Effect of low inspired oxygen fraction on respiratory indices in mechanically ventilated horses anaesthetised with a constant rate infusion of isoflurane and medetomidine

A.H. Taylor *, C.J. Seymour

Department of Clinical Sciences and Services, Royal Veterinary College, Hawkshead Lane, North Mymms, Hatfield, Hertfordshire AL9 7TA, United Kingdom

* Corresponding author. Tel.: +852 3650 3000.
E-mail address: alantaylor1963@yahoo.com (A. H. Taylor).

Highlights

- Poor oxygenation can be a major problem in horses during anaesthesia.
- Low FiO_2 is used to minimise atelectasis to improve respiratory function and oxygenation.
- Determination of invasive respiratory indices are difficult clinically, so non-invasive respiratory indices were substituted.
- Use of low FiO_2 did not result in significant improvement in respiratory indices.
- The calculated F-shunt was not lower in the low FiO_2 group.

Abstract

Horses may become hypoxaemic during anaesthesia despite a high inspired oxygen fraction (FiO_2). A lower FiO_2 is used commonly in human beings to minimise atelectasis and to improve lung function, and previously has been shown to be of potential benefit in horses in experimental conditions. Other studies suggest no benefit to using a FiO_2 of 0.5 during clinically relevant conditions; however, low FiO_2 (0.65) is commonly used in practice and in a large number of studies. The present study was performed to compare the effect of a commonly used FiO_2 of 0.65 versus 0.90 on calculated respiratory indices in anaesthetised mechanically ventilated horses in a clinical setting. Eighteen healthy Thoroughbred horses anaesthetised for experimental laryngeal surgery were recruited into a prospective, non-blinded, randomised clinical study. Before anaesthesia, the horses were randomly allocated into either low (0.65) or high (0.90) FiO_2 groups and arterial blood gas (ABG) analysis was performed every 30 min during anaesthesia to allow for statistical analysis of respiratory indices. As expected, PaO_2 was significantly lower in horses anaesthetised with a low FiO_2, but was sufficient to fully saturate haemoglobin. There were no significant improvements in any of the other respiratory indices. There is no obvious benefit to be gained from the use of a FiO_2 of 0.65 compared to 0.90 for mechanically ventilated Thoroughbred horses anaesthetised in lateral recumbency with isoflurane and a medetomidine constant rate infusion.

Keywords: Equine; Anaesthesia; Atelectasis; FiO_2; PaO_2; Respiratory indices

Introduction

General anaesthesia in horses may lead to hypoxaemia, hypercapnia and a large alveolar (A) arterial (a) difference in the partial pressure of oxygen ($P(A\text{-}a)O_2$), even with maximal fractional inspired oxygen (FiO_2) (Hall et al., 1968). The main causes of hypoxaemia during anaesthesia, which can be difficult to treat, are intrapulmonary shunt and ventilation-perfusion (V_A:Q) mismatch (Rees et al., 2010). Other potential causes of hypoxaemia include (1) hypoventilation, which can be corrected by mechanical ventilation; and (2) diffusion limitation, which although unlikely to be encountered in healthy horses, occurs at high intensity exercise (Wagner et al., 1989).

Atelectasis is caused by compression of the thorax by the abdominal contents (Moens et al., 1995; Sorenson and Robinson, 1980), absorption of alveolar gas (Nyman and Hedenstierna, 1989; Rothen et al., 1995b, c;) and reduced surfactant function, as seen in human beings (Magnusson and Spahn, 2003). Atelectasis develops early in the anaesthetic period and gas exchange impairment is semi-quantitatively related to the area of atelectatic lung (Nyman et al., 1990).

During anaesthesia, functional residual capacity (FRC) is reduced (Sorenson and Robinson, 1980), potentially below closing capacity, leading to small airway closure (Hedenstierna and Edmark, 2010). Normal alveolar gas exchange results in oxygen absorption and CO_2 expulsion from the blood, with minimal nitrogen exchange; however, in trapped alveoli, there is no net inspired ventilation and so gas absorption occurs, leading to atelectasis (Briscoe et al., 1960; Dantzker et al., 1975; Joyce et al., 1993). The rate of collapse of a closed gas pocket or lung area is greater when it contains a high concentration of oxygen (Piiper et al., 1962; Joyce et al., 1993). This may be reduced using a low FiO_2; one study using helium and oxygen suggests that pulmonary gas exchange is better preserved with a low FiO_2 (Staffieri et al., 2009). Horses anaesthetised with isoflurane in low FiO_2 (0.6) had significantly lower PaO_2 and lower $P(A\text{-}a)O_2$, but similar PaO_2:FiO_2 ratios and similar numbers of hypoxaemic animals, when compared to horses

