

Partial intravenous anaesthesia in 5 horses using ketamine, lidocaine, medetomidine and halothane

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ABSTRACT

A partial intravenous protocol was used successfully to maintain anaesthesia in 5 healthy horses. Horses were premedicated with acepromazine, romifidine and butorphanol, induced with guaifenesin and ketamine and maintained on a constant rate infusion of lidocaine, ketamine and medetomidine together with halothane inhalation anaesthesia. Mean end-tidal halothane concentration to maintain a surgical plane of anaesthesia was 0.8 ± 0.2 %. Mean dobutamine requirement to maintain mean arterial pressure above 9.31 kPa was 0.42 ± 0.3 $\mu\text{g/kg/min}$. The administration of relatively low doses of lidocaine, ketamine and medetomidine together with halothane resulted in haemodynamically stable anaesthesia, followed by smooth recovery.

Keywords: anaesthesia, halothane, horse, ketamine, lidocaine, medetomidine.

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INTRODUCTION

In recent years, many reports have added potentially beneficial drugs to the equine anaesthetist's arsenal. Volatile anaesthetics such as halothane cause significantly greater cardiorespiratory depression than intravenous anaesthetic agents and are associated with an increased risk of perioperative complications and mortality^{12,17,18,25}. Halothane is often used in South Africa for maintenance of anaesthesia in equines. It is characterised by good muscle relaxation and poor analgesia⁷. It causes dose-dependent cardiorespiratory depression and has been shown to sensitise the myocardium to catecholamines, increasing the risk of developing arrhythmias^{7,16,17,25,30}.

Balanced anaesthesia for equine patients has come to include intravenous infusions of sedatives, muscle relaxants, analgesics and anaesthetic agents in order to decrease volatile anaesthetic requirement and preserve cardiovascular function^{3,14,32,33}. In addition to reducing the minimum alveolar concentration (MAC) of volatile anaesthetic agents, beneficial effects of such combinations are numerous. Ketamine produces beneficial haemodynamic effects during halothane anaesthesia¹⁹. Combining guaifenesin and keta-

mine with halothane increases anaesthetic stability and decreases the need for dobutamine compared with halothane alone²³. The use of guaifenesin, ketamine and medetomidine with sevoflurane results in better transition and maintenance phases, improves cardiovascular function and reduces the number of attempts to stand compared with sevoflurane alone³². Ketamine and lidocaine intravenous infusions improve cardiovascular stability during isoflurane anaesthesia¹⁰. Lidocaine administration during halothane anaesthesia is antinociceptive²⁰. Using medetomidine with isoflurane decreases the dobutamine requirement compared with isoflurane alone²¹.

In a recent review³, lidocaine, ketamine and medetomidine were singled out as the main drugs used together with volatile anaesthetics for balanced anaesthesia. To our knowledge there is no report where all 3 these drugs have been used together with halothane for balanced anaesthesia.

MATERIALS AND METHODS

Five healthy horses that were presented for elective surgical procedures are included in this report (Table 1). Food, but not water, was withheld for 8 hours prior to premedication. Preanaesthetic examination of each patient included a physical examination, detailed cardiac and thoracic auscultation (including rebreathing bag), haematology, total serum protein and

electrocardiogram (ECG). No abnormalities were detected. Preoperative treatment included tetanus vaccination and intramuscular procaine penicillin (20 mg/kg). After recovery from anaesthesia, phenylbutazone (4.4 mg/kg) was administered intravenously.

