acceptable for inhalation induction of anaesthesia. Sevoflurane may be 100fold more vulnerable to metabolism than desflurane. Sevoflurane unlike others do not metabolize to reactive acyl halide intermediates with the potential to produce hepatotoxicity and cross sensitivity between drugs. It does not form carbon monoxide (stoelting., 1999).

Sevoflurane in veterinary species

Ovine

Sevoflurane MAC is 3.3 V%. (haemostat application to coronary band for 60s). After discontinuation of sevoflurane anaesthesia recovery occurs in less than 7 minutes. When sevoflurane doses increases from 1.0 to 1.5-2.0 MAC, significant decrease in mean arterial blood pressure is produced (lukasik *et al.*, 1998).

Equine

In adult horses sevoflurane MAC is 2.31V%. Inhalation anaesthesia with sevoflurane at 8V% in 10 minutes oxygen flow in horses produce central nervous system excitation, starting at 2.7 minutes. Slight transient excitation occurs at 5.7minutes. After 20 minutes recumbency is established. Recovery occurs in 10minutes when anaesthesia without sedation is given (Aida *et al.*, 1996).

At 1.0, 1.5 and 2.0 sevoflurane MAC respiratory acidosis is produced in spontaneously breathing adult horses . Also occurs a significant decrease in cardiac output, stroke volume and arterial blood pressure (Aida *et al*, 1996).

Canine

In adult beagles sevoflurane MAC is 2.36 V% /Recovery time is standing after sevoflurane anaesthesia is 10.4 minutes (Johnoson *et al*). A significant increase in heart rate and decrease in significant cardiovascular

resistance stroke volume and arterial blood pressure are produced at 1.5 and 2.0 MAC sevoflurane anaesthesia. Cardiac index remains constant due to increase in heart rate. Respiratory depression occurs at 2 MAC of sevoflurane (Mutoh *et al* 1997, Paddolford, 1999).

Feline

In adult cats MAC is 2.58% (tail clamp) .At 2.0 MAC sevoflurane decrease respiratory rate and hypercapnia , respiratory acidosis and hypotension occurs (Hikasa *et al* 1997).

Xenon

Xenon an inert gas, have many characters of inhaled anaesthetics. Its MAC in humans is 71%. More potent than nitrous oxide, whose MAC is 104%in human beings .its un reactive, non odourless,. Non explosive, non pungent gas producing minimal cardiac depression. It is prepared y fractional distillation of atmospheric air. Xenon has blood gas coefficient of 0.14%, which is lower than that of other clinically useful anaesthetics and even lower than that of nitrous oxide (0.46), sevoflourane (0.69) and desflurane (0.42). Emergence from xenon anaesthesia is two to three times faster than that equal MAC nitrous oxide plus isoflurane or sevoflurane. Disadvantage is that there exists a risk of recall but has not been observed in small numbers of patients (Stoelting, 1999).

Isoflurane

Isoflurane is the most recently available anaesthetic agent in the market when compared to other inhalant anaesthetic agents like halothane and methoxyflurane. Isoflurane is most preferable considering its pharmacological properties in certain clinical situations, these clinical situations include avian anaesthesia, geriatric patients with cardio vascular disease and hepatic disease, critically ill and unstable patients such as brachiocephalics whose upper area obstruction is a concern during recovery, patients where increase in intracranial pressure should be avoided and caesarean section. For outpatient surgeries rapid recovery seen with isoflurane may be an advantage.

Isoflurane in veterinary species:

Halothane and isoflurane produces similar circulatory and pulmonary effects during spontaneous and control ventilation accept for reduced depression of cardiac output and stroke volume with isoflurane during controlled ventilation in horses(Steffey *et al* 1980).

When ponies anaesthetised with isoflurane, very quiet and prolonged sternal recumbency with excellent coordination upon standing is observed.

In avian anaesthesia isoflurane has been used for wide range of species of birds. It shows very rapid induction (five minutes or less). It is considered as agent of choice for avian anaesthesia (Susane, E.D, 1996).

Halothane

Halothane was the most widely used volatile anaesthetic agent in veterinary practice but now a days this is not widely used, induction is fast because of its volatility. It is fat soluble hence its recovery from long anaesthetic in fatty animals may be prolonged. It has been widely used in veterinary anaesthesia for around 50 years (Steffey E. P., 1996).

Nitrous oxide

It is usually added to inhalant anaesthetic protocol to reduce the amount of more potent gas or injectable anaesthetic required to induce or to maintain anaesthesia. Diffusion of nitrous oxide is very rapid. MAC is above 100% and is less potent in animals than in human beings. The MAC of nitrous oxide in animals is close to 200% leading low clearance in inhalant anaesthetic MAC. Blood :gas partition coefficient of nitrous oxide is 0.46 (Stoelting, 1999). It cannot be used unless the anaesthetic machine has an oxygen deficit alarm. Also nitrous oxide should not be used in ruminants or horses unless the animal's blood gas analysis is available. It is regarded as pharmacologically safe anaesthetic but contraindicated in conditions like pneumothorax, air embolism and obstructed bowel. (Steffey, P. et al 2015)

II. CONCLUSIONS

The new inhalation anaesthetics obviously lead a path to show their usefulness in veterinary medicine. The number of experimental studies in this area are less so far. Therefore no specific recommendations are achieved. Desflurane having a very less solubility may allow faster induction and recovery times also permit a rapid change in the anaesthetic plane when an anaesthetic emergency present or when there is autonomic or central response to noxious stimulations. The clinical use of desflurane shall be achieved if the cost issues are solved. Sevoflurane is already in clinical use. Although sevoflurane have certain disadvantageous than isoflurane. halothane even though still exists in clinical practices, more potent inhalant anaesthetic reduces its

demand. Nitrous oxide is mainly used for its second gas effect so as to enhance the action of more potent inhalant anaesthetic. Xenon is still ongoing preclinical evaluation in human beings where its production cost make it prohibitive for animal use. However research and animal studies have been undergoing in species like cats, dogs, or some laboratory animals such as rats and mice.

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