anaesthetised with isoflurane in a higher FiO_2 (0.78) (Schauvliege et al., 2015). In two additional studies using oxygen/air mixtures, there was no benefit in using a FiO_2 of 0.5, with no improvement in oxygen delivery and significant hypoxaemia (Hubbell et al., 2011; Crumley et al., 2013).

Medetomidine is a selective and potent α_2 adrenoceptor agonist used for sedation and analgesia in veterinary anaesthesia (Virtanen et al., 1988; Pertovaara, 1993). When administered as a constant rate intravenous infusion (CRI) as a component of partial intravenous anaesthesia (PIVA), it reduces the minimum alveolar concentration (MAC) of isoflurane in horses (Neges et al., 2003) and improves the quality of recovery (Ringer et al., 2007). Medetomidine, like other α_2 agonists, causes cardiopulmonary effects, including reduction in cardiac output (*Qt*), biphasic changes in arterial blood pressure (ABP), bradycardia and arrhythmias (England and Clarke, 1996). With the exception of changes in ABP, these effects of bolus administration are not substantially different from pre-sedation values when steady state CRI values are reached (Bettschart-Wolfensberger et al., 1999). Other effects of medetomidine include a decrease in respiratory rate (f_R) and changes in $PaCO_2$ and PaO_2, although these are not always statistically or clinically significant (Wagner et al., 1991; Bettschart-Wolfensberger et al., 1999).

In view of the continued clinical use of low FiO_2 in practice and other clinical studies, the aim of this study was to compare calculated non-invasive respiratory indices in mechanically ventilated horses anaesthetised with isoflurane and a medetomidine CRI, using a FiO_2 of either 0.65 or 0.90. It was hypothesised that a low FiO_2 would improve calculated respiratory indices compared to a high FiO_2 but lower overall PaO_2.

Materials and methods

Animals

Eighteen Thoroughbred racehorses, retired due to laryngeal problems but otherwise healthy, were randomly assigned to receive either a low (0.65; ML) or a high (0.90; MH) FiO_2 during an experimental surgical procedure. All horses were included in the final results and all horses recovered uneventfully from anaesthesia. This prospective, randomised clinical study was approved by the Ethics and Welfare committee of the Royal Veterinary College (approval number RVC PURN: 2012 1179; date of approval 18 October 2012). The research horses were recruited from another study being performed under Home Office Licence regulations.

Anaesthesia

Horses were fasted for 10-12 h before anaesthesia for elective laryngeal surgery; access to water was not restricted. Flunixin meglumine (1.1 mg/kg IV; Flunixin Injection, Norbrook Laboratories) was infused through a 14 G x 13 cm jugular catheter (Milacath Extended Use, Mila). Gentamicin (6.6 mg/kg IV; Genta-kel, Kela; or GentaEquine, Dechra) was administered 30 min before anaesthesia. Procaine penicillin (20000 IU/kg IM; Norocillin, Norbrook Laboratories) was administered 60-90 min prior to anaesthesia. Acepromazine (0.04 mg/kg IM; Calmivet, Vetoquinol) was administered 60 min before anaesthesia.

Medetomidine (0.007 mg/kg IV; Sedastart, Animalcare) and morphine (0.2 mg/kg IV; Morphine Sulphate, Martindale Pharmaceuticals) were administered for sedation and analgesia. Anaesthesia was induced with ketamine (2.2 mg/kg; Ketaset, Zoetis) and midazolam (0.04 mg/kg; Hypnovel, Roche Products) given simultaneously IV. After induction of anaesthesia and endotracheal (ET) intubation, each horse was positioned in right lateral recumbency on the operating table and the ET tube connected to a large animal anaesthetic machine (Mallard Medical 2800C, AB Medical Technologies). Isoflurane (Isoflo, Abbott Laboratories) was delivered at an initial concentration of 3% V/V in a fresh gas flow of 5 L/min, with either 3.5 L/min oxygen plus 1.5 L/min medical air (ML) to provide a FiO_2 of 0.65, as commonly used in practice, or 100%

