Maintenance of anaesthesia in sheep with isoflurane, desflurane or sevoflurane

A. R. Mohamadnia, G. Hughes, K. W. Clarke

Rapid recovery from anaesthesia is advantageous in small ruminants, to reduce the risk of regurgitation. Theoretically, the least soluble inhalation agents should result in the fastest recoveries, but using additional injectable agents may negate this advantage. This study compared three inhalation agents for the maintenance of anaesthesia in sheep. Eighteen ewes that were to undergo orthopaedic surgery were allocated to one of three groups. Each group was premedicated with xylazine (0·1 mg/kg intramuscularly), anaesthesia was induced using ketamine (2 mg/kg) and midazolam (0·03 mg/kg) intravenously and analgesia provided by buprenorphine (0·008 mg/kg intramuscularly). Anaesthesia was then maintained with either isoflurane, sevoflurane or desflurane. Cardiopulmonary parameters were monitored throughout. All three inhalation agents provided adequate stable anaesthesia and there was no significant difference between the groups in their cardiopulmonary parameters or their recovery times. The mead (sd) postanaesthetic times to first swallow, first chewing attempts and ability to maintain their head lifted for five minutes were, respectively, 3·95 (2·53), 6·37 (3·68) and 32·8 (18·1) minutes for isoflurane, 3·62 (0·98), 7·66 (0·78) and 38·8 (16·6) minutes for sevoflurane, and 4·37 (1·65), 6·95 (1·52) and 29·8 (11·5) minutes for desflurane. Two sheep had poor quality recoveries after the use of sevoflurane, but all the other sheep recovered uneventfully. All three inhalation agents were suitable for the maintenance of anaesthesia in sheep but, as used in this study, there were no differences between them in speed of recovery.

SMALL ruminants such as sheep and goats are frequently used as a model for experimental surgery. Several anaesthetic induction techniques have been used, but anaesthesia is usually maintained with inhalation agents, because they make it possible to modify the depth and duration of anaesthesia without unduly extending the time taken to recover. Small ruminants are not the best candidates for anaesthesia because their intestinal physiology means that they are susceptible to bloat and the regurgitation of gut contents when recumbent, with potentially fatal consequences. These hazards are minimised initially by inducing anaesthesia with an intravenous agent, and securing the airway with a cuffed tube while the animal is still in sternal recumbency. However, the dangers return during the recovery period, until the animal has regained good control of its pharyngeal and laryngeal reflexes and can maintain sternal recumbency (Hall and others 2001). An anaesthetic protocol that results in a rapid and complete recovery should therefore reduce these risks.

The inhalation agents that have been most commonly used for the maintenance of anaesthesia are halothane and isoflurane, but two new agents, desflurane and sevoflurane, have recently been introduced into clinical practice. Desflurane is a fluorinated methyl ethyl ether. It is a clear, colourless and virtually odourless fluid, with a boiling point of 23·5°C, thus necessitating a heated vaporiser to ensure an accurate supply of vapour. Sevoflurane is a fluorinated ether with a boiling point of 58·5°C, with low pungency, and it produces little to no airway irritability compared with isoflurane and desflurane (Doi and Ikeda 1993, Inomata and others 1994).

The physicochemical properties of the two agents have been described by Eger (1992, 1995), Brown (1995) and Clarke (1999). The blood:gas and brain:blood partition coefficients of desflurane are 0·42 and 1·3 respectively and those for sevoflurane are 0·68 and 1·7; in comparison those of isoflurane are 1·4 and 1·6. Their lower blood:gas coefficients result in a more rapid equilibration of blood and brain levels with alveolar gases and a more rapid induction of anaesthesia. Speed of recovery, particularly after a long period of anaesthesia, is dependent not only on the solubility of the gas in blood, but also on its solubility in tissues with a poor blood supply, such as fat. The lower partition coefficient of desflurane in all tissues including fat (fat: blood coefficient 27) means that recovery from prolonged anaesthesia should theoretically be more rapid and complete than that from isoflurane (fat:blood coefficient 45) or sevoflurane (fat:blood coefficient 48) (Clarke 1999). The cardiopulmonary effects of desflurane and sevoflurane are similar to those of isoflurane, except that in most species studied so far the heart rate is slowest with sevoflurane. All three cause a dose-dependent decrease in arterial blood pressure and systemic vascular resistance and, at higher doses, myocardial depression and a decrease in cardiac output (Hikasa and others 1996, Mutoh and others 1997, Clarke 1999, Alibhai 2001, Steffey and others 2005a, b). In experimental studies in which anaesthesia has been induced with the inhalation agent, the speed of recovery has always been more rapid with desflurane and sevoflurane than with isoflurane (Matthews and others 1998, Hikasa and others 2000).

In clinical practice anaesthesia is usually induced by using injectable agents, often after premedication with sedatives and the administration of opioids for perioperative analgesia, all of which might influence the recovery of an animal from the inhalation anaesthetic agent.

