Total Intravenous Anesthesia with Propofol for Experimental Surgical Transposition of the Carotid Artery in Sheep

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ABSTRACT

Background: The carotid artery transposition may be used in research when continuous measurements of arterial pressure or serial blood sampling are needed. In sheep, this procedure has usually been performed under inhalational or barbiturate anesthesia; however, these anesthetic techniques may cause cardiorespiratory depression and delayed recovery. Conversely, propofol is a general anesthetic that promotes rapid induction, smooth recovery, and hemodynamic stability. The aim of this study was to assess physiological and anesthetic effects of total intravenous anesthesia with propofol to establish its safety and efficacy for performing permanent carotid transposition, in sheep.

Materials, Methods & Results: Seven young healthy ewes, weighing 35.00 ± 4.43 kg and subjected to a new technique of permanent transposition of the carotid artery were used. Propofol was administered by constant rate infusion (0.5 mg/kg/min; IV) after anesthetic induction with this same drug. Heart rate (HR), cardiac rhythm, oxyhemoglobin saturation (SpO₂), respiratory rate (f), rectal temperature (RT), systolic arterial pressure (SAP), and venous blood gas parameters (SvO₂, PvO₂, PvCO₂, and HCO₃⁻) were evaluated before induction and every 10 min up to 1 h of anesthesia. Recovery period was also evaluated. Data were submitted to Shapiro-Wilk normality test followed by one-way repeated measures analysis of variance and Tukey-Kramer multiple comparisons test (P < 0.05) to analyze possible effects over time. There was no occurrence of apnea or regurgitation after anesthetic induction; however, all sheep presented hypersalivation. In relation to baseline, HR was greater at 10 min, whereas PvO₂, PvCO₂, and SvO₂ increased at all evaluation points, and HCO₃⁻ was higher at 40 min and 60 min. There was a decrease in RT from 20 min to 60 min and pH was lower from 10 min to 30 min, and at 60 min. No significant differences were noted in SpO₂, SAP, and f. Mean time ± SD to extubation, sternal recumbency, and standing were 4.00 ± 1.41, 10.50 ± 3.21, and 14.00 ± 3.29 min, respectively, and recovery phase was classified as good in all animals.

Discussion: Increase, reduction or stability of HR have been reported during anesthesia with propofol, so the rise in HR at 10 min might be consequence of vagal blockade caused by this drug; however, no arrhythmias were recorded. Decrease in blood pressure after induction with propofol is proportional to elevation of drug plasma concentration, which is related to the rate of injection. Thus, the slow application of propofol performed in this study resulted in a smooth induction and precluded high arterial concentrations of propofol and occurrence of hypotension. Respiratory acidosis, reduction in f and hypercapnia can occur in propofol anesthesia. Therefore, decrease in venous pH probably was due to elevation of PvCO₂ resulted by a decline in CO₂ elimination. Good anesthetic recovery phase is desirable for ruminants because excessive struggling and prolonged decubitus can be deleterious for success of carotid artery transposition, because animals may injury the site of surgery. Longer food withdrawal times did not affect recovery time, but regurgitation is increased and quality of anesthesia is decreased. In this study, animals were fasted for 18 h and free access to water was allowed up to 6 h before anesthesia. So, this fasting regimen used might be the responsible for the absence of regurgitation and good anesthetic recoveries. In conclusion, total intravenous anesthesia with propofol does not promote major changes in the physiological parameters evaluated. Moreover, propofol provides short recovery periods from anesthesia without complications, and may be, therefore, considered safe and effective for carotid artery transposition in healthy sheep.

Keywords: carotid arteries, general anesthesia, intravenous anesthesia, sheep.
INTRODUCTION

In animal research, when continuous measurement of arterial pressure and serial blood sampling are needed, the carotid artery transposition is commonly used [9,12]. In sheep, this technique has been performed under anesthesia with halothane or barbiturates, which may cause cardiorespiratory depression and delayed recovery [12,19]. Propofol is a general anesthetic widely used to induce and maintain anesthesia in different domestic animals, given its characteristics as rapid induction, adequate anesthetic depth, quick and smooth recovery, hemodynamic stability, and absence of environmental pollution [2,5,8,12,20]. In this research, propofol was administered by intravenous continuous infusion in sheep subjected to a new technique of permanent transposition of the carotid artery to evaluate the usefulness of this anesthetic modality for this surgical procedure. Additionally, physiological and anesthetic effects of propofol were assessed to corroborate previous studies of this anesthetic in sheep.

MATERIALS AND METHODS

Animals

Seven young healthy Santa Ines sheep weighing 35.00 ± 4.43 kg were used. These animals were treated for possible parasitic diseases and underwent physical and laboratory examinations to be considered healthy before being included in this study. Sheep were kept in paddocks with Tifton grass, received commercial feed twice daily and had free access to water and mineral salt. Animals were fasted for 18 h and water was withdrawn 6 h before anesthesia.