oxygen (MH). All horses were mechanically ventilated with a tidal volume (V_T) of 12 mL/kg and at an f_R to maintain an end-tidal CO_2 tension ($P_{ET}CO_2$) between 35 and 55 mmHg. All horses received compound sodium lactate (CSL) solution (Vetivex 11, Dechra Veterinary Products) at a rate of approximately 7 mL/kg/h during anaesthesia. A surgical plane of anaesthesia was maintained using isoflurane and a CRI of medetomidine at a dose of 3.5 μg/kg/h. Ketamine boluses (0.1-0.2 mg/kg IV) were used if the horse was deemed to be lightly anaesthetised. Dobutamine (Dobutamine, Hameln Pharmaceuticals) was infused at a dose of up to 5 μg/kg/min, if required, to maintain mean arterial blood pressure (MAP) > 70 mmHg.

Monitoring and data collection

ABP was measured using a multiparameter monitor (Datex-Ohmeda S/5, GE Healthcare) using a catheter placed in the left dorsal metatarsal artery. This catheter was also used to collect samples for arterial blood gas analysis (ABG), which was started as soon as practicable after induction of anaesthesia and thereafter at 30 min intervals. Each sample was analysed immediately using an IRMA TruPoint (QCR) blood gas analyser. Parameters recorded were isoflurane vaporiser setting (%), inspired (FiIso) and end-tidal (F_{ET}Iso) isoflurane concentrations, heart rate (HR), f_R, FiO_2, expired percentage of oxygen ($F_{ET}O_2$), saturation of haemoglobin with oxygen (SpO_2), $P_{ET}CO_2$, V_T, peak inspiratory pressure (PIP) and positive end-expiratory pressure (PEEP). A rescue protocol for PaO_2 < 80 mmHg, an accepted level for hypoxaemia in equines (Haskins, 2007), was prepared but not used. All data were recorded manually every 5 min and study parameters collated between first and last ABG, so that the mean ± standard deviation for each parameter measured was within ABG measurements.

Data collation and analysis

Data were entered into a spreadsheet (Excel 2011 for Mac, Microsoft) before importation into a statistical programme (SPSS Statistics 21 for Mac, IBM) for analysis. After testing each sub-

group for normality (Kolmogorov-Smirnov test), independent sample *t* tests were used to compare means of continuous data between low and high FiO_2 sub-groups. The means tested were age, weight, duration of procedure, average dobutamine infusion rate, HR, V_T, V_T/weight, f_R, V_M, PIP, PEEP, SpO_2, MAP, $F_{ET}Iso$, FiO_2, PaO_2, barometric pressure (PB), PAO_2, oxygen partial pressure ($P(A\text{-}a)O_2$), arterial oxygen pressure ratio (PaO_2:FiO_2), respiratory index ($P(A\text{-}a)O_2/PaO_2$), ratio of dead space to V_T (V_D:V_T) and the calculated ratio of the oxygen partial pressure differences between alveolar-arterial and arterio-venous values (F-shunt) (Table 1).

Independent samples Mann-Whitney *U* tests were used for analysis of American Society of Anesthesiologists (ASA) health status[1], body condition score (BCS) and quality of recovery; the χ^2 test was used for analysis of sex. Statistically significant results ($P < 0.05$) were taken forward into multivariate analysis, using a general linear model (GLM), along with risk factors from any test in which $P \leq 0.1$, or which had been shown previously to affect PaO_2 in other studies, including age, BCS and weight, and refined until only independent predictors with a $P < 0.05$ remained in the final model. A linear mixed effects (LME) model was then performed on the data to examine the effect of group and time on PaO_2.

Results

Demographic and clinical data are shown in Table 2. Cardiorespiratory data are shown in Table 3. There were no significant differences in age, weight, BCS or ASA category between the eight males and one female in the ML group, or the seven males and two females in the MH group. Duration of anaesthesia, haemoglobin concentration, additional analgesic drug usage, dobutamine usage, duration of anaesthesia, and length and quality of recovery were not significantly different between groups (Table 3).