Horses were premedicated with intramuscular acepromazine (Aceprom 10, Bayer) at 0.02 ± 0.004 mg/kg (mean dose 9 ± 2.2 mg), 60 min prior to induction. Intravenous (IV) Romifidine (Sedivet 2 %, Boehringer Ingelheim) at 40 ± 7 $\mu\text{g/kg}$ (mean dose 17.4 ± 4.3 mg), and IV butorphanol (Torbugesic, Fort Dodge Animal Health) at 20 ± 4 $\mu\text{g/kg}$ (mean dose 10.6 ± 1.3 mg) were given 5 minutes prior to induction. Horses were induced intravenously, first with a 5 % guaifenesin solution (GGE, Kyron Laboratories) at 1.3 ± 0.1 ml/kg (mean dose 620 ± 84 ml), infused until they became ataxic, followed by a ketamine (Anaket-V, Bayer) bolus at 2.4 ± 0.13 mg/kg (mean dose 1140 ± 261 mg), in a padded induction room, intubated and connected to a circle anaesthetic machine. Ventilation was controlled with intermittent positive pressure ventilation and end-tidal carbon dioxide concentration (ETCO₂) maintained between 4 and 6 %. Anaesthesia was maintained during the 1st 10 min with an end-tidal halothane (EThal) concentration of 1.2 % and fresh gas flow rate set to 30 ml/kg/min. Thereafter the fresh gas flow rate was reduced to 10 ml/kg/min and the EThal maintained in a range between 0.6–0.85 % when combined with a constant-rate infusion (CRI) of lidocaine (2 mg/kg/hour), ketamine (2 mg/kg/h) and medetomidine (1 $\mu\text{g/kg/h}$), delivered *via* an infusion pump (Injectomat Agilia, Fresenius Kabi SA, Halfway House). The EThal maintenance concentration and CRI rate used in this report were previously determined in routine surgical cases from the Onderstepoort Veterinary Academic Hospital (OVAH) to minimise risk of movement during surgery (unpublished results). When the EThal concentration during surgery decreased to 0.6 %, the vaporiser setting was temporarily increased to 5 % until the EThal concentration increased to 0.85 %. Any spontaneous muscle move-

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Table 1: Signalment of 5 healthy horses presented for elective surgery maintained with halothane in oxygen and a constant-rate infusion of a combination of lidocaine, ketamine and medetomidine.

Horse no.	1	2	3	4	5	Mean ($\pm$ SD)
Age (years)	4	8	11	14	14	10.2 $\pm$ 3.8
Weight (kg)	362	410	563	558	432	465 $\pm$ 81.2
Breed	Arab	Cross	TB	TB	Fresian	–
Sex	Mare	Gelding	Mare	Gelding	Gelding	–
Procedure	Tenoscopy	Excenteration	Curet cyst on P3	Tie-back	Palmar digital neurectomy	–

TB, Thoroughbred

Table 2: Mean ($\pm$ SD) cardiorespiratory values, anaesthetic time, end-tidal halothane concentration and dobutamine doses for individual horses and combined in 5 healthy horses during anaesthesia maintained with halothane in oxygen and a constant-rate infusion of a combination of lidocaine, ketamine and medetomidine.

Parameter	Horse no.					Mean ($\pm$ SD)
	1	2	3	4	5	
Time (min)	90	95	90	95	105	95 $\pm$ 6.1
RR (breaths/min)	7.5 $\pm$ 1.0	7.4 $\pm$ 0.9	6.2 $\pm$ 0.7	6.4 $\pm$ 0.8	5.8 $\pm$ 1.2	6.7 $\pm$ 1.1
ET CO ₂ (%)	6.0 $\pm$ 0.6	6.6 $\pm$ 0.8	6.6 $\pm$ 0.1	6.1 $\pm$ 0.5	5.9 $\pm$ 0.4	6.2 $\pm$ 0.6
ET halothane (%)	0.8 $\pm$ 0.2	0.73 $\pm$ 0.1	0.71 $\pm$ 0.1	0.85 $\pm$ 0.2	0.61 $\pm$ 0.2	0.8 $\pm$ 0.2
HR (beats/min)	33 $\pm$ 3	32 $\pm$ 2	24 $\pm$ 3	28 $\pm$ 1	28 $\pm$ 4	29.2 $\pm$ 4.0
SAP (kPa)	15.0 $\pm$ 1.4	19.6 $\pm$ 2.0	14.9 $\pm$ 1.7	14.8 $\pm$ 1.6	17.4 $\pm$ 2.6	16.4 $\pm$ 2.7
DAP (kPa)	8.7 $\pm$ 1.0	10.6 $\pm$ 1.4	9.2 $\pm$ 0.9	9.2 $\pm$ 0.8	8.7 $\pm$ 1.1	9.3 $\pm$ 1.3
MAP (kPa)	10.7 $\pm$ 1.1	13.0 $\pm$ 1.8	11.1 $\pm$ 1.2	10.8 $\pm$ 1.1	11.0 $\pm$ 0.9	11.4 $\pm$ 1.5
Total dobutamine (mg)	0.31	0.8	10.3	16.7	35	12.6 $\pm$ 14.3
Dob rate (μ g/kg/min)	0.72	0.1	0.2	0.3	0.77	0.42 $\pm$ 0.3

