Cardiopulmonary effects of prolonged anesthesia via propofol-medetomidine infusion in ponies

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Objective—To determine cardiopulmonary effects of total IV anesthesia with propofol and medetomidine in ponies and effect of atipamezole on recovery.

Animals—10 ponies.

Procedure—After sedation was induced by IV administration of medetomidine (7 µg/kg of body weight), anesthesia was induced by IV administration of propofol (2 mg/kg) and maintained for 4 hours with infusions of medetomidine (3.5 µg/kg per hour) and propofol (0.07 to 0.11 mg/kg per minute). Spontaneous respiration was supplemented with oxygen. Cardiopulmonary measurements and blood concentrations of propofol were determined during anesthesia. Five ponies received atipamezole (60 µg/kg) during recovery.

Results—During anesthesia, mean cardiac index and heart rate increased significantly until 150 minutes, then decreased until cessation of anesthesia. Mean arterial pressure and systemic vascular resistance index increased significantly between 150 minutes and 4 hours. In 4 ponies, PaO₂ decreased to < 60 mm Hg. Mean blood propofol concentrations from 20 minutes after induction onwards ranged from 2.3 to 3.5 µg/ml. Recoveries were without complications and were complete within 28 minutes with atipamezole administration and 39 minutes without atipamezole administration.

Conclusions and Clinical Relevance—During total IV anesthesia of long duration with medetomidine-propofol, cardiovascular function is comparable to or better than under inhalation anesthesia. This technique may prove suitable in equids in which prompt recovery is necessary. (Am J Vet Res 2001;62:1428–1435)

In human anesthesia, mortality rate has greatly reduced since the 1980s, from an incidence of 0.02 to 0.01%. In contrast, there has been no decrease in mortality in equine anesthesia during the past 30 years, and the overall mortality rate of 1.6% is far greater than the mortality rates reported in humans and small animals.

Generally, prolonged anesthesia in horses is performed by use of volatile agents, and the cardiovascular depressant effects of these may contribute to the problems that develop.

In recent years, total IV anesthesia (TIVA) protocols have become widely used in humans. In horses, a variety of TIVA techniques have been used for short procedures in the field, but for longer procedures, maintenance of anesthesia by use of TIVA has been limited to combinations of muscle relaxants, α₁-adrenoceptor antagonists, or both, with ketamine. Although cardiopulmonary function during their use is acceptable, these techniques are limited in duration by accumulation of the ketamine metabolite, norketamine, causing poor recoveries with signs of apparent ketamine overdose.

Propofol has the ideal pharmacokinetic profile for infusion, but it provides poor surgical analgesia, and in humans and other species it is used in combination with sedatives, analgesics, or both for TIVA. Propofol has been used for TIVA in horses, but adequate anesthesia to enable surgical procedures with relatively low doses of propofol and with acceptable cardiopulmonary function was only achieved when propofol was combined with a ketamine infusion, which again limited its use for prolonged anesthesia.

One of the most important features of anesthesia in horses is maintenance of good cardiovascular function. Propofol decreases arterial blood pressure and cardiac output in a dose-dependent manner, probably because of reduction in preload by direct venodilation. In dogs, this effect is attenuated if propofol is combined with medetomidine. Thurmon et al stated that the decrease in vascular tone induced by propofol could help to alleviate the vasoconstriction caused by medetomidine if appropriate doses were used. Other authors reported variable adverse cardiopulmonary effects after the use of medetomidine in combination with propofol in dogs, depending on the dose used.

Results of a previous study performed in our laboratory indicated that the combination of propofol and medetomidine for infusion in ponies could provide anesthesia adequate to prevent response to supramaximal stimuli. Minimal infusion rate (MIR) is a standard for injectable anesthetics and allows comparison of the adverse cardiopulmonary effects caused by equipotent doses of different agents. Results of the previous study defined this minimal infusion rate of propofol in combination with medetomidine and indicated that the propofol infusion rates necessary to prevent positive responses from controlled stimuli were in the ranges of...
Infusion of propofol via the jugular catheter. Anesthesia was maintained with an IV solution-filled lines via transducers. After a further 10 minutes, anesthetic monitor. The monitor had been calibrated and the transducers were placed at the level of the heart. The Swan-Ganz catheter was advanced along the jugular vein and into the pulmonary artery. The location was confirmed by the characteristic pressure trace for each chamber of the heart.