[1] See: http://www.asahq.org/For-Members/Clinical-Iformation/ASA-Physical-Classification-System.aspx.

There were no significant differences in SpO_2, Pa, F_{ET}, P(A-a), HR, f_R, V_T, V_M, MAP, PIP, PEEP, V_D:V_T, CaO_2 or CcO_2 during anaesthesia. There were no significant differences in P(A-a)O_2 (P = 0.106), PaO_2:FiO_2 (P = 0.112) or F-shunt (P = 0.396) between the ML group and the MH group. Horses in the ML group had significantly lower PaO_2 (337.7 ± 56.4 mmHg) and PAO_2 (396.1 ± 19.1 mmHg) than those in the MH group (496.8 ± 52.5 and 581.9 ± 21.3) (P < 0.001 for both parameters). When taken into the GLM, only the FiO_2 sub-group was a significant independent predictor of PaO_2 (P < 0.001). In the LME model, time was not a significant factor (P = 0.285), while group (ML versus MH) again was significant for PaO_2 and PAO_2 (P < 0.001).

Discussion

The main finding of this study is that reducing FiO_2 to 0.65 in isoflurane and medetomidine anaesthetised horses does not result in a statistically significant improvement in pulmonary indices, compared to a FiO2 of 0.90. Therefore, the hypothesis that pulmonary function, as measured by pulmonary indices, would be improved by the use of a low FiO_2 of 0.65 is not supported.

Using low FiO_2 in an attempt to improve pulmonary function in horses is related to attempts to improve overall anaesthetic risk in this species. Significant proportions of peri-anaesthetic deaths in horses are caused by cardiac arrest or cardiovascular collapse (33%), myopathy (7%) and limb fractures (25%) (Johnston et al., 2002). Hypoxaemia may play a part in some or all of these deaths by contributing to inadequate myocardial oxygenation or poor peripheral oxygen delivery (Schatzmann, 1995).

High FiO_2 administered to human beings in the peri-anaesthetic period has detrimental effects, such as atelectasis and reformation after alveolar recruitment manoeuvres (Hedenstierna, 1990; Rothen et al., 1995a, b; Akca et al., 1999; Benoit et al., 2002; Hedenstierna and Edmark, 2010), increased intrapulmonary shunts in horses (Steffey et al., 1987; Marntell et al., 2005) and

increased systemic vascular resistance and reductions in cardiac index and heart rate in human beings (Anderson et al., 2005). In addition, hyperoxia may lead to tissue damage through oxygen toxicity in many species (Davis et al., 1983; Clutton et al., 2011). However, high FiO_2 ensures a higher PaO_2 during anaesthesia, which may be beneficial for wound healing (Greif et al., 2000). Oxygenation in the recovery period also improves the PaO_2 in horses (De Moor et al., 1974).

Use of a lower FiO_2 improves lung aeration and lowers atelectasis formation in dogs, cats and human beings, as well as decreasing pulmonary shunting and improving gas exchange (Hedenstierna, 1990; Rothen et al., 1995b; Staffieri et al., 2007, 2010). Improved $P(A\text{-}a)O_2$ in horses was demonstrated using a FiO_2 of 0.3 compared to 0.8 (Cuvelliez et al., 1990) and decreased pulmonary shunting observed with FiO_2 of 0.21 versus > 0.8 (Marntell et al., 2005). Use of a helium-oxygen (Heliox) mixture allowed adequate oxygenation in horses with an FiO_2 of 0.4 (Driessen et al., 2003), whilst a low FiO_2 of 0.25 and then stepwise increases in FiO_2 to > 0.9, again using Heliox, better preserved pulmonary gas exchange than in horses breathing FiO_2 > 0.9 (Staffieri et al., 2009). In the current study, there were no significant improvements noted for any of the respiratory indices and, whilst no pulmonary index improved with low FiO_2, the horses in both groups had more than adequate SpO_2 and PaO_2 throughout, with no horse becoming hypoxaemic.

Hubbell et al. (2011) and Crumley et al. (2013) demonstrated an improved $P(A\text{-}a)O_2$ with a FiO_2 of 0.5; furthermore, Staffieri et al. (2009) showed that a step-wise increase in FiO_2 >0.5 significantly worsened $P(A\text{-}a)O_2$, indicating oxygen absorption in areas of low V_A:Q, without replenishment, and a progressive collapse of alveoli. The critical inspired ventilation:perfusion ratio (V_{AI}:Q) describes lung areas where V_A:Q is so low that net absorption of alveolar gas occurs, despite airways remaining open, leading to significant alveolar collapse (Dantzker et al., 1975) and increased shunt formation.

