



Intravenous administration of halothane in ethanol (5% v/v) for general anaesthesia in sheep: A preliminary study

H P AITHAL¹, AMARPAL², P KINJAVDEKAR³, A M PAWDE⁴, K PRATAP⁵ and G R SINGH⁶

Indian Veterinary Research Institute, Izatnagar, Uttar Pradesh 243 122 India

Received: 21 September 2010; Accepted: 29 December 2010

Key words: General anaesthesia, Halothane, Intravenous administration, Sheep

Inhalation anaesthetics have the advantage of less cardio-pulmonary side effects and rapid elimination through lungs. However, the main disadvantage of inhalation anaesthetics is the need of a vaporizer for its administration, which may not be available in field conditions. However, intravenous administration of liquid halothane resulted in acute respiratory distress or even death in animals (Kopriva and Lowenstein 1969, Sutton *et al.* 1971, Berman and Tattersall 1982, Dwyer and Coppel 1989). Musser *et al.* (1999) studied the physiologic effects of intravenous administration of halothane liquid emulsion (5% v/v) in swine and reported lack of toxicity of IV administration of liquid halothane. However, they recommended that further work is necessary to evaluate the optimal carrier solution. Ethanol is used as a solvent for many drugs with limited aqueous solubility. It was hypothesized that ethanol might be a novel method of delivery for a volatile anaesthetic like halothane. Hence, in the present study, clinical and certain physiological effects of intravenously administered halothane (5%) in ethanol were evaluated in sheep.

Adult sheep (5), 1–2 year-old, weighing between 22 and 37 kg, were maintained in the Divisional sheds and observed for physiological parameters for 15 days prior to the start of experiment, to rule out the possibility of any disease condition.

A 5% solution of halothane in ethanol was prepared in a 100 ml glass bottle (IV drip bottle) by mixing 5 ml of liquid halothane in 95 ml of ethanol. The mixture was thoroughly shaken and inspected visually and microscopically to ensure complete mixing before administration.

All the animals were fasted for 24 h before the start of

experiment. The animals were premedicated with diazepam administered intramuscularly @ 0.5 mg/kg body weight; 10 min later, the animals were restrained in right lateral recumbency and the jugular vein was accessed. The anaesthetic solution (5% halothane in ethanol) was administered intravenously as a drip. The initial rate of administration (2–5 drops/kg/min) was determined by the response of the animal, i.e. the degree/stage of anaesthesia and the cardiovascular response. Once anaesthesia was achieved, the rate of administration was reduced and the anaesthesia was maintained by adjusting the flow of anaesthetic solution. The anaesthesia was maintained up to 60 min and thereafter the halothane administration was discontinued. The animals were constantly monitored for anaesthesia, respiratory rate, heart rate and untoward reactions, if any. Different parameters like the onset, rate of administration of halothane for induction and maintenance for 60 min, and recovery time after discontinuation of anaesthetic solution were determined.

Ethanol is used as a solvent for delivery of drugs with limited aqueous solubility. Preliminary trials in our laboratory showed that 5% halothane was completely miscible in ethanol and isopropyl alcohol. Ethanol being more commonly used and easily available, it was tried as a carrier to deliver halothane intravenously. This study reports the first successful intravenous administration of liquid halothane using ethanol as a carrier.

The time of induction of anaesthesia varied from 5 to 15 min and it mostly depended on the rate of administration of the anaesthetic solution. As the rate increased, the induction time reduced. Induction of surgical anaesthesia required a mean time of 13.40 ± 2.13 min at the speed of administration of anaesthetic mixture at 2.80 ± 0.26 drops/min/kg body weight.

Anaesthesia was maintained up to 60 min (starting from the initiation of halothane administration). The state of anaesthesia altered quickly based on the rate of administration of halothane-ethanol solution. Hence, strict monitoring was required to maintain a constant level of anaesthesia. For

Present address: ^{1,2} Senior Scientist (¹e mails: aithal@ivri.up.nic.in; hpaithal@rediffmail.com; ²e mail: amarpal@ivri.up.nic.in); ^{3,4} Principal Scientists (e mails: pk@ivri.up.nic.in; apawde@ivri.up.nic.in), ⁵Ex-Head (e mail: kpratap@indiatimes.com), Division of Surgery.

⁶ Dean (e mail: cvsc_dean@yahoo.co.in), College of Veterinary Sciences, Selesih, Aizawl, Mizoram.

