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Influence of recumbency on the pulmonary shunt in sevoflurane-anaesthetised sheep

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ABSTRACT: *This study assessed the impact of different recumbency on sevoflurane-anaesthetised sheep. Seven female sheep were premedicated with 0.1 mg.kg^{-1} butorfanol and subsequently administered a combination of 3 mg.kg^{-1} ketamine and 0.5 mg.kg^{-1} midazolam. Animals were maintained on sevoflurane anaesthesia with pressure-controlled ventilation (12 cm H_2O peak inspiratory pressure) and f of 10 mpm. During the anaesthetic procedure, animals underwent one out of three different recumbency: dorsal, left lateral, or right lateral positions. Treatments lasted 120 min with a 48-h washout period in between the treatments. Arterial and central venous blood samples were withdrawn for blood gas and electrolytes analysis and pulmonary shunt fraction (Qs/Qt) CaO_2, $CcvO_2$, and CcO_2 were calculated accordingly. Results showed that Qs/Qt greatly decreased from 0 to 120 min in all the groups (dorsal: 69.3% to 27.3%; left lateral: 59.1% to 25.0%; right lateral: 67.2% to 32.4%). CaO_2, $CcvO_2$ and CcO_2 improved over time points, with no difference among treatments. PaO_2 and PAO_2 showed higher values for 60 and 120 min compared to the 0 min value in all groups, with no differences among treatments as well. $PaCO_2$ and $ETCO_2$ in the lateral groups were higher than those in the dorsal group at 120 min. Pressure-controlled ventilation improved gas exchanges in sheep, thereby reducing pulmonary shunt. Recumbency did not interfere with pulmonary shunt, nevertheless, special attention must be paid to lateral recumbency.*
Key words: *inhalation anesthesia, mechanical ventilation, pulmonary shunt, ruminant anesthesia, sevoflurane.*

Influência do decúbito na ocorrência de shunt pulmonar em ovinos anestesiados com sevoflurano

RESUMO: *O estudo avaliou o impacto de diferentes decúbitos em ovelhas anestesiadas com sevoflurano. Sete ovelhas foram pré-medicadas com 0,1 mg.kg^{-1} de butorfanol e induzidas à anestesia com 3 mg.kg^{-1} de cetamina e 0,5 mg.kg^{-1} de midazolam. Os animais foram mantidos em anestesia por sevofluorano, em ventilação mecânica controlada por pressão, com pico inspiratório em 12 cm H_2O e f de 10 mpm, sendo mantidos por 120 minutos. Durante esse período os animais foram submetidos a um dos três tratamentos: decúbito dorsal, lateral esquerdo ou lateral direito, com intervalo de no mínimo 48 horas entre eles. Amostras de sangue arterial e venoso central foram colhidas para análise de gases sanguíneos e eletrólitos, bem como para cálculo da fração de shunt pulmonar (Qs/Qt), CaO_2, $CcvO_2$ e CcO_2. Os resultados mostraram que Qs/Qt diminuiu expressivamente de 0 a 120 minutos em todos os grupos (dorsal: 69,3% para 27,3%; lateral esquerdo: 59,1% para 25,0%; lateral direito: 67,2% para 32,4%). Os índices de CaO_2, $CcvO_2$ e CcO_2 melhoraram ao longo do tempo, sem diferença entre tratamentos. PaO_2 e PAO_2 apresentaram valores maiores, em todos os grupos, nos minutos 60 e 120 em comparação ao momento 0, não havendo diferenças entre tratamentos. $PaCO_2$ e $ETCO_2$ apresentaram maiores valores nos grupos laterais em comparação ao grupo dorsal ao final do procedimento. Conclui-se que a ventilação controlada por pressão melhorou as trocas gasosas em ovelhas anestesiadas com sevoflurano, reduzindo o shunt pulmonar. O decúbito não interferiu na formação de shunt pulmonar, porém, deve ser dada atenção especial aos decúbitos laterais.*
Palavras-chave: *anestesia de ruminantes, anestesia inalatória, sevoflurano, shunt pulmonar, ventilação mecânica.*

INTRODUCTION

Sheep has been one of the most used experimental models in biomedical research, since it seems to mimic human clinical conditions. Some characteristics make this species scientifically acceptable, such as easy handling, bone composition, and remodelling like in humans (EGERMANN et al., 2005). It is also suitable for studying the main physiological systems such as cardiovascular, endocrine, respiratory, renal, and reproductive systems (MCMILLEN, 2001).

