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ORIGINAL RESEARCH

Sevoflurane or isoflurane anaesthesia? A prospective, randomised blinded clinical trial in horses undergoing elective surgery

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Abstract

Background: Isoflurane is the only volatile anaesthetic agent licensed for equine use in the United Kingdom, but sevoflurane is also commonly used. The two agents have rarely been compared for use in clinical elective surgery.

Methods: This single centre, prospective, randomised, blinded clinical investigation recruited 101 healthy client owned horses undergoing elective surgery. Anaesthesia was standardised and horses randomly assigned to receive isoflurane (I) or sevoflurane (S) for maintenance of anaesthesia in 100% oxygen. Horses were ventilated to normocapnia and received intravenous fluid therapy and haemodynamic support with dobutamine to maintain mean arterial blood pressure above 60 mm Hg. Recovery was timed and video-recorded to allow offline evaluation by two experienced clinicians unaware of the volatile agent used. No post-anaesthetic sedation was administered.

Results: There was no significant difference between groups in terms of haemodynamic support required during anaesthesia nor in quality or duration of recovery. Inotropic support to maintain MAP above 60 mm Hg was required by 67 of 101 (67%) of horses. Five horses in the I group required additional ketamine or thiopentone to improve the plane of anaesthesia.

Conclusions: Haemodynamic support needed during anaesthesia as well as the duration and quality of recovery were similar with isoflurane and sevoflurane.

KEYWORDS
anaesthesia, horse, isoflurane, recovery, sevoflurane

INTRODUCTION

One of the first published studies performed using sevoflurane in horses concluded that the drug was straightforward to use and suitable for horses undergoing surgery.[1] The study evaluated the use of sevoflurane in 40 equids undergoing surgery following a combination of intravenous anaesthetic protocols. The depth of anaesthesia was easy to control, and recovery was generally very satisfactory, although intravenous xylazine was often included. Cardiopulmonary function and biochemical effects with sevoflurane anaesthesia were similar to isoflurane[2]; these findings were supported by other similar studies at the time.[3,4] A small scale study in Arabian horses not undergoing surgery concluded that the quality of recovery was superior following sevoflurane compared to isoflurane[5] but this again involved xylazine in the protocol. The longer lasting alpha 2 agonists were not in widespread use at that time. The use of sevoflurane was more widespread in Japan compared to the USA, Canada and Europe resulting in early publications and research from that country defining the sevoflurane minimum alveolar concentration (MAC) in horses. The MAC for sevoflurane in horses has been reported as 2.31%[6] and 2.84%[7] and its cardiovascular, pulmonary effects[8,9] and influence on biochemistry values have also been studied.[7] Sevoflurane decreased mean arterial blood pressure, cardiac output, stroke volume, respiratory rate (RR) and minute volume in a dose-dependent manner[8] similar to those changes seen with isoflurane. One study reported that horses

anaesthetised with sevoflurane may require less inotropic support for maintenance of blood pressure[10] which may be due to less suppression of vasomotor tone by sevoflurane compared to isoflurane. Furthermore the low blood/gas solubility of sevoflurane (0.69 compared to 1.38 for isoflurane) and low tissue solubility[11] should produce more rapid control of the depth of anaesthesia and rapid recovery, often desirable in equine anaesthesia. One more recent study in 77 horses undergoing general anaesthesia for MRI showed no difference in quality of recovery between isoflurane and sevoflurane; however, this study did not involve surgery and may have been underpowered to detect differences in recovery quality.[12] The aim of our study was to compare the course of anaesthesia and recovery in horses anaesthetised with isoflurane or sevoflurane for elective surgery under the conditions of conventional clinical equine practice.

MATERIALS AND METHODS

Study design

The study was designed as a prospective, randomised, blinded, controlled clinical trial. It was conducted under an Animal Test Certificate (ATC-S-107) and approval from the University of Nottingham, School of Veterinary Medicine and Science ethics committee (2631 181108). The study was undertaken at one equine hospital in the United Kingdom. Following informed client consent, horses were allocated to receive isoflurane (I) or sevoflurane (S) for maintenance of anaesthesia using a pre-prepared randomisation chart (GraphPad QuickCalcs 2019). Recovery from anaesthesia was filmed, and two experienced ECVAA diplomate anaesthetists not involved with the cases and unaware of the volatile agent used awarded the recovery score for each case.