The hypothesis tested in this study was that the recovery times of sheep, which had been sedated with xylazine, in which anaesthesia had been induced with ketamine/midazolam, which had been given a long-acting opioid (buprenorphine), and in which anaesthesia had then been maintained with isoflurane, desflurane or sevoflurane, would not differ significantly.

MATERIALS AND METHODS

One of the authors (A. R. M.) who was aware of the anaesthetic agent in use, performed all the practical parts of the study, including the administration of the anaesthetic, and the monitoring of the animals' intraoperative and recovery parameters.

Animals

Eighteen healthy (Masham and mule breed) ewes, aged two to four years and weighing between 65 and 90 kg were used. They were anaesthetised for a variety of experimental orthopaedic procedures, carried out under licence by the UK Home Office. The sheep were housed indoors at ambient temperature, bedded with straw and fed hay and proprietary sheep

Veterinary Record (2008) **163,** 210-215

A. R. Mohamadnia, DVM, DVSc,
Department of Clinical Sciences, College of Veterinary Medicine, 2 Saman Road, University of Shahrekord, Shahrekord, 88186/34141, Iran
G. Hughes, HND(Ag), HNC(Sci),
K. W. Clarke, MA, VetMB, DVetMed, DipECVA, DVA, FRCVS,
Royal Veterinary College, Hawkshead Lane, Hatfield, Hertfordshire AL9 7TA

pellets. Food was withheld for 24 hours before the procedures but the animals had free access to water.

Anaesthesia

The sheep were transported from their pens to the anaesthetic room on a trolley and then sedated with 0·1 mg/kg xylazine administered intramuscularly (Rompun; Bayer). Fifteen to 25 minutes later a jugular vein was catheterised with an 18 G Angiocath (Becton Dickinson). Anaesthesia was induced with 2 mg/kg ketamine (Ketaset; Fort Dodge Animal Health) and 0·03 mg/kg midazolam (Hypnovel; Roche Products) mixed in the same syringe and injected through the jugular catheter. Immediately after the induction of anaesthesia, the trachea was intubated with a 10 mm internal diameter endotracheal tube and the cuff was inflated. A stomach tube was inserted into the rumen. Buprenorphine (0·008 mg/kg) (Vetergesic; Alstoe Animal Health) was administered intramuscularly after the induction of anaesthesia to provide perioperative analgesia. The sheep were transported to the operating room, positioned as required for the surgery, and then connected to a circle breathing system (Cyprane; Boyle International 2). The carbon dioxide absorbent used was soda-lime (Sodasorb; W. R. Grace). Anaesthesia was maintained with the allocated inhalation agent, delivered to the breathing system in oxygen from a suitable temperature-compensated calibrated vaporiser (Isotec [Datex-Ohmeda] for isoflurane, Tec 6 [Datex-Ohmeda] for desflurane and Sigma Delta [Penlon] for sevoflurane) situated out of circuit. During the early period of anaesthesia, the fresh gas oxygen flow rate was set at 4 l/minute and the vaporisers were set to obtain end-tidal concentrations approaching the published minimal alveolar concentration (MAC) for the agent concerned. Once the concentration was close to this value, the flow of oxygen was reduced to 10 ml/kg per minute and the vaporiser settings were adjusted according to the sheep's autonomic responses (changes in blood pressure, heart and respiratory rates and changes in eye position) to surgical stimulation. Lactated Ringer's solution was administered intravenously at approximately 5 ml/kg per hour throughout the period of anaesthesia.

Anaesthesia was maintained in six of the sheep with isoflurane (Isoflurane-Vet; Merial Animal Health), in another six with desflurane (Suprane; Baxter Healthcare) and in the other six with sevoflurane (SevoFlo; Abbott Animal Health). They were not allocated to these groups at random, because it was necessary to ensure that the mean duration of anaesthesia for the sheep in each of the groups was similar. Each surgical procedure was classified as expected to be short, less than 90 minutes, medium, 90 to 140 minutes, or long, more than 140 minutes, on the basis of its complexity, and for each anaesthetic equal numbers of sheep were allocated to each time group.

Measurements

During the period of anaesthesia the following parameters were measured. Expired gases were sampled from an adapter located between the Y-piece and the endotracheal tube, and from these, end-tidal carbon dioxide (CO_2) and end-tidal agent concentration were measured continuously using side-stream spirometry with a calibrated gas analyser (Orcaap 7296; Kontron Instruments). Heart rate was measured by electrocardiogram, rectal temperature, blood oxygen saturation (SpO2) by pulse oximetry, and oscillometric non-invasive arterial blood pressures (systolic, diastolic and mean) with a Minimon 7137 (Kontron instruments), using an inflatable cuff on the metacarpal region, with zero taken as the level of the right atrium. The pulse oximeter probe was placed on the tongue or the ear.