Drug administration—The ponies were sedated 10 minutes after completion of preinduction instrumentation by IV administration of medetomidine (7 µg/kg of body weight) via the jugular catheter. After a further 10 minutes, anesthesia was induced with propofol (2 mg/kg, IV) administered via the jugular catheter. Anesthesia was maintained with an IV infusion of propofol administered by a syringe pump immediately after induction of anesthesia. Individual infusion rates were 0.1 mg/kg per minute greater than previously determined as the minimal infusion rate (MIR; Fig 1). Endotracheal intubation was performed, and the ponies were allowed to breathe spontaneously. Inspired air was supplemented by oxygen flow (2 L/min per 100 kg of body weight) via narrow bore pressure tubing placed into the endotracheal tube. Anesthesia was maintained for 4 hours.

An IV infusion of medetomidine was started at 3.5 µg/kg per hour after 20 minutes of anesthesia and maintained through the remainder of the anesthetic period. This was achieved by diluting medetomidine with saline solution to a concentration of 100 mg/ml and administering the solution via a syringe pump through the jugular catheter. After 4 hours of anesthesia, the infusions were discontinued, the endotracheal tube was removed, and the ponies continued to breathe oxygen-enriched air via a nasal tube. Ponies were randomly assigned into 2 groups for recovery.

Materials and Methods

Ponies—Ten healthy ponies that were between 3 and 7 years of age (mean ± SD, 4.8 ± 1.1 years) and weighed between 157 and 294 kg (mean ± SD, 216 ± 41 kg) were used for the study. Subcutaneous transposition of 1 carotid artery had been performed in 6 of the ponies at least 4 months prior to the study. The ponies were maintained on grass pasture with supplemental feeding of hay. Food was withheld 12 hours prior to each experiment. The study was performed under the United Kingdom Home Office project license No. PPL 80/00844 in accordance with the Animals Act (Scientific Procedures, 1986).

Instrumentation—A 14-gauge 160-mm jugular venous catheter was placed in the right jugular vein. A triple-lumen 7-F 110-cm Swan-Ganz balloon-tipped thermistor catheter was introduced into the left jugular vein by use of a Tuohy-Borst introducer set. Preinduction instrumentation was completed at least 10 minutes prior to sedation. After anesthesia had been induced, the ponies were positioned in left lateral recumbency on a foam-padded mattress, and instrumentation was completed. The transposed carotid artery or metatarsal artery was catheterized with a 22-gauge 25-mm catheter for collection of arterial blood samples and to measure arterial blood pressure, a 3-lead ECG instrument was attached by use of a modified base-apex lead system, and the ends of Swan-Ganz and arterial catheters were connected through saline (0.9% NaCl) solution-filled lines via transducers to a hemodynamic monitor. The monitor had been calibrated and the transducers were placed at the level of the heart. The Swan-Ganz catheter was advanced along the jugular vein and into the pulmonary artery. The location was confirmed by the characteristic pressure trace for each chamber of the heart.

Cardiovascular variables and blood gas values were measured by use of conventional methods as described in detail elsewhere. Cardiac output (CO) measurements were made by use of a thermal dilution technique with 10 ml of ice cold 5% dextrose per 100 kg. All data were analyzed by use of a hemodynamic computer and displayed on a monitor. Cardiac index (CI) was calculated from CO and corrected for body weight. Systemic vascular resistance index (SVRI), stroke volume (SV), mean arterial pressure, and mean pul-
monary arterial pressure (MPAP) were derived from standard formulas. For recording of data, the hemodynamic mon-
tor was connected to a computer that stored numeric data at 1-minute intervals and a video recorder that provided a per-
manent and continuous record of the monitor screen.