Animals

A sample size calculation indicated that 46 horses per group would be required to show a statistically significant clinically relevant difference. It was estimated that the size of the sample should be at least 92 horses to have an 80% power and 95% confidence level of detecting a 33% difference in recovery scores as assessed by a 0–5 Simple Descriptive Scale based on pilot studies, using an ordinal logistic regression model relying on a proportional odds assumption. Sample size calculation was performed using G*power (G*power 3.1).[13] The inclusion criteria for entry into the trial were defined as elective surgical cases in horses or ponies older than 6 months that had not received sedation in the preceding 24 h.

All horses were allowed access to hay and water until they were brought to the preparation area 45 min before induction of general anaesthesia. Patients were weighed and underwent a full clinical examination prior to premedication. All were classified as ASA 1 under the American Society of Anaesthesiologists classification.

Anaesthesia premedication

A 12-gauge intravenous catheter (Intraflow, Vygon Ltd) was secured in a jugular vein. At least 30 min prior to induction of anaesthesia, all horses received 0.03 mg/kg of acepromazine (Neurotranq, Alfasan) and 1.1 mg/kg of flunixin (Pyroflam, Norbrook) intravenously (i.v.). Perioperative antibiotics were determined by the clinician in charge of the case and consisted of 12 mg/kg procaine benzylpenicillin (Depocillin, MSD) intramuscularly (i.m.) with or without 6.6 mg/kg of gentamicin (Genta-Equine, Dechra) or 5 mg/kg oxytetracycline (Engemycin) i.v. Ten minutes before induction 80 mcg/kg romifidine (Sedivet, Boehringer Ingelheim) and 0.2 mg/kg morphine (Morphine sulphate, Martindale Pharmaceuticals) were administered i.v., and the horse was left undisturbed.

Anaesthesia induction and maintenance

Anaesthesia was induced with an i.v. bolus of 0.06 mg/kg diazepam (Diazepam injection BP) and 3 mg/kg ketamine (Ketavet, Zoetis UK Ltd) and horses became recumbent without manual restraint. Once the horse was laterally recumbent, the trachea was intubated with an appropriately sized cuffed, silicone endotracheal tube and connected to a large animal anaesthetic machine (JD LAVC 2000, JD Medical). Horses were mechanically ventilated (Bird Mark 7, JD Medical Phoenix USA) with a positive inspiratory pressure of 15–20 cmH_2O, a tidal volume of 10−12 ml/kg and a RR chosen by the anaesthetist to maintain end tidal carbon dioxide pressures ($P_E'CO_2$) of 40−45 mm Hg (5.3−6.0 kPa). Anaesthesia sufficient for the surgical procedure was maintained with isoflurane (Isoflo, Zoetis UK Ltd) or sevoflurane (Sevoflo, Zoetis UK Ltd) in oxygen. Vaporiser settings were selected to maintain end tidal isoflurane ($F_E'ISO$) between 1%−1.5% and end tidal sevoflurane ($F_E'SEVO$) between 2%−2.5%. Lactated Ringer's solution (Vetivex (Hartmann's) 11, Dechra) was infused i.v. at 5 ml/kg/h for the first hour and then 2 ml/kg/h thereafter. Dobutamine solution (Dobutamine concentrate, Hamelm Pharmaceuticals) was infused (HK-100VET infusion pump, VETisco) to horses requiring haemodynamic support to maintain mean arterial blood pressure (MAP) above 60 mm Hg using a prepared rate scale starting at 0.25 μg/kg/min to a maximum of 2 μg/kg/min. The total amount of dobutamine administered over the duration of the anaesthetic was recorded. A urinary catheter was placed in all horses before surgery started. If the horse developed nystagmus or moved a ketamine or thiopentone i.v., bolus was administered to improve the plane of anaesthesia.