In the present study, there were no significant differences in F-shunt values between the ML and MH groups, similar to the findings of Hubbell et al. (2011). In contrast, Marntell et al. (2005) found that a FiO_2 of 0.21 significantly reduced F-shunt values. These results suggest that a FiO_2 of 0.90 does not lead to greater shunt formation than a FiO_2 of 0.65 or 0.5. The lack of a reduction in shunt formation with a lower FiO_2, in comparison with maximal, also suggests that absorption atelectasis as described is minimal and unlikely to be a major component of the relatively poorer PaO_2 in the ML group (Nyman and Hedenstierna, 1989; Hubbell et al., 2011).

No horses in this study or the Heliox studies, all of which were positioned in lateral recumbency, were hypoxaemic (PaO_2 < 60 mmHg). However, hypoxaemia has been observed in some horses in other studies using air or an oxygen-air mixture; in the studies performed by Hubbell et al. (2011) and Crumley et al. (2013), horses were positioned in dorsal recumbency, whilst in the study by Marntell et al. (2005), horses were positioned in lateral recumbency. Horses in dorsal recumbency and spontaneously breathing horses in lateral recumbency breathing a FiO_2 of 0.21 were at risk of hypoxaemia. Posture, especially dorsal recumbency, affects pulmonary function by reducing effective lung area and FRC (Sorenson and Robinson, 1980; Day et al., 1995; Whitehair and Willits, 1999), leading to PaO_2 values significantly below those in standing, sternal or laterally recumbent horses, and contributing to large $P(A\text{-}a)O_2$ differences (Nyman and Hedenstierna, 1989; Day et al., 1995). Mechanical ventilation instituted immediately after induction of anaesthesia results in higher PaO_2 than when mechanical ventilation is delayed (Day et al., 1995; Wolff and Moens, 2010). In the present study, mechanical ventilation was instituted immediately in all horses to achieve similar values for $P_{ET}CO_2$.

Medetomidine CRI was used in this study in addition to morphine for analgesia, since the analgesia provided by other protocols (PIVA with romifidine CRI or ketamine CRI plus morphine) was inadequate to prevent movement in other research horses undergoing the same procedure,

253 despite liberal use of ketamine and morphine boluses. In this study, only two horses per group
254 required additional ketamine doses, and none of the horses moved, indicating that the PIVA
255 combination of isoflurane and medetomidine, with morphine, was sufficient to provide adequate
256 anaesthesia with F_{ET}Iso of 1.1-1.2%.
257
258 Morphine and medetomidine have cardiopulmonary effects, but these are likely to be similar
259 in both groups and thus would not be expected to alter the results overall. Morphine has different
260 reported effects on the cardiopulmonary system of horses anaesthetised with isoflurane, including
261 none (Nolan et al., 1991), reduced PaO_2 (Love et al., 2006) and increased $PaCO_2$ with serious
262 respiratory depression (Steffey et al., 2003), depending on dose of morphine given. Medetomidine
263 CRI reduces the MAC of isoflurane (Bettschart-Wolfensberger et al., 2001; Neges et al., 2003) and
264 is a potent analgesic. In addition to cardiovascular effects, α_2 adrenergic agonists cause respiratory
265 depression, leading to lower f_R, reduced or minimally changed PaO_2 (Wagner et al., 1991;
266 Bettschart-Wolfensberger et al., 1999; Neges et al., 2003) and increased $PaCO_2$ (Bryant et al.,
267 1996).
268
269 There were no statistically significant differences between ML and MH groups in time to
270 recover to standing or in unassisted recovery quality. Although there were significant differences in
271 PaO_2, this did not significantly influence the recovery to standing of horses in our study. In previous
272 studies, oxygen delivery (DO_2) was either not significantly different between groups (Hubbell et al.,
273 2011) or was significantly lower at one time point in the FiO_2 0.21 group (Marntell et al., 2005).
274
275 The IRMA TruPoint ABG analyser has not been validated for measuring equine
276 haemoglobin (Hb) concentrations, so this may have introduced some errors into our F-shunt
277 calculations, but these errors would occur in both ML and MH groups and thus would have minimal
278 effects on results. A further limitation of this study is that we used the human value of 3.5 mL/dL