Recovery

At the end of surgery the animals were placed in sternal recumbency on a trolley. The vaporiser was switched off, the expiratory valve was opened, the reservoir bag was emptied and the system was refilled using the oxygen flush. This was repeated twice, and fresh oxygen was allowed to flow into the circle system at 4 l/minute until extubation. The times at which the sheep made the first swallowing attempt and the first chewing movements were recorded, and the endotracheal tube was then removed. The sheep were then returned to their barn and positioned in sternal recumbency supported by hay bales on each side. Their recovery was recorded on video film, and their recovery features were determined from this film. Recovery from anaesthesia to the point at which the sheep could maintain sternal recumbency, and therefore no longer required continual observation, was taken as the time at which it could lift its head and keep it raised for a continuous period of five minutes.

After they had recovered from anaesthesia, the sheep were kept under close observation until they were able to stand and eat. They were observed carefully for behavioural signs of pain, and further doses of buprenorphine were administered as required and in relation to the surgery performed.

Data analysis

The cardiopulmonary data recorded 35, 50, 65 and 80 minutes after the induction of anaesthesia were selected for analysis. The hypothesis that the mean times to positive swallowing, chewing and adequate recovery after the end of the period of anaesthesia would not differ significantly between the treatments was assessed using a one-way analysis of variance. A repeated measures analysis of variance was used to determine whether the two main effects, time and treatment, were significant for the variables end-tidal CO_2, SpO_2, diastolic, systolic and mean blood pressure, temperature and heart rate.

$P \leq 0{\cdot}05$ was considered significant. The results are presented as mean (sd) unless stated otherwise. The analyses were carried out using the Windows statistical packages SAS 9.1 (SAS Institute) and SPSS 12.

RESULTS

Demographic data

The periods of anaesthesia were not always as expected, with some procedures taking longer than anticipated. The numbers of sheep undergoing short, medium or long periods of anaesthesia are shown in Table 1 and were not equal for each group as originally intended. Table 2 gives the mean times from when the sheep were sedated with xylazine, and from when anaesthesia was induced to the end of the period of administration of the inhalation agent. The mean duration of anaesthesia was longest in the sheep anaesthetised with isoflurane, but the difference was not statistically significant.

Intraoperative observations

A suitable and stable depth of anaesthesia was achieved easily with all three anaesthetic agents, and there were no untoward or unexpected occurrences. An irregular pattern of respiration was recorded in the majority of cases, several rapid breaths being followed by a short period of apnoea.

Table 3 and Fig 1 detail the parameters that were measured while the sheep were anaesthetised. There were no significant differences between the groups in any of the parameters. The end-tidal concentrations of the inhalation agents could not be compared directly, but the mean concentrations when the vaporisers were switched off were 1·55 (0·20) per cent for isoflurane, 2·25 (0·15) per cent for sevoflurane, and 7·21 (0·48) per cent for desflurane.

Recovery

Table 4 gives the times taken by the sheep to their first swallow, their first chewing attempt, and being able to maintain

TABLE 1: Numbers of sheep undergoing short, medium or long surgical procedures

Anaesthetic agent	Short (less than 90 minutes)	Medium (between 90-140 minutes)	Long (more than 40 minutes)
Isoflurane	1	2	3
Sevoflurane	2	1	3
Desflurane	2	2	2

TABLE 2: Mean (sd) duration of anaesthesia and sedation (minutes) in the sheep anaesthetised with the three agents

Anaesthetic agent	Time from induction of anaesthesia until withdrawal of volatile agent	Time from xylazine premedication until withdrawal of volatile agent
Isoflurane	169·0 (67·1)	188·0 (67·7)
Sevoflurane	131·8 (63·7)	152·7 (61·7)
Desflurane	121·5 (56·5)	148·7 (56·3)

their head lifted for five minutes. There were no significant differences between the groups.

All the sheep anaesthetised with isoflurane and desflurane recovered calmly and uneventfully, but two of the sheep anaesthetised with sevoflurane recovered violently. These animals showed excitation at the time of extubation and attempted to jump off the trolley. They were physically restrained and transferred to the recovery pen, after which they took about an hour before they could maintain their head lifted for five minutes.

DISCUSSION

The results of this study support the hypothesis that the differences in recovery time between the three inhalation anaesthetics would be clinically insignificant once sedative, anaesthetic and analgesic agents had also been administered. The agents used perioperatively were xylazine, ketamine, midazolam and buprenorphine. Steffey and others (1991) demonstrated that in horses there was a significant reduction in MAC three to four hours after the administration of 1 mg/kg xylazine. Ruminants, including sheep, are very sensitive to the sedative effects of xylazine, the duration of which is dose-dependant (Knight 1980). However, there are variations in response between breeds of sheep (Ley and others 1990), and between individuals within a breed. Garcia-Villar and others (1981) reported that the half-life of elimination of xylazine in sheep was 22 minutes but that its duration of action did not seem to be related to its blood concentration. Grant and Upton (2004) showed that in sheep a dose of 0·05 mg/kg xylazine had measurable analgesic effects after 90 minutes. In this study, the average time from administration of xylazine to the end of the period of anaesthesia was 148 minutes, but its effect on the recovery of the sheep cannot be discounted.