In large surgeries, inhalation anaesthesia is recommended; however, some issues in sheep inhalation anaesthesia must be considered. The rumen occupies about three quarters of the abdominal cavity in sheep and its proximity to diaphragm can interfere with ventilation during the procedure (EWING,

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1990) resulting in hypoxaemia and hypercapnia when they are positioned in lateral or dorsal recumbency (BLAZE et al., 1988). Furthermore, those animals produce a large amount of saliva, and inadequate fasting can lead to regurgitation, obstruction, aspiration, asphyxia and pneumonia in the postoperative period (TRANQUILLI, 1986).

Ventilation impairment during inhalation anaesthesia can lead to pulmonary ventilation-perfusion mismatch (PETERSSON & GLENNY, 2014). Impaired gas exchanges during inhalation anaesthesia have been related to inspired gases ventilation mismatch, reduced lung volume, airway obstruction, and pulmonary hypoxia (GALATOS, 2011). Pulmonary shunt is defined as the pathological condition in which the pulmonary alveoli are normally perfused, but ventilation fails to supply the perfused region (LOVERING et al., 2015).

Reduced lung volume is the main cause of shunt in sheep undergoing inhalation anaesthesia (DUECK et al., 1984), and it can be worse, depending on the recumbency (GALATOS, 2011). Diaphragmatic compression that occurs due to rumen distension, by reduced organ activity or atony, substantially reduces lung compliance, especially when animals are placed in lateral or dorsal recumbency (MEYER et al., 2010). Lateral recumbency is associated with potentiation of diaphragmatic compression's deleterious effects on pulmonary ventilation (FUJIMOTO & LENEHAN, 1985). In dorsal recumbency with reverse *Trendelenburg* position, there is no improvement in respiratory function or worsening in cardiovascular function (ARAÚJO et al., 2017). Conversely, better ventilatory stability and tissue oxygenation in mechanically-ventilated sheep has been proposed (FUJINO et al., 2001).

The importance of studying different recumbency lies in different possible impacts on sheep anaesthesia, potentiating ventilation-perfusion mismatches. Thus, this study verified the impact of three different recumbency positions in sheep under inhalation anaesthesia. We hypothesized that the recumbency position determines the pulmonary shunt magnitude, and the left lateral recumbency is related to increased pulmonary shunt.

MATERIALS AND METHODS

Seven female adult half-blooded Dorper sheep (body weight range 40 to 60 kg) were used in this study. Health status was checked by clinical assessment and laboratory tests (complete blood cell count, gama-glutamyltransferase, aspartate-aminotransferase, urea, and creatinine). The animals were subjected to one of three different treatments, namely: dorsal, right lateral, and left lateral recumbency, each one corresponding to an experimental group. The treatments lasted 120 min and recumbency selection order was defined by a block randomisation design, avoiding treatment sequence repetition. Washout period was at least 48 h.

Food was withheld 12 h preceding the experimental days, without water restriction. A central venous catheter was introduced and fixed into the animals 24 h before the first assessment day, through the left jugular vein until it reached the right atrium. For the procedure, animals were given a premedication with 0.1 $mg.kg^{-1}$ butorfanol IM. After a 10-minute period, sheep were administered a combination of 3 $mg.kg^{-1}$ ketamine and 0.5 $mg.kg^{-1}$ midazolam IV.

On experimental days, sheep were given the same anaesthetic protocol as mentioned before. Immediately after induction, arterial and central venous blood samples were collected (1 mL each) from the auricular artery and the jugular vein, for blood gas analysis. Thereon, animals were orally intubated with an appropriate cuffed tracheal tube, placed on the drawn recumbency (dorsal, right lateral or left lateral), and connected to a circle circuit system. Anaesthesia maintenance was performed with sevoflurane in 95 ± 2% O_2, at a flow rate of 1.5 $L.min^{-1}$.