TABLE 1 Recovery score. The number of attempts to stand was also counted, and a free text box was available for comments

Recovery score	Description
0	Very violent ('wall of death') self-inflicted injury, prolonged struggling, unable to stand after the end of anaesthesia
1	Excitement when recumbent, persistent unsuccessful attempts to stand, severe ataxia and falls once standing, aimless walking, high risk of self-inflicted injury
2	Excitement paddling when recumbent, several attempts to stand, severe ataxia when standing, danger of self-inflicted injury
3	Some staggering and ataxia, a few unsuccessful attempts to stand, ataxic immediately after standing up
4	Slight ataxia and staggering, stood up at first/second attempt, no serious instability
5	No ataxia, no struggling, stood up at first attempt as if fully conscious

Monitoring

A 22 or 20-gauge catheter (Intraflow, Vygon) was placed in a facial or dorsal metatarsal artery for arterial blood pressure measurement. Heart rate, systolic (SAP), mean (MAP) and diastolic (DAP) blood pressure, RR, and arterial oxygen haemoglobin saturation (SPO_2), end tidal expired carbon dioxide pressure ($P_E'CO_2$) were continuously displayed using a multiparameter monitor (Lightning Multiparameter Monitor, Vetronic) and manually recorded every 5 min. End tidal volatile agent and carbon dioxide values (F_E'ISO, F_E'SEVO, $P_E'CO_2$) were measured separately (Masimo ISA agent monitor, Masimo). Monitoring devices were calibrated prior to use according to the manufacturer's instructions.

Anaesthesia recovery

At the end of surgery horses were moved into a padded recovery box. Ventilation was assisted using a demand valve (Oxygen Demand Valve, JD Medical Phoenix USA) until spontaneous respiration resumed. Once spontaneous ventilation was deemed satisfactory by the attending anaesthetist, the endotracheal tube was removed and the horse left to recover unassisted. The entire recovery phase was timed and scored by the attending anaesthetist and filmed by a camera (Dahua IP Camera system) situated above the recovery box. Films were saved as MP4 files and stored securely for off-line analysis by two anaesthetists (KW and PT) unaware of the volatile agent used. The time from disconnection to extubation, sternal recumbency and standing were recorded. The quality of the anaesthesia recovery was evaluated using a previously reported recovery score system for horses[14] from 5 being the best to 0 being the worst (Table 1). The authors discussed and agreed on the application of the scoring system, and several 'practice runs' were undertaken on clinical cases anaesthetised before the trial began.

Data analysis

The normality of the data was evaluated using the D'Agostino and Pearson test. Categorical data were analysed using Fisher's exact test or chi-square, and kappa was calculated for inter-rater reliability. Continuous data and physiological variables were analysed using the unpaired Students' t test for normally distributed data or the Mann-Whitney U test for non-parametric data. A general linear regression model was used to analyse recovery score data with the different observers as the within-subjects factor and the volatile agent as the between-subjects factor. Differences were considered significant when $p \leq 0.05$.

RESULTS

One hundred and three horses were recruited to the study between February and November 2019. Two horses were excluded because the recovery films were not available. The final analysis included 49 horses who received isoflurane and 52 who received sevoflurane.

There were no significant differences between the groups for age, bodyweight, sex, duration of surgery, duration of anaesthesia, type of surgery, position of horse during anaesthesia or antibiotic administration. The demographics of the horses are summarised in Table 2.

MAC multiples at each time point were calculated as end tidal volatile agent divided by the MAC of the volatile agent. Averaged MAC multiples for I and S groups were different ($p < 0.0001$), but there was no difference at the final reading prior to disconnection ($p = 0.05$). When averaged over the entire anaesthetic, total anaesthetic exposure calculated as MAC hours was very similar between groups (Table 3). Four horses in the I group required additional doses of ketamine ($p = 0.04$), and one horse received thiopentone. There was no significant difference between groups for the number of horses receiving dobutamine or the μg/kg infused ($p = 0.2$). One horse in each group received a phenylephrine infusion to increase arterial blood pressure, in both cases for less than 20 min. Notwithstanding the infusion of dobutamine and phenylephrine, a hypotensive index can also be calculated to quantify the magnitude and duration of hypotension occurring below a pre-determined value. The hypotensive indexes for blood pressure below 60 and 70 mm Hg were also calculated. There were no differences in cardiopulmonary variables between I and S groups (Table 4).

The median time to extubation was identical in both groups, but the range was significantly different.