Time, anaesthetic time; RR, respiration rate; ET CO₂, end-tidal carbon dioxide concentration; HR, heart rate; SAP, systolic pressure; DAP, diastolic pressure; MAP, mean arterial pressure; Total Dobutamine, total dobutamine dose administered; Dob rate, dobutamine infusion rate.

ment could have been countered with a single or multiple 100 mg IV ketamine boluses but this was not required.

Blood volume was maintained with an IV isotonic crystalloid solution (PlasmaVet, Sabax) administered at 10 ml/kg/h and mean arterial pressure (MAP) maintained with an IV infusion of dobutamine administered at an initial dose rate of 2 μ g/kg/min. Thereafter the dose rate was adjusted to maintain MAP between 9.31 and 11.97 kPa. Clinical parameters used to evaluate anaesthetic depth were the palpebral reflex, corneal reflex, nystagmus and spontaneous skeletal muscle movement. In addition, capillary refill time of the oral mucous membrane was monitored. Other parameters were monitored with a multi-parameter anaesthesia monitor (GE Datex-Ohmeda Cardiocap/5, GE Healthcare, Helsinki, Finland) on a continuous basis, recorded at 5-minute intervals, and included ECG, heart rate (HR), invasive systolic arterial blood pressure (SAP), diastolic arterial blood pressure (DAP), MAP, ET_{hal} and ET_{CO₂}, inspired oxygen concentration, and peripheral oxyhaemoglobin saturation (SpO₂) with the pulse oximeter probe placed on the tongue. Recording of parameters started 15–20 min after induction of anaesthesia.

At the end of surgery, intravenous anaesthetic infusions were stopped and the horses allowed to breathe spontane-

ously. Thereafter the horses were disconnected from the anaesthetic machine, moved into the padded recovery room, positioned appropriately and extubated. Oxygen was administered *via* nasal insufflation (15 l/min) to prevent hypoxaemia. To avoid possible upper airway obstruction, a small-animal endotracheal tube (10–14 mm) was placed in the ventral meatus of 1 nostril and taped in position in order to ensure a patent airway despite oedema that may have developed during recumbency. Horses were sedated with romifidine (40 μ g/kg) at the 1st sign of movement. Recovery was assisted with head and tail ropes. Recovery times were not recorded.

RESULTS

Individual and group mean ($\pm$ SD) cardiorespiratory variables are summarised in Table 2 and Fig. 1. Changes in variables over time were not statistically significant for HR ($P = 0.46$), SAP ($P = 0.36$), DAP ($P = 0.49$), MAP ($P = 0.44$), RR ($P = 0.32$), ET-CO₂ ($P = 0.53$). Capillary refill time remained normal (<2 s), but the oral mucous membranes became progressively paler over time. This was associated with an inability of the pulse oximeter to measure SpO₂ due to the plethysmographic wave amplitude becoming a nearly flat line.

Horse 3 had a 2nd-degree atrioventricular (AV) block in the stable prior to

premedication that disappeared with mild exercise and did not recur during anaesthesia. Horse 5 had a 2nd-degree AV block that persisted for the 1st 40 min of anaesthesia, during which time dobutamine was infused at 2 μ g/kg/min to maintain MAP above 9.31 kPa. After the arrhythmia ceased, there was no further need for dobutamine in this patient. This horse did not demonstrate a 2nd-degree AV block on preanaesthetic ECG examination.

Horse 3 blinked spontaneously twice, at 5 min and 55 min. No nystagmus was seen in any of the horses at any time during anaesthesia. In all horses, corneal reflexes were strong and palpebral reflexes absent for the duration of the anaesthetic period. Muscle relaxation was considered suitable for surgery, anaesthetic depth was appropriate in all 5 horses at all times and no intra-operative movement occurred. Horse 2 dribbled urine during the procedure. His bladder was catheterised and emptied prior to recovery. Time to complete recovery ranged from 40–60 min and horses stood on the 1st or 2nd attempt. Recovery was coordinated and free from excitation.