Muscle blockade was done by 0.12 $mg.kg^{-1}$ rocuronium, IV, and all sheep were mechanically ventilated in pressure-controlled ventilation (PCV) mode with a 12 cm H_2O peak inspiratory pressure in a zero end-expiratory pressure, *f* adjusted to 10 mpm and inspiratory-to-expiratory ratio 1:2 (WATO EX-20, Shenzhen Mindray Bio-Medical Electronics Co., Ltd.). When necessary, animals were administered a quarter of the rocuronium loading dose. End-tidal sevoflurane concentration (FE'Sevo) was maintained at a level of 2.03 ± 0.11% during the entire procedure. Heart rate (HR), hemoglobin oxygen saturation (SpO_2), arterial blood pressures, body temperature, end-tidal carbon dioxide concentration ($ETCO_2$) and FE'Sevo, were assessed by a multiparameter monitor (Digicare® LifeWindow™ Lite, Digicare Biomedical Technology, Boynton Beach, Florida, USA). Body temperature was measured by an oesophageal thermometer and obtained in Celsius. Ringer's lactate solution was infused intravenously to all sheep at a rate of 3 $mL.kg^{-1}.h^{-1}$.

Arterial and venous blood gas analysis were performed immediately after induction (0

min), maintaining the animal in ventral recumbency, and at 60 min and 120 min after induction, from the auricular artery and central venous catheter for immediate analysis (CG8+, Abbott®, São Paulo, Brazil). Potential of hydrogen (pH), carbon dioxide partial pressures (PCO_2), oxygen partial pressures (PO_2), and oxygen saturations (SO_2) were assessed by a portable blood gas analyser (i-STAT, Abbott®, São Paulo, Brazil). Fraction of inspired oxygen (FiO_2) was obtained directly by the anaesthetic machine (WATO EX-20, Shenzhen Mindray Bio-Medical Electronics Co., Ltd.).

A mathematical approach was done to determine the arterial oxygen content (CaO_2), central venous oxygen content ($CcvO_2$), capillary oxygen content (CcO_2) and pulmonary shunt fraction (Qs/Qt), according to LUMB (2000) and STAUB (1963). These parameters were calculated as follows:

$CaO_2 = (Hb \times 1.34)\ (SaO_2) + (PaO_2 \times 0.0031)$;
$CcvO_2 = (Hb \times 1.34)\ (SvO_2) + (PvO_2 \times 0.0031)$;
$CcO_2 = (Hb \times 1.34)\ (ScO_2) + (PAO_2 \times 0.0031)$;
$Qs/Qt = (CcO_2 - CaO_2) / (CcO_2 - CcvO_2)$.

Hemoglobin (Hb) values were obtained by blood cell count ($g.dL^{-1}$); 1.34 is the oxygen-carrying hemoglobin capacity ($mL.g^{-1}$); SaO_2 is the arterial oxygen saturation; $ScvO_2$ is the central venous oxygen saturation; ScO_2 is the pulmonary end-capillary oxygen saturation [assumed to be 100% (ie, 1)]; 0.0031 is the solubility coefficient of plasma oxygen; and PAO_2 is the alveolar partial pressure of oxygen (mmHg).

The PAO_2 was calculated as follows (LUMB, 2000): $PAO_2 = [FiO_2(PB - PH_2O)] - (PaCO_2/R)$, where FiO_2 is the fraction of inspired oxygen, PB is the local barometric pressure (708,75 mmHg); PH_2O is vapor pressure of water (47 mmHg), $PaCO_2$ is the arterial partial pressure of carbon dioxide, and R is the respiratory quotient, assumed to be 0.8.

At the end of the treatment, the animals were given 0.05 $mg.kg^{-1}$ neostigmine IV and 0.1 $mg.kg^{-1}$ hyoscine IM for reversal of neuromuscular block. All of the sheep were assisted throughout the anaesthetic recovery and placed in sternal recumbency to eliminate ruminal gases by belching, and the tracheal tube was removed when the animals showed laryngotracheal reflex.

Data analysis

Data (mean ± standard deviation) were considered parametric if they were normally distributed, according to the Shapiro–Wilk test, and had a coefficient of variation of less than 0.2; otherwise, they were considered nonparametric data (median [interquartile range]). All parametric data were analysed by two-way ANOVA followed by Bonferroni's post-hoc test for comparisons within each group, and by Tukey's post-hoc test for moments among groups comparisons. The alveolar-arterial oxygen gradient [$P(A\text{-}a)O_2$] and the arterial-end-tidal carbon dioxide gradient [$P(a\text{-}ET)CO_2$] were performed using the Friedman's test with Dunn's multiple comparison post-test. Paired sample t-test was used for FiO_2, HR, MAP and FE'Sevo comparisons between 60 and 120 min, within each group. Values were expressed as mean ± standard deviation or as median and interquartile range, when appropriate. Significance level of 5% was considered ($P < 0.05$) accordingly.