Cardiopulmonary measurements were not taken before adminis-
tration of the drugs. Heart rate (HR), arterial blood pressure, pulmonary artery pressure, and central venous pres-
sure (CVP) were measured continuously from induction until the end of the medetomidine-propofol infusion. Pulmonary
capillary wedge pressure (PCWP) and CO were monitored 10 and 20 minutes after induction, then every 20 minutes during the
first 2 hours of anesthesia and every 30 minutes during the remaining 2 hours of anesthesia. At these times arterial blood
samples were obtained anaerobically for blood gas analyses and blood temperature and respiratory rate were recorded. Samples
for blood gas analyses were stored in ice water and analyzed within 2 hours by use of a calibrated blood gas machine.7

To determine blood concentrations of propofol during anes-
thesia, 10 to 17 blood samples/pony were collected into tubes containing potassium oxalate, cooled immediately, and stored at 4°C until analysis. Samples were obtained 10, 20, and 30 minutes after induction, then at 15-minute intervals or if the infusion rate was changed. Blood concentrations of
propofol were determined within 3 weeks of sampling in the
pharmacology laboratories of the University of Glasgow
according to a described method.27

**Statistical analysis**—Data were recorded as mean ± SD values. Hemodynamic data were analyzed by use of ANOVA
for repeated measures. When appropriate, the Scheffe test
was used to determine differences between time points. To
detect differences in recovery times between groups that did
or did not receive atipamezole, the Wilcoxon signed rank test
was used. Significance was set at \( P < 0.05 \).

**Results**

**Anesthesia induction**—Induction of anesthesia was scored as good (4) in all 10 ponies. Induction was similar in all ponies and typical of that described else-
where for propofol induction.11,13-15,24 The ponies took
several deep breaths and then became recumbent, falling suddenly onto their side. Paddling of the limbs ceased
within 1 minute after becoming recumbent, and the ponies were relaxed during the remainder of the
anesthetic period. Ease of endotracheal intubation was
assessed as excellent in all ponies.

**Infusion rates of propofol**—Propofol infusion rates
given to individual ponies ranged from 0.07 to 0.11
mg/kg per minute. Two ponies started chewing the
endotracheal tube within 5 minutes of the dose being
reduced by 0.01 mg/kg per minute. One pony moved its
ears twice at a dose rate of 0.07 mg/kg per minute. In
these ponies, propofol infusion rate was increased by
0.01 mg/kg per minute, although there was no need for
a bolus dose of propofol to be administered.

**Cardiovascular effects**—All cardiovascular vari-
ables except PCWP had some significant variations
with time (Fig 2; Tables 1 and 2). Cardiac index and
HR increased during the first 150 minutes of anesthe-
sia, then decreased toward the end of anesthesia. The
SVRI was unchanged for the first 150 minutes of anes-
thetia and then increased until the end of the monitor-
ing period. The CI, HR, and SV reached their lowest
recording values after 240 minutes of anesthesia, at the
same time SVRI was at its highest recorded value. The
only significant change in MPAP was between its value at
60 minutes and at 150 minutes.

One pony had sinus arrhythmia for 60 minutes
after anesthesia induction, and another had sinus arrhythmia from 80 minutes after anesthesia induction
until the end of the observation period. In the second
pony, the arrhythmia coincided with a low \( \text{PaO}_2 \) of
approximately 60 mm Hg.

**Respiration and arterial blood gases**—Individual
arterial oxygen tensions had large variations during
anesthesia but did not vary in a predictable manner with
time (Table 3). Two ponies had an intermittent breath-
ing pattern during the entire anesthetic period, with 3 to
4 deep breaths followed by a pause of 20 to 40 seconds.
A similar pattern of breathing was observed in 2 ponies
for the first 40 minutes of anesthesia and in 1 pony for
the first 60 minutes of anesthesia. Two ponies had vari-
able breathing patterns that changed with time. Only 3
ponies breathed regularly from induction onwards; however, there was no apparent connection with the respiratory rate or pattern in any individual pony and the occurrence of low PaO₂ or high PacO₂.

Base excess and bicarbonate concentrations increased significantly with time (Table 4). After 100 minutes of anesthesia, mean base excess was significantly higher than at the first recording at 10 minutes after induction and then continued to increase toward the end of the infusion. Bicarbonate concentrations were only significantly different from the 20-minute value at 180 minutes and continued to increase toward the end of the infusion.