TABLE 2 Demographic data, procedural times and types of surgery of horses undergoing anaesthesia maintained with isoflurane ($n = 49$) or sevoflurane ($n = 52$)

	Isoflurane (I) $n = 49$	**Sevoflurane (S) $n = 52$**	**95% CI**	***p* value**
Age	6 (7 months-18 years)	7 (2 years- 23 years)	−1 to 2	0.4
Sex				0.2
Female	15	24		
Male	34	28		
Castrated	29	24		
Stallions/colts	5	4		
Breed				N/A
Pony (Connemara, Welsh)	6	6		
Cob	4	4		
Standardbred	1	0		
Thoroughbred and thoroughbred x	2	6		
Warmblood (Hannovarian, Holsteiner, Sport Horse)	26	20		
Irish Sport Horse	5	12		
Irish Draft Horse	3	0		
Arab	0	1		
Unspecified	2	3		
Weight (kilogrammes)	578 (288−706)	570 (370−752)	−24–40	0.7
Duration of anaesthesia (minutes)	100 ± 30	106 ± 26	−4.6–17.4	0.7
Duration of surgery (minutes)	45 (10−100)	40 (10−100)	−15–5	0.2
Types of surgery				N/A
Arthroscopy/tenoscopy/bursoscopy (1)	15 [†]	15 [‡]		
Arthroscopy/tenoscopy/bursoscopy (> 1)	12[†]	11		
Neurectomy	4	8		
Annular ligament desmotomy	3	1		
Splint bone removal	0	1		
Airway surgery	1	4		
Sarcoid removal	2	1		
Castration and cryptorchid surgery	1	3		
Wounds and abscess debridement	8	6		
Dental	1	1		
Unspecified	2	1		
Antibiotic administration				0.3
Perioperative penicillin	17	12		
Perioperative penicillin and gentamicin	28	36		
Perioperative oxytetracycline	2	3		
No perioperative antibiosis	2	1		
Recumbency				0.1
Dorsal	29 [§]	34		
Right lateral	12	6		
Left Lateral	6	12		
Unspecified	2	0		

Normally distributed data are presented as mean ± SD and nonparametric data as median (minimum-maximum). *p* value was calculated for continuous data using Student's *t* test or Mann-Whitney test, and categorical data were compared using Fisher's exact test or chi-square test. *p* value represents differences between groups, and confidence intervals (CI) are calculated for that difference.

[†]One horse had an additional procedure.

[‡]Two horses had an additional procedure.

[§]Two horses in the I group were moved from dorsal to right and left lateral recumbency during anaesthesia.

TABLE 3 Anaesthetic data for the two groups of horses. Values are expressed as mean ± SD or median (minimum-maximum). *p* value represents differences between groups, and confidence intervals (CI) are calculated for that difference

	Isoflurane (I)	Sevoflurane (S)	95% CI	*p* value
Dobutamine dose (μg/kg/min) infused during anaesthesia	0.3 (0.04–0.6) $n = 35$	0.2 (0.02–0.6) $n = 32$	−0.1–0.02	0.2
Additional ketamine (mg/kg)	0.8 (0.6–2.2) $n = 4$	0	0	0.04
Additional thiopentone (mg/kg)	0.75 $n = 1$	0	N/A	N/A
End tidal volatile agent (%)	1.2 (0.8–1.5) $n = 49$	2.2 (1.8–2.6) $n = 52$	N/A	N/A
MAC multiple	0.9 (0.6–1.1) $n = 49$	1.0 (0.8–1.8) $n = 52$	0.03–0.08	< 0.0001
MAC multiple at disconnection	0.9 (0.6–1.1) $n = 49$	1.0 (0.9–1.1) $n = 52$	0–0.07	0.05
MAC hours	1.3 ± 0.4 $n = 49$	1.3 ± 0.4 $n = 52$	−0.2–0.1	0.8

MAC multiples were calculated as end tidal volatile agent divided by isoflurane MAC of 1.3 vol%[15] or a sevoflurane MAC of 2.3 vol%[6].
MAC hour was calculated as (average end-expired volatile agent concentration/$MAC_{Volatile\ agent}$) x hours of volatile agent anaesthesia) based on an isoflurane MAC of 1.3 vol%[15] and a sevoflurane MAC of 2.3 vol%[6].
Abbreviation: MAC, minimum alveolar concentration.