Ketamine, usually in combination with a benzodiazepine or an alpha-2 agonist, has been used widely as an anaesthetic in sheep (Nowruzian and others 1981, Coulson and others 1989, Taylor 1991). Waterman and Livingston (1978) and Waterman (1978) found that its half-life of elimination in sheep was 33 minutes and that the dose used in their study (11·6 mg/kg) gave 15 to 20 minutes of anaesthesia. Combinations of xylazine and ketamine provide a longer period of anaesthesia. Hughan and others (2001) showed that a combination of 0·02 mg/kg xylazine and 1 mg/kg ketamine given during anaesthesia delayed the recovery of sheep, both to extubation and to standing, after they had been anaesthetised with halothane.

In human beings midazolam, a water-soluble benzodiazepine, is shorter acting but three to four times more potent than diazepam (Hall and others 2001). When used on its own in sheep, intravenous doses of 0·1 mg/kg may either sedate or excite them (Raekallio and others 1998), but in combination with ketamine it can be used to induce anaesthesia. In human beings premedication with midazolam reduces the differences in recovery times between desflurane and sevoflurane, and the use of benzodiazepines (including midazolam) has been shown to increase the incidence of emergence delirium (Valley and others 2003, Lepouse and others 2006).

TABLE 3: Mean (sd) cardiopulmonary measurements, end-tidal concentrations of the anaesthetic agents and body temperatures of groups of six sheep anaesthetised with the three agents at intervals after the induction of anaesthesia

Anaesthetic agent	Parameter	Time from induction of anaesthesia (minutes) 35	50	65	80
Isoflurane	HR (bpm)	83·5 (18·0)	77·5 (13·7)	77·5 (17·3)	81·2 (13·4)
	SpO_2 (%)	97·8 (3·06)	96·8 (3·65)	96·8 (2·64)	97·7 (2·73)
	SAP (mmHg)*	101·7 (24·3)	109·8 (13·3)	123·3 (15·7)	118·0 (12·8)
	DAP (mmHg)	51·2 (25·2)	56·7 (8·89)	70·2 (17·8)	70·2 (15·1)
	$ETCO_2$ (kPa)	6·60 (1·52)	7·68 (0·91)	7·51 (0·90)	6·77 (1·53)
	ETISO (%)	1·38 (0·13)	1·40 (0·21)	1·45 (0·08)	1·48 (0·09)
	Temp (°C)*	38·7 (0·58)	38·2 (0·70)	37·9 (0·73)	37·7 (0·72)
Sevoflurane	HR (bpm)	79·3 (7·03)	76·3 (6·02)	75·7 (2·80)	74·5 (4·27)
	SpO_2 (%)	96·7 (4·08)	98·7 (1·03)	97·8 (2·63)	96·5 (4·72)
	SAP (mmHg)	117·2 (14·7)	116·7 (11·9)	120·0 (11·0)	118·5 (14·3)
	DAP (mmHg)	55·5 (9·09)	62·8 (6·08)	62·3 (7·02)	69·0 (11·7)
	$ETCO_2$ (kPa)	6·31 (2·20)	6·26 (1·83)	6·31 (1·86)	8·17 (1·51)
	ETSEVO (%)	1·96 (0·13)	2·03 (0·08)	2·20 (0·11)	2·28 (0·19)
	Temp (°C)	38·5 (0·77)	38·4 (0·93)	38·3 (0·96)	38·9 (0·28)
Desflurane	HR (bpm)	78·5 (17·4)	82·3 (13·6)	81·3 (14·9)	76·8 (14·4)
	SpO_2 (%)	98·5 (1·87)	98·7 (1·96)	98·2 (2·22)	98·5 (1·76)
	SAP (mmHg)	108·2 (15·6)	109·5 (12·1)	110·8 (17·3)	109·5 (19·6)
	DAP (mmHg)	64·2 (21·6)	59·0 (19·3)	61·7 (18·7)	58·2 (21·1)
	$ETCO_2$ (kPa)	7·80 (1·33)	7·84 (1·14)	7·33 (1·31)	7·71 (1·22)
	ETDES (%)	7·1 (0·81)	6·98 (0·50)	6·91 (0·46)	7·15 (0·45)
	Temp (°C)	37·9 (1·45)	38·5 (0·55)	38·4 (0·47)	38·2 (0·58)