**Blood propofol concentrations**—The largest variation between individuals occurred during the first 10

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**Table 1**—Cardiovascular values (mean ± SD range) in 10 ponies during 4 hours of total IV anesthesia with propofol and medetomidine

**Table 2**—Cardiovascular values (mean ± SD range) in arterial blood samples in 10 ponies during 4 hours of total IV anesthesia with propofol and medetomidine

**Table 3**—Respiratory physiologic values (mean ± SD range) in arterial blood samples in 10 ponies during 4 hours of total IV anesthesia with propofol and medetomidine

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PaO₂ had been then stood immediately. Two of the ponies in which stood after 15.3 and 15.5 minutes, respectively, fell treated group. Two ponies that received atipamezole pamezole-treated group, compared with the placebo-treated group, spent in sternal recumbency was longer in the atipamezole group. The time between the end of the infusion and the first time each pony lifted its head was significantly shorter in the atipamezole-treated group, compared with the placebo-treated group. Duration of time spent in sternal recumbency was longer in the atipamezole-treated group, compared with the placebo-treated group. Two ponies that received atipamezole stood after 15.3 and 15.5 minutes, respectively, fell down again after 5.8 and 1.2 minutes, respectively, but then stood immediately. Two of the ponies in which PaO₂ had been <60 mm Hg had signs of depression for 2 hours after standing. There was no significant difference in recovery score between groups.

Other effects—Blood temperature did not change significantly with time; maximal individual changes were ±0.3°C. All ponies urinated 1 to 2 times spontaneously during anesthesia.

Discussion

The propofol infusion rate used in this study was higher than the infusion rates reported previously; the increase was necessary, because 4 ponies had signs of lightening of the depth of anesthesia in the study reported here. The inability to maintain a steady-state of anesthesia may be attributable to time-dependent kinetics of propofol. Another explanation is that during determination of minimal infusion rate, the higher infusion rates used at the beginning of the study may have caused saturation of body tissues. In the study reported here, no pain stimuli were applied. However, on the basis of the previous study in which supramaximal stimuli were applied, it can be assumed that propofol infusion rates used in the study reported here would have provided a suitable depth of anesthesia for surgery. This assumption has been confirmed in subsequent clinical studies.

To assess all the effects of an anesthetic, it is ideal to compare standing resting cardiopulmonary data with the correlating data during general anesthesia. Nevertheless we did not determine cardiopulmonary data before administration of any drugs for several reasons. Many authors have measured cardiopulmonary function in standing horses, and mean resting reference range values are available. The cardiopulmonary data in our group of ponies was measured in a previous study in which supramaximal stimuli were used, it can be assumed that propofol infusion rates used in the study reported here would have provided a suitable depth of anesthesia for surgery. This assumption has been confirmed in subsequent clinical studies.

Table 4—Respiratory physiologic values (mean ± SD [range]) in venous blood samples in 10 ponies during 4 hours of total IV anesthesia with propofol and medetomidine

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Table 5—Elapsed time and other measurements of recovery (mean ± SD [range]) after cessation of administration of anesthetic after 4 hours of total IV anesthesia with propofol and medetomidine in 10 ponies that did (n = 5) or did not (5) receive atipamezole 10 minutes after anesthesia

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<th>Measurement</th>
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<th>No atipamezole</th>
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<tr>
<td>Into sternal recumbency (min)</td>
<td>19.7</td>
<td>20.2</td>
</tr>
<tr>
<td>Standing (min)</td>
<td>28.1</td>
<td>30.3</td>
</tr>
<tr>
<td>Attempts to stand (min)</td>
<td>26.3</td>
<td>27.5</td>
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<tr>
<td>No. of attempts to stand</td>
<td>2.8</td>
<td>3.5</td>
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<tr>
<td>Recovery score</td>
<td>5 (n = 1); 3 (n = 4)</td>
<td>5 (n = 3); 3 (n = 2)</td>
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*Significant (P < 0.05) difference between groups.
sedative action through the prevention of release of nor-
epinephrine and, therefore, are ineffective against the
adrenergic transmitter substances already released.\textsuperscript{36} Thus, in our study we did not want to excite the ponies
more than necessary before induction of anesthesia.