RESULTS

Anaesthetic induction was considered satisfactory in all sheep, without complications. The arterial and central venous blood samples were collected after 229 ± 58 seconds for the dorsal recumbency group, 190 ± 58 seconds for the right lateral recumbency group, and 199 ± 49 seconds for the left lateral recumbency group, with no differences among them.

The Qs/Qt reduced from 0 minute (69.3%) to 60 (33.7%) and 120 min (27.3%) in the dorsal recumbency group ($P < 0.01$). The same pattern was observed in the left lateral recumbency group (0=59.1%; 60=29.9%; 120=25.0%; $P < 0.01$). For the right lateral recumbency group, difference was only reported between 0 minute (67.2%) and 120 min (32.4%) ($P < 0.01$). Difference between groups was only observed at 60 min, when the Qs/Qt was higher in the right lateral recumbency group compared to the left one (P=0.033) (Figure 1).

CaO_2, $CcvO_2$, CcO_2, PAO_2, $P(A\text{-}a)O_2$ increased from 60 min to 120 min compared to 0 min ($P < 0.05$) (Table 1). Higher CaO_2 levels in animals from the left lateral recumbency group were observed at 0 min (9.9±1.43 $mL.dL^{-1}$) compared to the dorsal recumbency group (8.9±1.4 $mL.dL^{-1}$) (P=0.018). No differences between treatments were observed for $CcvO_2$, CcO_2 and PAO_2. The left lateral recumbency group showed lower $P(A\text{-}a)O_2$ values at 0 min (P=0.012) and 60 min compared to the right lateral recumbency group (P=0.028). No differences were reported in V_T and V_M in all treatments and between time points, and the same was observed for $P(a\text{-}ET)CO_2$ values (Tables 1 and 2).

Main physiological variables are described in the table 2. FiO_2, HR and FE'Sevo showed no statistical difference at different time points. MAP

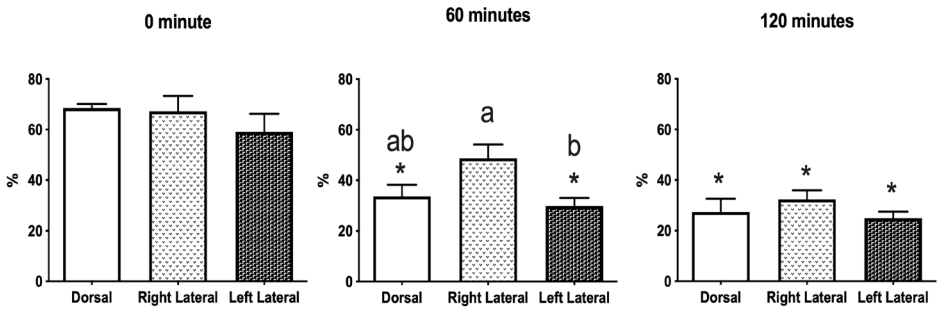

Figure 1 – Mean ± SED of the pulmonary shunt fraction (Qs/Qt) of sevoflurane-anaesthetised sheep, mechanically-ventilated under dorsal, right lateral or left lateral recumbency. *Statistical difference from 0 minute; Different letters indicate statistical difference between groups ($P \leq 0.05$).

was lower on the dorsal recumbency group at 120 min compared to the right and left lateral recumbency groups (P=0.043). Increasing in the pH was observed at 60 min (P=0.017) and at 120 min (P=0.029) in the dorsal recumbency group, and at 60 min in the left lateral group when compared to 0 minute (P=0.017). Furthermore, pH for the dorsal recumbency group was significantly higher when compared to the other treatments at 120 min (P=0.039). PaO_2 showed higher values at 60 and 120 min for all the groups, when compared to the 0 minute ($P < 0.01$). $PaCO_2$ followed the same pattern, but only for the right and left lateral recumbency groups. Conversely, the dorsal recumbency group showed stable $PaCO_2$ throughout the anaesthesia period, thus, being different from the others at 120 min.