* Significant change with time within the same group
HR Heart rate, SpO_2 Blood oxygen saturation, SAP Systolic arterial blood pressure, DAP Diastolic arterial blood pressure, ET End-tidal concentration, CO_2 Carbon dioxide, ISO Isoflurane, SEVO Sevoflurane, DES Desflurane

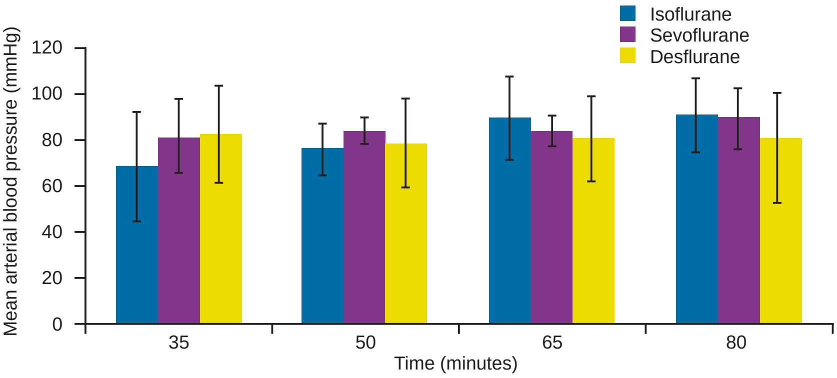

FIG 1: Mean (sd) arterial blood pressures measured in three groups of six sheep at intervals while anaesthesia was maintained with isoflurane, sevoflurane or desflurane

TABLE 4: Recovery times (minutes) from cessation of the administration of the three anaesthetic agents

Anaesthetic agent	First swallowing attempt	First chewing attempt, extubation	Maintained head lifted for five minutes
Isoflurane	3·95 (2·53)	6·37 (3·68)	32·8 (18·1)
Sevoflurane	3·62 (0·98)	7·66 (0·78)	38·8 (16·6)
Desflurane	4·37 (1·65)	6·95 (1·52)	29·8 (11·5)

Buprenorphine is a long-acting partial agonist opioid, which may provide up to four hours analgesia in sheep (Nolan and others 1987, Taylor 1991). In human beings its effect on recovery time is uncertain. Van den Berg and others (1994) found that its use resulted in severe postoperative respiratory depression and somnolence, whereas Takahashi and others (2001) found that it did not delay recovery from sevoflurane anaesthesia.

An indication that the residual effects of the combination of injectable agents discussed above were having an effect throughout the anaesthetic period is given by the end-tidal concentrations of the anaesthetics required to prevent autonomic responses to surgery, which were similar to or less than the mean of the published MAC for each of them. On the basis of published MAC values, the end-tidal concentration of isoflurane (1·55 per cent) was 0·75 to 1·18 times its MAC, the 2·25 per cent for sevoflurane was 0·63 to 0·75 times its MAC and the 7·21 per cent for desflurane was 0·67 to 0·83 times its MAC. The MAC values published for adult sheep are, for isoflurane, 1·01 to 1·58 per cent (Palahniuk and others 1974, Bernards and others 1996) and for desflurane, 9·5 per cent (Lukasik and others 1998b). The only report of the MAC of sevoflurane in sheep is 3·3 per cent (Lukasik and others 1998a). This is exceptionally high in comparison with its value in other species; in goats for example it is reported as 2·3 to 2·7 per cent (Hikasa and others 1998, Alibhai 2001). In herbivores, methane can interfere with infra-red measurements of end-tidal halothane (Taylor 1990) and, to a lesser extent, of isoflurane (Dujardin and other 2005). In this study, any error so generated would have increased the end-tidal isoflurane measurements and was considered minimal because the fresh gas flow rates were high, and the monitor used had previously been validated as accurate in ruminants for the measurement of all three anaesthetic agents (Alibhai 2001) by the method of Gootjes and Moens (1997).

Theoretical considerations suggest that if the inhalation anaesthetics had been used without other medication, recovery should have been fastest with desflurane, followed by sevoflurane and slowest with isoflurane, the difference between desflurane and the other two agents being accentuated after prolonged periods of anaesthesia. In experimental studies Alibhai (2001) compared the three inhalation agents in goats. Following mask induction, the goats recovered significantly more quickly from desflurane and sevoflurane than from isoflurane, but the differences between desflurane and sevoflurane were not significant. Several comparisons in human beings and animals of two of the three agents have recorded similar results, or that recovery after desflurane is the most rapid (Eger 1993, Eger and others 1997, Hikasa and others 1998). However, Johnson and others (1998) did not observe any significant differences between the recovery times of dogs anaesthetised with isoflurane and sevoflurane. Similarly, Steffey and others (2005a, b) observed no significant difference in horses between sevoflurane and desflurane, although they recorded that recovery times increased as the period of anaesthesia increased. In clinical studies in horses in which injectable anaesthetics were used for induction, Matthews and others (1998) observed a more rapid recovery from sevoflurane than from isoflurane, but Polis and others (2001) did not observe a similar difference in dogs. The present study most closely resembles the clinical studies quoted above, in that the recovery of the sheep could have been influenced by factors relating to the duration of the different surgical procedures. The protocol had attempted to compensate for this variation by allocating equal numbers of sheep in each anaesthetic group to procedures expected to be short, medium or long. Some of the surgical procedures took longer than expected (a common situation in clinical practice), but the surgery performed was that originally intended. Overall, there was no significant difference in the duration of the period of anaesthesia between the three groups.