Maintenance of CO is an important feature of a
successful anesthetic protocol, to maintain muscular
blood flow and thus reduce the risk of postanesthetic myopathy.\textsuperscript{26} Cardiac indices in standing unsedated
horses and ponies range from 60 to 80 ml/kg per
minute.\textsuperscript{10,20,23} During anesthesia in our study, mean CI
ranged from 31.1 to 31.7 ml/kg per minute, representing
a reduction from typical values of about 30 to 50% and
with the lowest values occurring during the last
hour of anesthesia. These changes are comparable to\textsuperscript{8,10}
or slightly more profound than those reported during
shorter-duration TIVA involving ketamine combined with α2-agonists, benzodiazepines, or guaifenesin.\textsuperscript{7,9}

Because none of the authors that used ketamine com-
binations maintained anesthesia for a duration compa-
rable to that evaluated in our study, it is unknown
whether CI is maintained for as long as 3 hours by use
of ketamine-based TIVA protocols. The PaCO\textsubscript{2} values in
our study (7.5 to 15 mm Hg) were lower than during the
discussed TIVA regimes. This could explain the
differences in CI, because PaCO\textsubscript{2} in horses is posi-
tively related with CO and norepinephrine and epi-
nephrine concentrations.\textsuperscript{31} In a study\textsuperscript{41} that used
xylazine and propofol, profound hypercapnia (mean
PaCO\textsubscript{2} 103 mm Hg) at high propofol infusion rate (0.25 mg/kg per minute) was associated with higher CI
(62 ml/kg per minute), compared with the lower infu-
sion rate of 0.15 mg/kg per minute that was associated
with lower PaCO\textsubscript{2} (72 mm Hg) and CI (35 ml/kg per
minute). A further possible cause for reduced CI in our
study could be the action of the α\textsubscript{2}-agonist, which low-
ers concentrations of norepinephrine and epinephrine by
suppressing their release in the locus coeruleus.\textsuperscript{37}

After 150 minutes of anesthesia CI and HR peaked,
whereas MAP and SVRI were lowest at this point. After
this time the mean CI decreased, but this was influenced
in part by a substantial decrease in 2 ponies that were
markedly hypoxic. We assume that pharmacodynamic
rather than pharmacokinetic mechanisms induced
these cardiovascular alterations. Propofol reduces blood
pressure and CI by direct vasodilatation;\textsuperscript{42} however, these
changes are not correlated to changes in blood propofol
concentrations. Medetomidine, like other α\textsubscript{2}-agonists,
may induce peripheral vasoconstriction through activa-
tion of peripheral α\textsubscript{2}-adrenoceptors.\textsuperscript{38} By central inhibi-
tion of sympathetic outflow or increase in vagal tone,
they cause a decrease in HR and vasodilation.\textsuperscript{22} The
influence of propofol on medetomidine kinetics is
unknown. Nevertheless, according to published data,\textsuperscript{31,38}
it is unlikely that changes in medetomidine plasma con-
centrations induced these cardiovascular changes.
Lagerweij et al\textsuperscript{31} compared the cardiovascular effects of
propofol infusion in dogs with and without medetomi-
dine administration. The only significant difference
detected was in arterial blood pressures, which were
increased with medetomidine administration. In the
absence of other influences on the cardiovascular sys-
tem, the relationship between medetomidine concentra-
tion and propofol concentration probably determines
which cardiovascular action is dominant. The relative
balance between these effects could explain the cardio-
vascular changes, which occurred throughout the 4-
hour observation period.

In our study, PaCO\textsubscript{2} did not change significantly
during anesthesia, and high PaCO\textsubscript{2}, as reported by oth-
ers,\textsuperscript{14,15} did not develop. The PaCO\textsubscript{2} values measured in
our study were comparable to those typically measured
in spontaneously breathing halothane-anaesthetized
horses\textsuperscript{b} but were lower than those found under isoflu-
rane anesthesia.\textsuperscript{40}

Propofol is a potent respiratory depressant in
humans and dogs, and oxygen supplementation has
been recommended.\textsuperscript{20,41} During propofol infusions in
spontaneously breathing dogs, PaCO\textsubscript{2} values increased
during the period of anesthesia.\textsuperscript{20,41} This is of little con-
cern in human anesthesia, because artificial ventilation
is common practice, but the equipment required for
this in horses is not always available to equine practi-
tioners. Thus, it was considered appropriate to investi-
gate the present anesthetic regime without artificial
ventilation and only with oxygen supplementation.
However, in the 4 ponies in which PaO\textsubscript{2} decreased to <
60 mm Hg, arterial hemoglobin would not have been
fully saturated. Whether the administration of a higher
percentage of inspired oxygen, artificial ventilation, or
both would prevent the development of hypoxemia is
not known.