TABLE 4 Cardiopulmonary data for the two groups of horses

	Isoflurane (I)	Sevoflurane (S)	95% CI	*p* value
Heart rate (beats per minute)	35 (20–62)	34 (26-76)	−3.7–0.05	0.05
PE' CO_2 (mm Hg)	39 (26-48)	39 (24-58)	−2–1	0.8
SpO_2 (%)	98 (67-100)	98 (74-100)	−0.2–0.4	0.2
Hypotensive index 60 (mm Hg/Hr) †	1.8 (0.05–17.4) $n = 13$	0.6 (0.05–21) $n = 21$	−4.6–0.5	0.4
Hypotensive index 70 (mm Hg/Hr) ‡	6.5 (0.05–45.9) $n = 44$	11 (0.1–42.3) $n = 38$	−0.3–6.3	0.09

Normally distributed data are presented as mean ± SD and nonparametric data as median (minimum-maximum). *p* value represents differences between groups, and confidence intervals (CI) are calculated for that difference.
†Hypotensive index = (60-lowest mean blood pressure) x time in hours the mean blood pressure was less than 60.
‡Hypotensive index = (70-lowest mean blood pressure) x time in hours the mean blood pressure was less than 70.

Horses in the S group attained sternal recumbency later than the I group ($p = 0.03$), but no difference in the time taken to stand or attempts to stand were discernible (Table 5).

Normally distributed data are presented as mean ± SD and nonparametric data as median (minimum-maximum). *p* value was calculated for continuous data using Student's *t* test or Mann-Whitney test. *p* value represents differences between groups, and confidence intervals are calculated for that difference

There was no significant difference in recovery score between the I or S groups for either of the blinded observers (Rater A and B) and the attending anaesthetist aware of the volatile agent used. Inter-rater agreement (kappa) for recovery scores for the two blinded observers was almost perfect for I (0.83) and S (0.84). Scores are summarised in Table 6, and a histogram of the distribution of the recovery scores for the observers is shown in Figure 1. Free text comments associated with the recovery scoring indicated that a few horses in both groups (9 I, 10 S) had repeated, frantic, unsuccessful attempts to stand. One horse (Group I), a 7-month-old warmblood was euthanised after a prolonged recovery and a tentative diagnosis of spinal cord malacia. The horse had undergone a stifle arthroscopy in dorsal recumbency.

DISCUSSION

This clinical prospective blinded comparison of the recovery of horses from isoflurane or sevoflurane anaesthesia found no significant difference in the quality of recovery or the haemodynamic support required. The clinical nature of the study deserves emphasis; it is a true representation of equine surgery and anaesthesia in a UK practice. The results are in agreement with the non-surgical clinical study comparing recovery after sevoflurane or isoflurane anaesthesia for MRI.[12]

Haemodynamic support did not differ between the groups; the hypotensive indexes which can be considered an outcome measure of the support given indicate group effects. Of the horses in the I group, 90% (44/49) experienced a period of time with mean blood pressure below 70 mm Hg in comparison to 73% (38/52) in the S group. For decades, equine anaesthetists have been acutely aware of the relationship between hypotension and reduced muscle perfusion,[16,17] hence the emphasis on correct positioning of the horse, padding and limiting hypotension during anaesthesia. Nevertheless, while the infusion of inotropes and vasopressors may mitigate against hypotension, this does not guarantee adequate muscle perfusion. No cases of post-anaesthetic myopathy were recorded in this cohort, and this may also be a

TABLE 5 Recovery characteristics of horses after isoflurane or sevoflurane anaesthesia

	Isoflurane	Sevoflurane	95% CI	*p* value
Attempts to stand	4 (1–25)	4 (1–17)	−2–1	0.5
Time to extubation (minutes)	5 (1–10)	5 (2–11)	0–2	0.02
Time to sternal (minutes)	18 (5–53)	21 (2–44)	0–6	0.03
Time to standing (minutes)	29 ± 11	32 ± 10	−1.2–7	0.2

TABLE 6 Recovery scores (0–5) of the two blinded observers and the attending anaesthetist aware of the volatile agent

	Recovery score attending anaesthetist	Recovery score blinded observer Rater A	Recovery score blinded observer Rater B	*p* value
Isoflurane	3 (0–5)	3 (0–5)	3 (0–5)	0.4
Sevoflurane	4 (2–5)	3 (2–5)	3 (1–5)	0.8

function of the relative vasodilation caused by isoflurane and sevoflurane[8,18] in contrast to the vasoconstriction incurred by horses receiving halothane in the past.