One difference between the studies quoted above is the indices used to assess recovery; for all species these include extubation, but whereas in people they include cognitive factors, in most veterinary studies final recovery is taken as the ability of the animal to stand, unless, as in this study, standing might be limited for orthopaedic reasons. Final recovery in the present study was taken as when the sheep could hold up its head for five minutes. This time was chosen after preliminary observations that showed that some sheep would lift up their head (particularly in response to noise stimulation) but would allow it to drop as soon as they were left undisturbed, and, if the bales supporting them moved, would go into lateral recumbency. When recovering from anaesthesia, sheep should not be left unattended until they can safely maintain themselves in sternal recumbency; preliminary trials showed that they could do this once they were sufficiently awake to maintain their head raised for five minutes. The more usual parameters of swallowing, chewing and extubation were also used to assess the stage of recovery and they also failed to demonstrate any significant difference in recovery time between the three agents.

The quality of recovery from anaesthesia is also important. In human beings there have been reports of 'emergence agitation' after sevoflurane anaesthesia (Cravero and others 2000, Moos 2005). A similar phenomenon has been reported in an experimental study in horses (Clarke and others 1996) but has not been reported from clinical veterinary studies in any species (Matthews and others 1998). A possible cause for a disturbed recovery could be pain, as the effect of the buprenorphine could have been waning if the procedure had lasted more than four hours (Taylor 1991). However, during the recovery excitement phase that occurred in two sheep given sevoflurane (one in a short and one in a long procedure), the animals then returned to a sleepy state, and did not show any signs indicative of pain until well after they were considered to have fully recovered from the anaesthesia.

The sheep's cardiopulmonary parameters were monitored throughout the study. There were no significant differences between the three agents in any of the parameters measured. This result was as expected from experimental comparisons in human beings and in a wide range of animals (Mutoh and others 1997, Hikasa and others 1996, Clarke 1999, Alibhai 2001, Steffey and others 2005a, b), although some of these studies have demonstrated a lower heart rate and a higher end-tidal CO_2 after anaesthesia with sevoflurane than with the other two agents.

The results of the present study show that the anaesthesia that had been induced in the sheep with parenteral agents could be maintained satisfactorily during orthopaedic surgery with isoflurane, sevoflurane or desflurane; that the cardiopulmonary changes were similar with all three agents, and that, under these circumstances in which buprenorphine had been used for analgesia, differences in the sheep's speed of recovery did not reach significant proportions. The excited behaviour of two of the sheep during their recovery from sevoflurane, despite the residual sedative effect of the parenteral agents, was an unwanted side effect that requires further investigation.

ACKNOWLEDGEMENTS

The authors thank the Deputy of Research, Shahrekord University for providing the funding for a sabbatical leave enabling A. R. M. to work at the Royal Veterinary College.

References

ALIBHAI, H. I. K. (2001) Aspects of inhalation anaesthesia in the goat. PhD thesis. London, University of London

BERNARDS, C. M., KERN, C. & CULLEN, B. F. (1996) Chronic cocaine administration reversibly increases isoflurane minimum alveolar concentration in sheep. *Anesthesiology* **85,** 91-95

BROWN, B., Jr (1995) Sevoflurane: introduction an overview. *Anesthesia and Analgesia* **81** (Suppl 1), 3

CLARKE, K. W. (1999) Desflurane and sevoflurane. New volatile anesthetic agents. *Veterinary Clinics of North America: Small Animal Practice* **29,** 793-810

CLARKE, K. W., SONG, D. Y., ALIBHAI, H. I. & LEE, Y. H. (1996) Cardiopulmonary effects of desflurane in ponies, after induction of anaesthesia with xylazine and ketamine. *Veterinary Record* **139,** 180-185

COULSON, N. M., JANUSZKIEWICZ, A. J., DODD, K. T. & RIPPLE, G. R. (1989) The cardiorespiratory effects of diazepam-ketamine and xylazine-ketamine anesthetic combinations in sheep. *Laboratory Animal Science* **39,** 591-597

CRAVERO, J. P., BEACH, M., DODGE, C. P. & WHALEN, K. (2000) Emergence characteristics of sevoflurane compared to halothane in pediatric patients undergoing bilateral pressure equalization tube insertion. *Journal of Clinical Anesthesia* **12,** 397-401