The cause of the variable breathing patterns was
unclear, but such patterns have been reported in ani-
mals of other species anesthetized with propofol and
medetomidine. After administration of medetomidine
alone in dogs, intermittent and irregular breathing pat-
terns have been described in dogs that were deeply
sedated.\textsuperscript{42,43} After the use of medetomidine in combina-
tion with propofol, Hall et al\textsuperscript{44} reported that some
dogs developed fast shallow breathing and others
developed slower and deeper breathing.

Individual ponies in our study had low PaO\textsubscript{2}
throughout the entire period of anesthesia. In these
ponies, these low values did not necessarily reflect
decreased CI, changes in pulmonary pressures,
diminished respiratory rate, or oxygen delivery.
Impaired gas exchange resulting in hypoxemia during anesthesia is
common in horses\textsuperscript{87,97} and dependent on many factors.
Other authors have also reported hypoxemia in propo-
fol-anaesthetized horses\textsuperscript{14,15} but did not report such
marked hypoxemia as found in the study reported here.
This can be explained, in part, by the fact that other
studies used inspired oxygen > 90%, and although
inspired oxygen was not measured in our study, it was
expected to be lower than this value. Medetomidine-
induced sedation in dogs enhances respiratory depres-
sion before induction with propofol.\textsuperscript{46} Other authors
reported that with propofol infusions in medetomidine-
sedated dogs, respiratory rate was reduced by 35.5%,
compared with unsedated dogs, but there were no sig-
nificant differences between groups for arterial blood gas
values.\textsuperscript{31} Sedation with medetomidine did not change
oxygen delivery to tissues, oxygen extraction ratio, or
venous admixture. The histopathologic changes seen in
the pulmonary parenchyma of ruminants after adminis-
tion of α₂-agonists\textsuperscript{19} have not been reported in horses but may represent another mechanism by which medetomidine affects pulmonary gas exchange.

Mean and minimal \(\text{PaO}_2\) values in our study were even lower than in the study that evaluated MIR of propofol in combination with medetomidine,\textsuperscript{24} although the ponies used and the anesthetic management were almost identical. In our study, propofol infusion rate at the beginning of anesthesia was lower than in the MIR study in all ponies; thus, it was surprising that individual ponies had lower \(\text{PaO}_2\) values from the beginning of anesthesia. Respiratory drive in horses in the previous propofol-medetomidine study\textsuperscript{24} may have been increased by the electrical stimuli applied regularly to determine depth of anesthesia. The lack of such stimulus in our study is the most likely explanation for the discrepancy in these results.

Arterial base excess and bicarbonate concentration increased significantly with time. This is of interest, because to our knowledge, this has not been reported in other species. In contrast, human children that were infused with propofol during a period of several days developed hyperlipidemia and metabolic acidosis.\textsuperscript{46}