DISCUSSION

Inhalation anaesthetic potency is expressed in terms of MAC, which is the concentration of anaesthetic that will

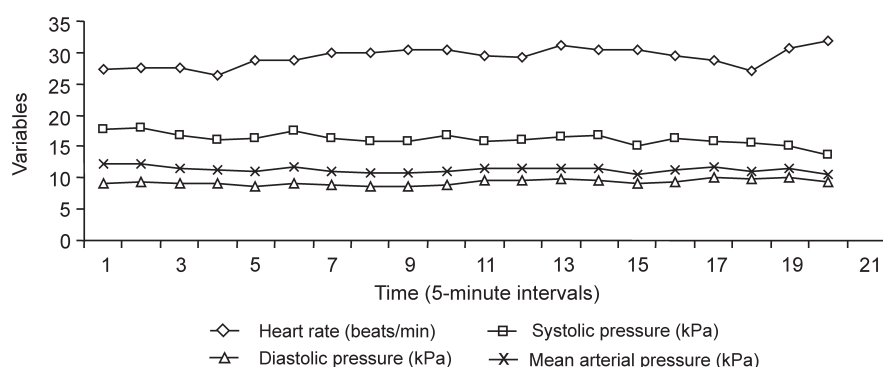


Fig. 1: Mean cardiovascular variables over time in halothane-anaesthetised horses and lidocaine-ketamine-medetomidine constant-rate infusion.

prevent purposeful movement in 50 % of animals^{5,9}. The MAC for halothane has been reported as 0.88 ± 0.03 %²⁶, 0.91 ± 0.04 %²⁵ and 0.94 ± 0.03 %⁷. To prevent movement in 100 % of cases, it is necessary to maintain an anaesthetic concentration of 1.2–1.5 MAC. This would require an ETal concentration of 1.2–1.4 %⁷ in the horse. Medetomidine, ketamine and lidocaine infused during this investigation contributed to a decrease in isoflurane requirement to maintain surgical anaesthesia.

Lidocaine has traditionally been used as a local anaesthetic and to treat premature ventricular contractions³. More recently, it has been shown to decrease the MAC of volatile anaesthetics in horses and ponies^{6,8}. The lidocaine dose recommended to decrease volatile anaesthetic MAC is a bolus of 1.5–2.5 mg/kg IV followed by a CRI of 0.03–0.05 mg/kg/min.^{1,7} The dose used for patients in the present report is 0.03 mg/kg/min without a loading dose. The effect of omitting the loading dose on MAC reduction has yet to be established.

Ketamine, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, has long been recognised as an important intravenous anaesthetic agent for induction and for use in both total (TIVA) and more recently partial intravenous anaesthetic (PIVA) maintenance protocols. It decreases the MAC of halothane and exhibits additive anaesthetic sparing effects when used together with lidocaine^{10,19}. Doses used to decrease volatile anaesthetic MAC range from 1–3.6 mg/kg/h^{10,14,32,33}. Ketamine infusion is reported to increase anaesthetic- and haemodynamic stability and decrease hypotension^{19,23}. It is the only anaesthetic agent used in horses that supports cardiovascular function³¹. In addition, it is an excellent analgesic and has now also been shown to have anti-inflammatory properties^{15,22}. Its sympathomimetic action minimises the bradycardia and hypotensive effects of sedatives such as medetomidine¹.

Medetomidine, is a α_2 -adrenergic agonist that has potent sedative, analgesic and anaesthetic-sparing properties in equines³, facilitates smooth anaesthesia and contributes to muscle relaxation¹¹. It is reported to be an ideal drug for CRI in ponies, owing to its short distribution half-life² and has been used to decrease volatile anaesthetic MAC in horses at 1.25–3.5 $\mu\text{g/kg/h}$ ^{3,14,21}.