DISCUSSION

Our study assessed the effect of three different recumbency upon pulmonary shunt in sheep during a period of 120 min of sevoflurane anaesthesia. Effects of dorsal, right and left lateral recumbency on blood gas analysis and acid-base status have been assessed in sheep, however, pulmonary shunt was not addressed so far (FUJIMOTO & LENEHAN, 1985). The effect of recumbency and lung recruitment manoeuvre on haemodynamic and blood gas analysis in sheep, under pressure-controlled ventilation, have also been recorded. However, data were not correlated to recumbency nor to pulmonary shunt (FUJINO et al., 2001).

Collecting central venous blood samples is a simple, less expensive technique, and less often associated with complications than withdrawing mixed venous blood by pulmonary artery catheters (WALLEY, 2011). Thus, measurement of $ScvO_2$ has been validated as an option for SvO_2 in healthy patients (AKMAL et al., 2007). Central venous Hb saturated with oxygen has been measured from the right atrium or superior vena cava (WALTON & HANSEN, 2018). However, some factors should be pointed out to make $ScvO_2$ reliable, such as catheter placement, anatomy and the physiological state of the patient. Thus, if the patient has no clinical complications, it has been accepted that only a 2-3% difference is noted from mixed venous blood, which makes it a reliable index (REINHART, 2004; HARTOG & BLOOS, 2014). Arterial and central venous oxygen saturations are essential variables used to calculate their respective oxygen content (COLLINS et al., 2015). The oxygen content indices used in our study had been calculated based on blood gas analysis, which also included SO_2 and PO_2. Thus, we understand the reliability of our data lies precisely in the fact that all variables used to obtain the pulmonary shunt were calculated and not just estimated.

Shunt was significantly higher in all groups right after induction. Indeed, it was expected low levels of PaO_2 at 0 minute, indicating hypoxaemia in the sheep. This problem was due to the rumen distension and abdominal pressure, which led to severe PaO_2 reduction following anaesthetic induction, even if $PaCO_2$ levels were eucapnic (TRIM, 1981). P(A-a) O_2 values were lower as well, suggesting poor gas exchange efficiency for non-ventilated alveoli and anatomical shunt areas contributed to this condition (ROBINSON, 2009; ARAOS et al., 2012).

Table 1 – Oxygen tension, content indexes and parameters of sevoflurane-anaesthetised sheep, mechanically-ventilated under dorsal, right lateral or left lateral recumbency.

Parameter	Treatment	0 minute	60 min	120 min
CaO_2 (mL.dL^{-1})	Dorsal	8.9±1.4^{a}	23.0±3.8*	23.7±3.8*
	Right Lateral	9.7±1.6^{ab}	20.8±3.4*	23.5±2.6*
	Left Lateral	9.9±1.4^{b}	23.6±1.7*	23.9±2.7*
$CcvO_2$ (mL.dL^{-1})	Dorsal	7.0±1.2	12.3±3.0*	11.9±2.9*
	Right Lateral	7.7±1.4	12.8±3.6*	13.6±3.7*
	Left Lateral	7.7±2.2	12.7±3.7*	12.2±2.9*
CcO_2 (mL.dL^{-1})	Dorsal	13.5±2.9	28.3±2.4*	28.2±2.4*
	Right Lateral	13.6±2.4	28.4±2.0*	28.1±2.1*
	Left Lateral	13.2±2.6	28.2±2.3*	27.9±2.4*
PaO_2 (mmHg)	Dorsal	47.2±4.4	408.8±53.3*	433.0±61.6*
	Right Lateral	48.6±9.7	333.0±80.1*	417.8±42.1*
	Left Lateral	51.4±6.0	429.8±43.0*	438.8±41.2*
PAO_2 (mmHg)	Dorsal	102.1±18.5	579.9±9.4*	576.5±7.7*
	Right Lateral	100.9±8.8	577.2±11.8*	567.7±8.2*
	Left Lateral	94.3±3.8	576.2±13.1*	567.6±9.2*
$P(A\text{-}a)O_2$ (mmHg)	Dorsal	45(43;71)^{ab}	162(133;212)^{ab*}	117(93;218)*
	Right Lateral	49(43;72)^{a}	225(184;294)^{a*}	139(110;197)*
	Left Lateral	39(37;52)^{b}	145(119;173)^{b*}	126(81;176)*
$PaCO_2$ (mmHg)	Dorsal	32.8±7.2	39.0±8.8	39.9±8.4^{b}
	Right Lateral	30.4±7.1	44.6±11.8*	50.5±12.0^{*a}
	Left Lateral	35.8±3.8	45.5±7.2*	50.6±7.7^{*a}
$ETCO_2$ (mmHg)	Dorsal	-	32.5±7.7	33.0±10.9^{b}
	Right Lateral	-	38.0±6.9	42.5±10.4^{a}
	Left Lateral	-	37.5±5.5	41.6±6.8^{a}
$P(a\text{-}ET)CO_2$ (mmHg)	Dorsal	-	6.8(4.2;8.5)	5.8(4.5;10.0)
	Right Lateral	-	6.6(2.6;12.0)	8.8(6.0;9.4)
	Left Lateral	-	9.4(4.9;10.0)	8.3(2.1;9.7)