Blood propofol concentrations were determined to ensure that a steady-state concentration was achieved. Samples were stored for no longer than 3 weeks prior to assay to maintain 98% of propofol concentration.\textsuperscript{27} Blood, rather than plasma, was used so that results could be compared with work by others.\textsuperscript{11,14,15,27} After induction of anesthesia with ketamine-medetomidine, propofol blood concentrations necessary to maintain anesthesia for 74 minutes in horses ranged from 3.27 to 9.44 µg/ml\textsuperscript{14} or from 3.5 to 9.1 µg/ml if additional acepromazine, butorphanol, and flunixin meglumine were administered.\textsuperscript{1} The propofol blood concentrations of these studies are within the same ranges as necessary to abolish any response to surgical stimulation in dogs.\textsuperscript{2,24} Mean propofol concentration in our study was 2.02, which was lower and had less individual variation than that of previous studies on propofol infusions in horses. Only 1 sample had a disproportionately low propofol concentration of 0.3 µg/ml. This was not associated with lightening of anesthesia and was considered to be attributable to sampling error. Lower mean concentrations of propofol necessary to maintain anesthesia in horses (1.9 to 2.7 µg/ml) have only been reported if propofol was combined with a constant infusion of ketamine.\textsuperscript{14} In dogs in which a 2-hour propofol infusion has been combined with medetomidine-induced sedation, propofol concentrations ranged from 3 to 6 mg/ml.\textsuperscript{2,11,23,24} In these studies, proper determination of the minimal dose necessary to allow surgery was not performed, and fixed constant infusion rates of propofol were chosen, leading to increased propofol blood concentrations with time that likely caused overdosage. Nolan and Reid\textsuperscript{22} infused dogs for 50 minutes with propofol at a constant rate. Because they measured increasing propofol blood concentrations, they stated that a zero-order infusion maintained for long periods could result in delayed recoveries from anesthesia because of accumulation of propofol in tissues.

In horses, prompt and controlled recovery from anesthesia is important to prevent muscle or nerve damage attributable to prolonged recovery\textsuperscript{29} and trauma attributable to poor-quality recoveries. During recovery, cardiopulmonary function cannot be monitored fully, and hypoxemia or hypotension are not recognized and treated immediately. After prolonged infusion of an injectable anesthetic agent, recovery is dependent on its context-sensitive half-life, which in the case of propofol is quite short.\textsuperscript{11} A previous study\textsuperscript{24} was not able to detect an influence of atipamezole on recovery from anesthesia with medetomidine and propofol in horses. Mean recovery times to standing in our study ranged from 28.1 minutes with atipamezole to 38.8 minutes without atipamezole. This is longer than reported elsewhere\textsuperscript{29} (20.2 and 20.9 minutes, respectively) but still represents a rapid recovery after a prolonged period of anesthesia. It is doubtful that differences in dose rates were responsible for these differences, but the use of electrical stimulation during the MIR study may have resulted in painful local inflammation, prompting a more rapid recovery. Recovery scores with and without atipamezole did not differ significantly; however, routine use of atipamezole is not recommended, because ponies that did not receive atipamezole seemed calmer during recovery, and 2 ponies fell down after recovery appeared complete after receiving atipamezole, presumably because of redistribution of propofol from body tissues. Administration of atipamezole after surgery would also antagonize medetomidine’s analgesic action. In horses that have delayed recoveries or severe cardiovascular problems (eg, life-threatening bradycardia), the use of atipamezole remains an alternative.

Our results suggest that medetomidine-propofol anesthesia in horses induces comparable or less severe changes in CI than other methods routinely used for prolonged anesthesia. The reduced cardiopulmonary effects may be explained in part by the action of medetomidine, which markedly reduces the minimal infusion rate of propofol, and by the opposing cardiovascular effects of the drugs, in that propofol may attenuate the vasoconstriction caused by medetomidine. If respiration is only supplemented with oxygen, hypocapnia may develop. Thus, endotracheal intubation with an inspired oxygen concentration > 90% is recommended. The protocol offers rapid and controlled recovery from anesthesia and may result in greater patient safety than for other anesthetic protocols.


\textsuperscript{3}Taylor PM, Fowden AL, Bloomfield MR. Propofol anesthesia for surgery in late gestation pony mares, in Proceedings. 6th Int Conf Vet Anaesth 1997;122.

\textsuperscript{4}Secalon, Ohmeda, Hatfield, UK.

\textsuperscript{5}SP5107H, Criticath, Ohmeda, Hatfield, UK.

\textsuperscript{6}Cook Veterinary Products, Queensland, Australia.

\textsuperscript{7}Insyte, Vialon, Becton-Dickinson UK, Oxford, UK.

\textsuperscript{8}Colormon, Kontron Instruments, Watford, UK.

\textsuperscript{9}T-130-AD, Viggo-Spectramed, Swindon, UK.

\textsuperscript{10}Domitor, Orion-Farmos, Turku, Finland; provided by ORION.

\textsuperscript{11}Rapinovet, Malinckrodt UK; provided by Malinckrodt.

\textsuperscript{12}4000, IVAC, Basingstoke, UK.
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