Table 1. Heart rate (HR) and respiratory rate (RR) at different intervals after IV halothane administration in sheep

Parameters	Intervals (min)								
	Before induction of anaesthesia		After induction of anaesthesia						
	0	10	5	10	15	20	30	45	60
HR	69.20±03.88	71.20±04.80	76.40±12.24	86.40±08.45	97.60±**04.12	99.20±*06.62	108.80±*08.14	98.40±*09.52	83.20±05.16
RR	41.60±02.04	28.40±04.67	25.20±02.65	35.20±06.38	37.20±03.20	41.20±04.72	46.40±06.40	35.80±03.90	32.00±03.85

** Value differ significantly ($P<0.01$) from the base value; * values differ significantly ($P<0.05$) from the base value.

maintenance of anaesthesia, the speed of administration required was 1.93 ± 0.28 drops/min/kg body weight. The total dose of halothane-ethanol mixture required for maintenance of anaesthesia for 60 min was 1.35 ± 0.19 ml/kg body wt., i.e. 0.0675 ± 0.009 ml/kg body weight of intact halothane, indicating that very less halothane was sufficient to induce and maintain anaesthesia.

Bradycardia is common during halothane anaesthesia (inhalation), apparently due to vagal stimulation (Hall *et al.* 2001). In the present study, however, heart rate gradually increased after halothane administration (IV) up to 30 min and it remained significantly ($P<0.05$) high from 15 to 45 min, subsequently it reduced (Table 1). It is not very clear why the HR increased in the present study.

Respiratory rate (RR) decreased transiently after diazepam administration, i.e. even before administration of halothane. The reduction was significant at 5 min after halothane administration (Table 1). Subsequently RR stabilized to reach near normal level in 15–20 min. Initial fall in RR might be attributed to depressant effect of diazepam. Inhalant halothane has also been shown to cause dose dependent respiratory depression both in depth and rate (Hall *et al.* 2001). Intravenous administration of intact halothane has been reported to produce acute respiratory failure (Sandison *et al.* 1970). In the present study, IV administration of halothane-ethanol mixture produced only transient depression in RR. However, acid-base status of the blood was not studied. Nevertheless, no serious respiratory effects were produced and all the animals recovered soon after the withdrawal of anaesthetic administration (5–10 min). The reason for lack/limited toxicity could be due to the use of very less quantity of halothane in a slow and steady rate, and the solubility of halothane in ethanol preventing a high free concentration of the drug directly exposing the pulmonary system.

The results of this preliminary study indicated that ethanol could be used as a carrier for IV administration of halothane. Five per cent halothane in ethanol could induce and maintain anaesthesia without any apparent cardio-pulmonary side effects, though it requires constant monitoring. Further studies are required to establish the pharma co-kinetics of halothane in ethanol and its safety in veterinary patients.

SUMMARY

The effects of intravenous halothane (5%) in ethanol were studied in sheep premedicated with diazepam administered intramuscularly @ 0.5 mg/kg body weight. Ten min after the administration of diazepam, halothane was given as a drip @ 2.5–5 drops/kg/min. After induction, anaesthesia was maintained up to 60 min. During the period, the animals were observed for respiratory rate, heart rate and any untoward reaction. The onset of anaesthesia, the rate of administration, total dose of the anaesthetic required for induction and maintenance of anaesthesia and recovery time were determined. All the animals recovered smoothly within 5 min of discontinuation of halothane. No significant changes were recorded in cardiopulmonary parameters, except for an increase in heart rate and transient decrease in respiratory rate. The results suggested that intravenous administration of 5% halothane in ethanol could be used for induction and maintenance of general anaesthesia in sheep under constant monitoring.

REFERENCES

- Berman P and Tattersall 1982. Self poisoning with intravenous halothane (letter). *Lancet* 1: 340.
- Dwyer R and Coppel D L. 1989. Intravenous injection of liquid halothane. *Anesthesia Analgesia* 69: 250–55.
- Hall L W, Clarke K W and Trim C M. 2001. *Veterinary Anaesthesia*. 10th edn, Pp 82, 138–139. W B Saunders, Philadelphia.
- Kopriva C J and Lowenstein E. 1969. An anesthetic accident: cardiovascular collapse from liquid halothane delivery. *Anesthesiology* 30: 246–47.
- Musser J B, Fontana J L and Mongan P D. 1999. The anesthetic and physiologic effects of an intravenous administration of a halothane lipid emulsion (5% v/v). *Anesthesia Analgesia* 88: 671–75.
- Sandison J W, Sivapragasam S, Hayes J A and Woo-Ming M O. 1970. An experimental study of pulmonary damage associated with intravenous injection of halothane in dogs. *British Journal of Anesthesia* 42: 419–24.
- Sutton J, Harrison G A and Hickie J B. 1971. Accidental intravenous administration of halothane. *British Journal of Anesthesia* 43: 513–20.