for the arterial-mixed venous oxygen content difference ($C(a\text{-}\bar{v})O_2$). In contrast, values of 4-7 mL/dL have been measured by Marntell et al. (2005), who reported mean shunt values of 5-13 ± 5% in spontaneously breathing anaesthetised horses in left lateral recumbency. The F-shunt values of 16-18 ± 7% calculated in the present study are broadly equivalent, given that they are likely to have been overestimated.

An additional and important limitation of this study is that the combination of immediate mechanical ventilation and lateral recumbency in lean ('flat-bellied') horses is likely to have reduced the risk of small airway closure and significant absorption atelectasis. Dorsal recumbency induces the greatest impairment to ventilation in the horse (McDonell and Hall, 1974; Sorensen and Robinson, 1980); furthermore, in all positions, anaesthetised 'round-bellied' horses also had a lower PaO_2 and larger $P(A\text{-}a)O_2$ than anaesthetised 'flat-bellied' horses (Moens et al., 1995). In dorsal recumbency, 'round' and 'flat-bellied' horses have similar distribution of air flow to each lung. In lateral recumbency, 'round-bellied' horses develop an uneven distribution of air flow, whilst 'flat-bellied' horses retain equal airflow distribution (Moens et al., 1995). Moreover, tall, lightweight, lean horses with a large thoracic circumference have a better PaO_2 when anaesthetised compared to 'round-bellied' horses (Mansel and Clutton, 2008). These studies support the general hypothesis that body shape and the pressure exerted by abdominal contents is a major contributor to poor respiratory function in horses during anaesthesia. The results of this study, in lean flat-bellied Thoroughbred horses, therefore cannot be related to all horses in all recumbencies or indeed those horses spontaneously ventilating.

Detrimental changes in the respiratory system in horses during anaesthesia usually occur early in the anaesthetic process and worsen with time (Nyman et al., 1988). This was not seen in this study in respect of PaO_2, which remained relatively high in both groups, with little upward or downward variation over the duration of each anaesthetic procedure. It may be that the combination

of anaesthetic protocol, young healthy Thoroughbred horses, immediate mechanical ventilation and positioning in lateral recumbency prevented any time effect from becoming evident. Furthermore, the low number of horses in the study may have reduced the power of the study.

Conclusions

Horses anaesthetised with a FiO_2 of 0.65 had a lower arterial oxygenation, but no significant improvement in pulmonary indices, compared to horses in which a higher FiO_2 was used. Hypoxaemia did not occur and low FiO_2 did not affect recovery quality and time to recovery; therefore, this combination may be acceptable for mechanically ventilated horses, anaesthetised with isoflurane and medetomidine CRI, positioned in lateral recumbency. The optimum overall anaesthetic strategy to maintain high PaO_2 and excellent pulmonary function in horses is still to be elucidated.

Conflict of interest statement

Neither of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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Table 1

Respiratory calculations.

Unit or index calculated	Calculation
Alveolar partial pressure of oxygen: PAO_2 (mmHg)	$PAO_2 = ([PB^a - PH_2O^b] \times FiO_2) - (PaCO_2/0.8)$
Pulmonary end-capillary oxygen content: $Cc'O_2$ (mL/dL)	$Cc'O_2 = ([Hb]^c \times \text{Hüfner's Constant}^d \times Sc'O_2^e) + (0.0031 \times Pc'O_2^f)$
Arterial oxygen content: CaO_2 (mL/dL)	$CaO_2 = ([Hb] \times \text{Hüfner's Constant} \times SaO_2^g) + (0.0031 \times PaO_2)$
Alveolar-to-arterial oxygen difference: $P(A\text{-}a)O_2$ (mmHg)	$P(A\text{-}a)O_2 = PAO_2 - PaO_2$
Arterial-to-inspired oxygen ratio (mmHg)	$PaO_2:FiO_2$
F-shunt (%)	$([Cc'O_2\text{-}CaO_2]/[Cc'O_2\text{-}CaO_2] + 3.5^h \text{ mL/dL}) \times 100$

[a] Barometric pressure (mmHg).