DOI, M. & IKEDA, K. (1993) Airway irritation produced by volatile anaesthetics during brief inhalation: comparison of halothane, enflurane, isoflurane and sevoflurane. *Canadian Journal of Anesthesia* **40,** 122-126

DUJARDIN, C. L., GOOTJES, P. & MOENS, Y. P. (2005) Isoflurane measurement error using short wavelength infrared techniques in horses: influence of fresh gas flow and pre-anaesthetic food deprivation. *Veterinary Anaesthesia and Analgesia* **32,** 101-106

EGER, E. (1992) Desflurane animal and human pharmacology: aspects of kinetics, safety and MAC. *Anesthesia and Analgesia* **75** (Suppl 4), 3-9

EGER, E. I., II (1993) New inhalational agents – desflurane and sevoflurane. *Canadian Journal of Anesthesia* **40,** R3-8

EGER, E. I., II (1995) New drugs in anesthesia. *International Anesthesiology Clinics* **33,** 61-80

EGER, E. I., II, BOWLAND, T., IONESCU, P., LASTER, M. J., FANG, Z., GONG, D., SONNER, J. & WEISKOPF, R. B. (1997) Recovery and kinetic characteristics of desflurane and sevoflurane in volunteers after 8-h exposure, including kinetics of degradation products. *Anesthesiology* **87,** 517-526

GARCIA-VILLAR, R., TOUTAIN, P. L., ALVINERIE, M. & RUCKEBUSCH, Y. (1981) The pharmacokinetics of xylazine hydrochloride: an interspecific study. *Journal of Veterinary Pharmacology and Therapeutics* **4,** 87-92

GOOTJES, P. & MOENS, Y. (1997) A simple method to correct infra-red measurement of anaesthetic vapour concentration in the presence of methane. *Journal of Veterinary Anaesthesia* **24,** 24-27

GRANT, C. & UPTON, R. N. (2004) Comparison of the analgesic effects of xylazine in sheep via three different administration routes. *Australian Veterinary Journal* **82,** 306-307

HALL, L. W., CLARKE, K. W. & TRIM, C. M. (2001) Veterinary Anaesthesia. 10th edn. London, W. B. Saunders. pp 350-353

HIKASA, Y., KAWANABE, H., TAKASE, K. & OGASAWARA, S. (1996) Comparisons of sevoflurane, isoflurane, and halothane anesthesia in spontaneously breathing cats. *Veterinary Surgery* **25,** 234-243

HIKASA, Y., SAITO, K., TAKASE, K. & OGASAWARA, S. (2000) Clinical, cardiopulmonary, hematological and serum biochemical effects of sevoflurane and isoflurane anesthesia in oxygen under spontaneous breathing in sheep. *Small Ruminant Research* **36,** 241-249

HIKASA, Y., YAMASHITA, M., TAKASE, K. & OGASAWARA, S. (1998) Prolonged sevoflurane, isoflurane and halothane anaesthesia in oxygen using a rebreathing or non-rebreathing system in cats. *Zentralblatt für Veterinärmedizin. Reihe A* **45,** 559-575

HUGHAN, S. C., LOOSE, J. M., CADDY, D. J., CANNY, B. J., TILBROOK, A. J. & YOUNG, I. R. (2001) Combined xylazine and ketamine as an analgesic regimen in sheep. *Australian Veterinary Journal* **79,** 207-211

INOMATA, S., WATANABE, S., TAGUCHI, M. & OKADA, M. (1994) End-tidal sevoflurane concentration for tracheal intubation and minimum alveolar concentration in pediatric patients. *Anesthesiology* **80,** 93-96

JOHNSON, R. A., STRILER, E., SAWYER, D. C. & BRUNSON, D. B. (1998) Comparison of isoflurane with sevoflurane for anesthesia induction and recovery in adult dogs. *American Journal of Veterinary Research* **59,** 478-481

KNIGHT, A. P. (1980) Xylazine. *Journal of the American Veterinary Medical Association* **176,** 454-455

LEPOUSE, C., LAUTNER, C. A., LIU, L., GOMIS, P. & LEON, A. (2006) Emergence delirium in adults in the post-anaesthesia care unit. *British Journal of Anaesthesia* **96,** 747-753

LEY, S., WATERMAN, A. & LIVINGSTON, A. (1990) Variation in the analgesic effects of xylazine in different breeds of sheep. *Veterinary Record* **126,** 508

LUKASIK, V. M., NOGAMI, W. M. & MORGAN, S. E. (1998a) Minimal alveolar concentration and cardiovascular effects of desflurane in sheep. *Veterinary Surgery* **27,** 167

LUKASIK, V. M., NOGAMI, W. M. & MORGAN, S. E. (1998b) Minimal alveolar concentration and cardiovascular effects of sevoflurane in sheep. *Veterinary Surgery* **27,** 168