CaO_2: arterial oxygen content. $CcvO_2$: central venous oxygen content. CcO_2: capillary oxygen content. PaO_2: arterial partial pressure of oxygen. PAO_2: alveolar partial pressure of oxygen. $P(A\text{-}a)O_2$: alveolar-arterial oxygen gradient. $PaCO_2$: arterial partial pressure of carbon dioxide. $ETCO_2$: end-tidal carbon dioxide. $P(a\text{-}ET)CO_2$: arterial-end-tidal carbon dioxide gradient. * Statistical difference from 0 minute; Different letters indicate statistical difference between groups ($P \leq 0.05$). Values expressed by mean ± SD. $P(A\text{-}a)O_2$ and $P(a\text{-}ET)CO_2$ expressed as median and interquartile range.

Table 2 – Physiological, blood gas parameters and end-tidal sevoflurane concentration of anaesthetised sheep, mechanically-ventilated under dorsal, right lateral or left lateral recumbency.

Parameter	Treatment	0 minute	60 min	120 min
FiO_2 (%)	Dorsal	-	0.95±0.01	0.95±0.02
	Right Lateral	-	0.96±0.02	0.95±0.03
	Left Lateral	-	0.96±0.02	0.95±0.01
V_T ($mL.kg^{-1}$)	Dorsal	-	10.0±2.2	9.2±2.3
	Right Lateral	-	9.0±2.2	8.2±2.4
	Left Lateral	-	9.3±1.8	9.0±1.9
V_M ($mL.kg^{-1}.min^{-1}$)	Dorsal	-	99.8±21.5	92.1±23.1
	Right Lateral	-	90.3±22.0	81.8±23.6
	Left Lateral	-	92.6±17.7	89.9±19.3
pH	Dorsal	7.39±0.04	7.51±0.11*	7.50±0.10*[a]
	Right Lateral	7.38±0.07	7.45±0.09	7.41±0.07[b]
	Left Lateral	7.38±0.05	7.45±0.07*	7.43±0.07[b]
HR (bpm)	Dorsal	-	108±20.5	98±22.5
	Right Lateral	-	99±16.9	99±19.5
	Left Lateral	-	102±16.1	100±20.4
MAP (mmHg)	Dorsal	-	67±3.2	71±4.4[a]
	Right Lateral	-	80±10.9	85±12.4[b]
	Left Lateral	-	79±13.5	88±12.3[b]
FE'Sevo (%)	Dorsal	-	1.80±0.14	1.83±0.22
	Right Lateral	-	1.73±0.18	2.00±0.28
	Left Lateral	-	1.82±0.15	2.00±0.21

FiO_2: fraction of inspired oxygen. V_M: minute volume. V_T: tidal volume. HR: heart rate. MAP: mean arterial pressure. FE'Sevo: end-tidal sevoflurane concentration. Values expressed by mean ± SD. *Statistical difference from 0 minute; Different letters indicate statistical difference between groups ($P \leq 0.05$).

Despite hypoxaemia after induction, the shunt values had decreased from 60 min as a consequence of the mechanical ventilation and the high FiO_2 as well. This is in accordance with studies conducted in horses (BRIGANTI et al., 2015) and sheep (ARAOS et al., 2012), that showed about 20 – 30% shunt at a 1.0 FiO_2. Likewise, the PaO_2 values higher than 300 mmHg are in accordance with those studies which had used similar FiO_2, showing that both FiO_2 and mechanical ventilation were effective on reversing hypoxaemia induction.