[b] Vapour pressure of water = 47 mmHg.

[c] Haemoglobin concentration.

[d] Oxygen carrying capacity of haemoglobin (1.36 mL/g).

[e] Pulmonary end capillary oxygen saturation (for $PAO_2 > 100$ mm Hg assumed = 1).

[f] Pulmonary end-capillary partial pressure of oxygen (mmHg), assumed to be PAO_2.

[g] Arterial haemoglobin oxygen saturation (%).

[h] Arterial-venous oxygen content difference $[C(a\text{-}\bar{v})O_2]$ in mechanically ventilated humans.

549 **Table 2**

550 Demographic and other data of 18 horses anaesthetised with isoflurane and medetomidine and mechanically ventilated
551 using either a low (0.65) or high (0.90) FiO_2.

552

	Low FiO_2 (n = 9)	High FiO_2 (n = 9)
Age (years) [a]	6.1 ± 1.2	5.8 ± 1.6
Sex (number of males:number of females)	8:1	7:2
Weight (kg) [a]	558.8 ± 34.5	550.4 ± 58.2
Body condition score (0-9)	4	3.9 (range 3-4)
ASA [b] category	1 (range 1-2)	1
Haemoglobin (g/dL) [a]	11.4 ± 1.24	10.9 ± 1.1
Duration of anaesthesia (min) [a]	200 ± 36.1	178.9 ± 30.4
Number of horses receiving additional ketamine (dose range in mg)	2 (200-400)	2 (200-600)
Number of horses receiving additional morphine (dose range in mg)	7 (60-90)	6 (60-90)
Number of horses receiving dobutamine	9	9
Dose of dobutamine (µg/kg/min) [a]	0.61 ± 0.4	0.54 ± 0.3
Time to recovery (min) [a]	50.1 ± 22.7	45.1± 12.5
Recovery quality (median)	2 (range 1-3)	2 (range 1-3)

553
554 [a] Mean ± standard deviation.
555 [b] American Society of Anesthesiologists health status.

Table 3

Measured and calculated cardiovascular and respiratory variables (mean ± standard deviation) of 18 horses anaesthetised with isoflurane and medetomidine CRI and mechanically ventilated using either a low (0.65) or high (0.90) FiO_2.

	Low FiO_2	High FiO_2
FiO_2 [a, b]	66.5 ± 2.9	92.4 ± 2.2
PaO_2 (mmHg) [a]	337.7 ± 56.4	496.8 ± 52.5
PAO_2 (mmHg) [a]	396.1 ± 19.1	581.9 ± 21.3
$P(A\text{-}a)O_2$ (mmHg)	58.42 ± 41.7	85.07 ± 49.6
PaO_2:FiO_2	505.6 ± 66.3	537.6 ± 53.2
F-shunt (%)	18.2 ± 7.2	16.5 ± 5.8
CaO_2 (mL O_2/dL)	15.3 ± 1.5	15.4 ± 1.4
CcO_2 (mL O_2/dL)	16.1 ± 1.6	16.1 ± 1.5
SpO_2 (%)	95.8 ± 1.9	96.9 ± 1.6
$PaCO_2$ (mmHg)	57.0 ± 5.6	57.7 ± 6.3
$F_{ET}CO_2$ (mmHg)	44.5 ± 3.6	45.2 ± 3.7
$P(A\text{-}a)CO_2$ (mmHg)	12.5 ± 3.6	12.5 ± 5.0
HR (beats/min)	30.0 ± 3.3	27.6 ± 2.9
fR (breaths/min)	7.8 ± 0.9	7.1 ± 0.6
V_T (L/breath)	6.9 ± 1.0	6.4 ± 0.8
V_T/weight (mL/kg)	12.3 ± 1.2	11.6 ± 1.4
V_M (L/min)	53.5 ± 7.9	45.5 ± 7.8
MAP (mmHg)	75.0 ± 8.9	75.7 ± 9.6
PIP (cmH_2O)	21.5 ± 2.3	20.6 ± 3.3
PEEP (cmH_2O)	3.7 ± 0.8	3.6 ± 0.6

[a] Significantly different between ML and MH groups ($P < 0.05$)

[b] Independent predictor of PaO2 from general linear model ($P < 0.05$).