Additional ketamine and thiopentone boli were only administered to horses in the I group. This might stem from easier control of the plane of anaesthesia with the less soluble sevoflurane as a result of the faster rate of response to change[19] thereby reducing the need for injectable anaesthetics. It might also indicate that the I horses were maintained at a lighter plane of anaesthesia. However, most horses in the I group did not require 'top-ups', and all surgery was completed successfully making the latter reason of limited clinical significance. The horses that received the ketamine and thiopentone boli underwent different procedures and had recoveries that ranged in quality from excellent (5) to requiring euthanasia (0). The horse requiring euthanasia in this study cohort results in a 1% death rate, as for other studies,[20,21] and a retrospective evaluation of all anaesthesia deaths in elective cases in the preceding 7 years at this one centre was found to be 0.6% (John F. R. Hird, personal communication). The aetiology of spinal cord malacia is still debated, but the cases reported in the literature include mostly large breed young male horses undergoing surgeries in dorsal recumbency, and spinal cord ischaemia is presumed to occur during the procedure.[22] Although this particular horse had a hypotensive (60) index of 5 and a hypotensive (70) index of 31.3 which may have been a factor, its haemodynamic record was not out with the range of whole group.

The debate about the quality of equine recovery from anaesthesia has persisted since isoflurane superseded halothane and became the agent of choice because of less deleterious haemodynamic effects[23,24] and liver toxicity for patients and theatre staff.[25,26] In order to compare the recovery from the two volatile agents meaningfully, careful consideration was given to standardising the protocol while maintaining a typical clinical caseload and choosing a suitable sample size. Recording of the recovery ensured all aspects of the process could be scrutinised, timed and scored without bias. The recovery scores of the attending anaesthetists were higher for sevoflurane recoveries than the blinded scorers, potentially indicating a preference for sevoflurane over isoflurane. Equine anaesthesia recovery is often characterised by emergence delirium and violent uncoordinated attempts to stand; the most common causes of death are the devastating fractures occurring in recovery.[20] It is postulated, at least in humans, that residual volatile agent in the brain may be responsible for a breakdown in intracortical and thalamocortical connectivity sufficient to facilitate dysphoria but insufficient to produce immobility and unconsciousness.[27]

There is hysteresis between the anaesthetic partial pressure in the CNS and the alveolar anaesthetic partial pressure (P_AA) in the lung; consequently, strategies aimed at improving recovery quality from

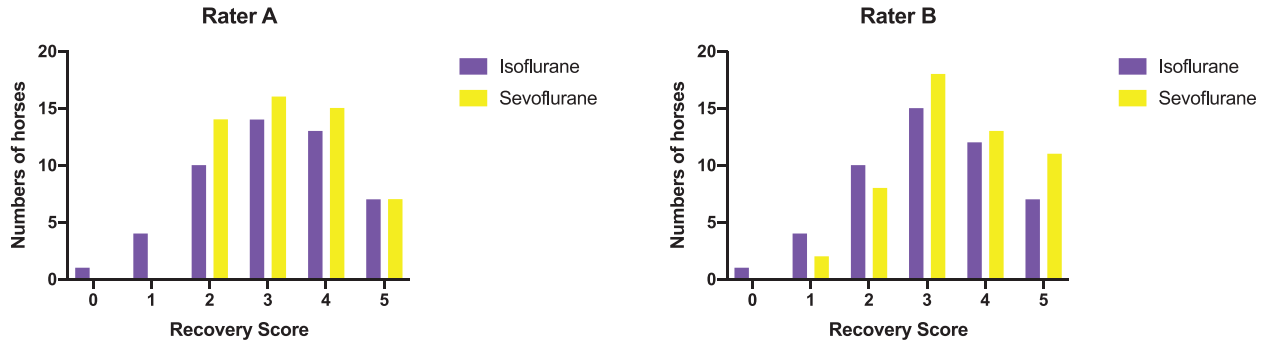

FIGURE 1 Histogram of recovery scores assigned by two experienced anaesthetists (Rater A and B) unaware of the volatile agent delivered during the anaesthesia. Recovery score is 0 (worst) to 5 (best)