A potential complication of lidocaine and ketamine anaesthesia is ataxia and excitation during the recovery period. Lidocaine infusions are reported to cause ataxia in the recovery period²⁹, while prolonged ketamine infusion may lead to muscle rigidity and excitation¹⁹. This problem can be overcome by discontinuing the lidocaine infusion 30 min prior to the end of surgery, decreasing the ketamine dose to 65 % after 50 min and discontinuing the ketamine infusion 15–20 min prior to the end of surgery^{3,10,29}. We did not observe increased ataxia or excitation when using the protocol described in this report compared with maintenance with halothane alone. Romifidine was administered during recovery to delay the 1st attempt to stand, and to allow more time for plasma levels of the infused and inhaled anaesthetic drugs to decline sufficiently for a strong, coordinated 1st attempt to stand. Subjectively assessed, the recovery times appeared longer compared with halothane-only anaesthesia used at this institution. A significant increase in the time to 1st movement, produced by combining guaifenesin, ketamine and medetomidine with sevoflurane anaesthesia, is reported to significantly decrease the number of attempts to stand³². Longer recoveries in equine patients may be better, because catastrophic post-operative complications occur when horses attempt to stand too soon after the end of anaesthesia. The use of head and tail ropes and romifidine may have contributed to the smooth recoveries observed here. In this investigation preference was given to romifidine for

recovery from anaesthesia as it is associated with reduced attempts to stand and improved coordination during recovery from anaesthesia⁴.

Medetomidine, like other α_2 -adrenergic agonists, causes mild, dose-dependent cardiovascular suppression in horses^{11,34}. The effect at 1 $\mu\text{g/kg/h}$ during anaesthesia may, however, be negligible, because a medetomidine CRI at 3.5 $\mu\text{g/kg/h}$ is reported to cause no cardiovascular suppression in conscious ponies³. Any potential cardiovascular suppression would, however, be offset by a reduction in halothane requirement. The α_2 -adrenergic agonists (most likely the romifidine premedication) would have caused the 2nd-degree AV block in 1 of the horses in this report¹¹. The observed progressive pallor of the oral mucous membranes is probably the result of peripheral vasoconstriction caused by medetomidine and also the reason for the inability of the pulse oximeter to obtain oxyhaemoglobin saturation readings from the mucous membrane of the tongue²⁷. It is important to note that eye reflexes should be brisker with medetomidine as an anaesthetic adjunct and insufficient anaesthetic depth is only indicated by nystagmus³. Anaesthesiologists should be aware that spontaneous blinking could occur at appropriate depths of anaesthesia during surgery. Alpha₂-adrenergic agonists cause a significant increase in urine production. One of the horses in this report demonstrated this effect by dribbling urine during anaesthesia. It is advisable to catheterise and empty the bladder prior to recovery in order to prevent post-operative discomfort in horses that received a medetomidine infusion, especially after prolonged anaesthesia³. The benefits of PIVA extend beyond merely decreasing the MAC of volatile agents. In addition to the anaesthetic-sparing effects, lidocaine contributes to antinociception and has anti-inflammatory properties^{15,22}.

Very low doses of dobutamine were required to keep MAP within acceptable limits. This may be attributed to a decrease in halothane MAC as well as ketamine's positive haemodynamic effects. The cardiovascular depressant effects of halothane are dose-dependent, resulting in a decrease in arterial blood pressure with increased dose²⁴. In addition, the peripheral vasoconstriction induced by medetomidine may also have contributed to the increase in blood pressure³⁴. Decreasing the requirement of dobutamine is beneficial to the patient, because dobutamine administration may be associated with supraventricular tachycardia, especially in colic patients^{28,35}.

Drug dose rates in this report are expressed in terms of the amount of drug given per kilogram, per time unit. The future of CRI drug therapy lies within the realm of target-controlled drug infusions (TCI), where pharmacokinetic models are used to calculate the dose rate necessary in order to attain a desired plasma concentration of the drug infused. A physiologically based pharmacokinetic model for ketamine in ponies has been developed¹³. Using such models in computer-controlled infusions, anaesthetists will have greater control during the anaesthetic period and perhaps even better recoveries in the future.

In conclusion, the constant-rate infusion of relatively low doses of lidocaine, ketamine and medetomidine during halothane anaesthesia resulted in haemodynamically stable anaesthesia, followed by smooth recovery.

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