MATTHEWS, N. S., HARTSFIELD, S. M., MERCER, D., BELEAU, M. H. & MACKENTHUN, A. (1998) Recovery from sevoflurane anesthesia in horses: comparison to isoflurane and effect of postmedication with xylazine. *Veterinary Surgery* **27,** 480-485

MOOS, D. D. (2005) Sevoflurane and emergence behavioral changes in pediatrics. *Journal of PeriAnesthesia Nursing* **20,** 13-18

MUTOH, T., NISHIMURA, R., KIM, H. Y., MATSUNAGA, S. & SASAKI, N. (1997) Cardiopulmonary effects of sevoflurane, compared with halothane, enflurane, and isoflurane, in dogs. *American Journal of Veterinary Research* **58,** 885-890

NOLAN, A., LIVINGSTON, A. & WATERMAN, A. E. (1987) Investigation of the antinociceptive activity of buprenorphine in sheep. *British Journal of Pharmacology* **92,** 527-533

NOWROUZIAN, I., SCHELS, H. F., GHODSIAN, I. & KARIMI, H. (1981) Evaluation of the anaesthetic properties of ketamine and a ketamine/xylazine/atropine combination in sheep. *Veterinary Record* **108,** 354-356

PALAHNIUK, R. J., SHNIDER, S. M. & EGER, E. I. (1974) Pregnancy decreases the requirements for inhaled anesthetic agents. *Anesthesiology* **41,** 82-83

POLIS, I., GASTHUYS, F., VAN HAM, L. & LAEVENS, H. (2001) Recovery times and evaluation of clinical hemodynamic parameters of sevoflurane, isoflurane and halothane anaesthesia in mongrel dogs. *Journal of Veterinary Medicine. A, Physiology, Pathology, Clinical Medicine* **48,** 401-411

RAEKALLIO, M., TULAMO, R. M. & VALTAMO, T. (1998) Medetomidine-midazolam sedation in sheep. *Acta Veterinaria Scandinavica* **39,** 127-134

STEFFEY, E. P., MAMA, K. R., GALEY, F. D., PUSCHNER, B. & WOLINER, M. J. (2005a) Effects of sevoflurane dose and mode of ventilation on cardiopulmonary function and blood biochemical variables in horses. *American Journal of Veterinary Research* **66,** 606-614

STEFFEY, E. P., WILLITS, N., WONG, P., HILDEBRAND, S. V., WHEAT, J. D., MEAGHER, D. M., HODGSON, D., PASCOE, J. R., HEATH, R. B. & DUNLOP, C. (1991) Clinical investigations of halothane and isoflurane for induction and maintenance of foal anesthesia. *Journal of Veterinary Pharmacology and Therapeutics* **14,** 300-309

STEFFEY, E. P., WOLINER, M. J., PUSCHNER, B. & GALEY, F. D. (2005b) Effects of desflurane and mode of ventilation on cardiovascular and respiratory functions and clinicopathologic variables in horses. *American Journal of Veterinary Research* **66,** 669-677

TAKAHASHI, S., TANAKA, M., MATSUMIYA, N., KONDO, T., MIYABE, M. & TOYOOKA, H. (2001) Dose-response study of preincisional buprenorphine on emergence time and postoperative analgesic requirement in patients anesthetized with sevoflurane. *Masui. The Japanese Journal of Anesthesiology* **50,** 256-260 (In Japanese)
TAYLOR, P. M. (1990) Interference with the Datex Normac anaesthetic agent monitor for halothane in horses and sheep. *Journal of the Association of Veterinary Anaesthetists of Great Britain and Ireland* **17,** 32-34
TAYLOR, P. M. (1991) Anaesthesia in sheep and goats. *In Practice* **13,** 31-36
VALLEY, R. D., FREID, E. B., BAILEY, A. G., KOPP, V. J., GEORGES, L. S., FLETCHER, J. & KEIFER, A. (2003) Tracheal extubation of deeply anesthetized pediatric patients: a comparison of desflurane and sevoflurane. *Anesthesia and Analgesia* **96,** 1320-1324
VAN DEN BERG, A. A., HONJOL, N. M., PRABHU, N. V., DATTA, S., ROZARIO, C. J., MURALEEDARAN, R. & SAVVA, D. (1994) Analgesics and ENT surgery. A clinical comparison of the intraoperative, recovery and postoperative effects of buprenorphine, diclofenac, fentanyl, morphine, nalbuphine, pethidine and placebo given intravenously with induction of anaesthesia. *British Journal of Clinical Pharmacology* **38,** 533-543
WATERMAN, A. (1978) Studies on the distribution and metabolism of ketamine in sheep. *Journal of Veterinary Pharmacology and Therapeutics* **1,** 141-147
WATERMAN, A. & LIVINGSTON, A. (1978) Some physiological effects of ketamine in sheep. *Research in Veterinary Science* **25,** 225-233