It was observed the $PaCO_2$ increased in both lateral recumbency, comparing to the 0 minute, but not for $ETCO_2$ and $P(a\text{-}ET)CO_2$. Despite no statistical evidence for these two variables, there is clinical relevance showing an increasing tendency of $P(a\text{-}ET)CO_2$ overtime, which may reflect alveolar dead space (NUNN & HILL, 1960), and statistical difference might have been reported if treatments had been kept for more than 120 min. In right and left lateral recumbency, the dependent lung (i.e., lowermost) is poorly ventilated due to atelectasis (PORCELLI, 1992). Thus, even high inspired oxygen concentrations would have minor effects over gas exchange and CO_2 elimination (WEST, 1977). It is important to point out even though shunt decreased over time, it was still higher from acceptable physiological values, i.e., less than 10% (LUMB, 2000). Perhaps a PEEP manoeuvre could prevent alveolar collapse and promote alveolar recruitment, as observed in horses (HOPSTER et al., 2011).

It should be highlighted that FiO_2 has a great influence over other variables. FiO_2 at 0 minute (0.21) was different from the other moments (0.95) and it might have directly influenced the PaO_2 and $P(A\text{-}a)O_2$ (OLIVEN et al., 1980), as pulmonary shunt ameliorated over time points. Thus, a statistical difference in the $P(A\text{-}a)O_2$ was expected among time points and even treatments. These values might be influenced by changes in FiO_2, barometric pressure and body temperature (GILBERT & KEIGHLEY, 1974). Blood flow from alveoli with low ventilation/perfusion ratio, non-ventilated alveoli, or anatomic shunt areas also contributed to elevated $P(A\text{-}a)O_2$ values (WEST, 1977), as observed at 60 and 120 min. In our study this may be due to the time that it took to equalise alveolar and pulmonary end-capillary PO_2, which created a relative diffusion defect, or to PO_2 losses, because of the very large partial pressure gradients, at 60 and 120 min. This finding was in line with those reported in anaesthetised sheep under different FiO_2 values (ARAOS et al., 2012).

V_M and V_T values remained constant throughout the experimental period, with no statistical differences between time points and treatments, even with the presence of gravitational forces and visceral weight continuously pressing the diaphragm of these animals. Our study used pressure-controlled ventilation, and it determined a rapid increase in alveolar pressure. Maintaining constant pressure during the inspiratory phase allows alveoli to remain open and, theoretically, guarantees lung compliance and gas exchange (CORONA & AUMANN, 2011), suggesting that this situation kept these variables constant. A similar situation was observed in cattle anaesthetised with sevoflurane under spontaneous ventilation (ARAÚJO et al., 2017), in which V_M and V_T remained without statistical difference throughout the 180-minute experimental period.

No statistical difference was observed in HR and MAP, except for MAP at 120 min from the sheep in the dorsal recumbency group. This could be a result of impaired venous return in dorsal recumbency once gravitational forces impacted directly over rumen and other viscera, reducing venous blood flow (GENÇCELEP et al., 2004). The result in healthy patients is decreased stroke volume and pressure, because no changes are observed on vasomotor tone from heart beats (SINGH & PINSKY, 2008).

CONCLUSION

This study demonstrated that pressure-controlled mechanical ventilation improves gas exchanges in sheep, reducing pulmonary shunt. Recumbency does not interfere with pulmonary shunt, nevertheless, special attention must be paid to lateral recumbency. High levels of FiO_2 are mandatory to ameliorate alveolar gas exchanges and reduce shunt incidence.

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BIOETHICS AND BIOSSECURITY COMMITTEE APPROVAL

Institutional Animal Use Ethics Committee (CEUA) of the Universidade de São Paulo (USP) approved the study under protocol n° 1240030918.

DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest. The funding agency did not interfere in the study design; collection, analysis, or data interpretation; in manuscript writing, and in the decision to publish the results.

AUTHORS' CONTRIBUTIONS

All authors contributed equally for the conception and writing of the manuscript. All authors critically revised the manuscript and approved the final version.

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