inhaled agents can include promoting alveolar ventilation in order to decrease P_AA as much as possible before the horse starts to move.[28] Administration of alpha 2 agonists during recovery can reduce alveolar ventilation and prolong recumbency[29] hence the current study design omitting this intervention with the aim of parsing out the recovery characteristics of the two volatile agents. The lower blood gas solubility of sevoflurane in theory should produce a shorter recovery time compared to isoflurane,[5,30,31] but in fact in both this current study and others[4,28] this was not the case, since it is assumed the predicted advantage is negated by the greater respiratory depression as a result of the sevoflurane. Furthermore, studies of volatile agents in rodents show these discrepancies can also be explained by the anaesthetics having different neural endpoints for amnesia, immobility,[32,33] proprioception, hyperalgesia and in humans higher cognitive functions. Horses took longer to reach sternal recumbency after sevoflurane than isoflurane. It seems unlikely that they were at a deeper plane of anaesthesia at disconnection as MAC multiples were the same at this point. It may reflect the alleged calmer recovery from sevoflurane compared with isoflurane,[5] although the final result was not different. A common approach to the potential for horses trying to stand before regaining normal cognition is to sedate the horses in recovery in order to control for the variable neural endpoints under the assumption that a longer period in lateral or sternal recumbency would ensure that the horse has passed the time period during which numerous uncoordinated attempts to stand occur. The 19 (9 I, 10 S) horses which had repeated, frantic, unsuccessful attempts to stand may have benefitted from sedation. Future studies incorporating standardised post-operative sedation comparing isoflurane with sevoflurane, and possibly desflurane in large clinical caseloads are indicated. Studies to date have shown sedation improves recovery quality but prolongs duration.[5,14,34] This may be an attractive trade off, but in practical terms, may not be universally viable since the sedated horse is occupying the padded box for a longer period of time, potentially resulting in surgical slow down, and further lengthening the working day and increasing staff costs.

A further limitation stems from the attending anaesthetists being inevitably aware which volatile anaesthetic was in use. Anaesthesia was provided by one of four different anaesthetists who were aware which volatile anaesthetic was in use. This may have introduced bias because experience with a particular anaesthetic may have led to slight differences in how each was administered. However, sufficient depth of anaesthesia for surgery within a narrow window of vaporiser settings coupled with the need not to depress cardiovascular function unnecessarily would suggest this was a minor problem. Five I horses but no S horses required IV supplementation with ketamine or thiopentone. This might reflect a lighter plane of anaesthesia in the I group, or as discussed above, the need for more rapid change in the depth of anaesthesia. It is also possible that it was simply a result of less familiarity with isoflurane than sevoflurane; and the need for a known rapid effect to ensure horses did not move during surgery. There was some discrepancy in the equality of MAC values between the groups, suggesting that the isoflurane horses may have been at a lighter plane of anaesthesia. The haemodynamic data suggest that this difference was not marked, as the cardiovascular support required was similar. Moreover, the relevance of equal MAC in a clinical setting is questionable; response to surgery is more relevant. Murrell et al[35] showed in rats that 'equipotent' concentrations of isoflurane cause more burst suppression in the EEG than sevoflurane. This demonstrates that the plane of anaesthesia required for the mixed stimuli of surgery may not be equivalent to MAC multiples. Rigid adherence to equality of MAC in a clinical setting appears less apposite than maintaining the best conditions for surgery.

In conclusion, isoflurane and sevoflurane provide similar anaesthetic conditions for elective surgeries. Isoflurane anaesthetics required more 'top ups' of ketamine and thiopentone. There was no difference in the haemodynamic support required during anaesthesia or the recovery profiles. In view of the fact that post-anaesthetic sedation is the standard of care at some practices, future prospective studies incorporating these aspects are advised.

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AUTHOR CONTRIBUTIONS

All authors were responsible for all the aspects of the planning, conduct and reporting of the study and are responsible for content as guarantors.

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