Anesthesia, monitoring and experimental design

Initially, sheep were physically restrained and left jugular vein was cannulated for administration of propofol and to provide venous sampling for blood gas analysis. Sheep received no preanesthetic medication, and as induction of anesthesia, propofol (Propovan 1%)1 was injected slowly (50 mg/min), at a maximum dose of 8.0 mg/kg. Propofol was administered until relaxation of the jaw and possibility of tracheal intubation, which was carried out with a laryngoscope. Animals were placed in left lateral recumbency and the endotracheal tube was connected to a semiclosed circle system for supplementation of 100% oxygen under spontaneous ventilation. Propofol constant rate infusion (0.5 mg/kg/min) was initiated immediately after intubation, for 1 h, via peristaltic infusion pump (Infusion Pump 660T)2, at an infusion rate of 10 mL/kg/h.

All animals were subjected to a permanent surgical transposition of the right common carotid artery, by the technique proposed by Gouvêa et al. [9]. Infiltrative local anesthesia was performed at the site of surgery with 2% lidocaine without vasoconstrictor (Xylestesin 2%)3. During surgical procedure, propofol was reserved for intraoperative administration (1.5 mg/kg, IV) if there was a need for complementary chemical restraint. The criteria for propofol administration were based on occurrence of sudden voluntary gross movements of animals in response to surgical stimulus. Anesthetic depth was monitored, and infusion rate of propofol was diminished if systolic blood pressure and respiratory rate decreased more than 30% of basal values and if corneal reflex was absent.

Heart rate (HR), cardiac rhythm, oxyhemoglobin saturation (SpO2), respiratory rate (f), rectal temperature (RT), systolic arterial pressure (SAP), and venous blood gas parameters (SvO2, PvO2, PvCO2, and HCO3−) were evaluated before anesthetic induction (basal) and every 10 min after the start of intravenous infusion, during a total period of 60 min. Subsequently to the end of infusion, animals were moved to a recovery room, and time to extubation, time to achieve sternal recumbency and time to standing were recorded. The quality of recovery was assessed immediately after extubation and classified as good, fair or poor, according to a description by Prassinos et al. [18].

The HR, cardiac rhythm, SpO2, and RT were measured by a multiparameter monitor (DX 2010 LCD)4. Electrodes for electrocardiography were placed in DII derivation and pulse oximeter probe was positioned on animals’ tongues. Systolic arterial pressure was assessed by Doppler method (DV10)4, with cuff of appropriate size placed on right pelvic limb over the metatarsal artery, and f was evaluated by observation of thoracic wall movements. Venous blood samples were taken anaerobically with syringes for blood gas analysis (BD Preset)5 and were immediately processed in an automatic analyzer (Omni C)6.

At the postoperative period, the animals received a single application of 10 mg of dexamethasone IV (Dexacort)7 to avoid severe edema of the manipulated area, and 1.1 mg/kg of flunixin meglumine IV (Banamine)8, every 24 h for 3 days, as analgesic treatment. Enrofloxacin (5.0 mg/kg, IM) [Zelotril 10%]9...
was administered every 24 h for 7 days. The surgical wound was protected with povidone-iodine moistened drapes fixed with micropore (Nexcare) and the suture was removed after 10 days of surgery.

**Statistical analysis**

Sample size estimation was carried out to establish an appropriate number of individuals for this study, and statistical power was set to 0.80 [7]. Data were assessed for normal distribution with Shapiro-Wilk normality test. One-way repeated measures analysis of variance and Tukey-Kramer multiple comparisons test were used to analyze possible significant effect of drug over time. The level of significance for the statistical tests was set at \( P < 0.05 \) [16]. The software GraphPad Prism for Mac version 5.00 (GraphPad Software Inc., La Jolla, CA, USA) was used to perform statistical analyses.

**Table 1.** Means and standard deviations (mean [SD]) of blood gases and other physiological parameters in sheep submitted to permanent carotid transposition under total intravenous anesthesia with propofol (n = 7).

<table>
<thead>
<tr>
<th>Physiological parameter</th>
<th>Time (min)</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td></td>
<td>102</td>
<td>128*</td>
<td>110</td>
<td>100</td>
<td>97</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>SAP (mmHg)</td>
<td></td>
<td>124</td>
<td>130</td>
<td>115</td>
<td>119</td>
<td>120</td>
<td>120</td>
<td>130</td>
</tr>
<tr>
<td>f (mov./min)</td>
<td></td>
<td>30</td>
<td>25</td>
<td>27</td>
<td>25</td>
<td>26</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>RT (°C)</td>
<td></td>
<td>39.1</td>
<td>38.8</td>
<td>38.5*</td>
<td>38.4*</td>
<td>38.1*</td>
<td>38.0*</td>
<td>37.8*</td>
</tr>
<tr>
<td>pH (units)</td>
<td></td>
<td>[0.6]</td>
<td>[0.6]</td>
<td>[0.7]</td>
<td>[0.6]</td>
<td>[0.7]</td>
<td>[0.9]</td>
<td>[0.7]</td>
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<tr>
<td>SpO₂ (%)</td>
<td></td>
<td>98.43</td>
<td>98.71</td>
<td>98.57</td>
<td>98.71</td>
<td>98.43</td>
<td>98.29</td>
<td>98.43</td>
</tr>
<tr>
<td>SvO₂ (%)</td>
<td></td>
<td>[0.79]</td>
<td>0.49</td>
<td>0.98</td>
<td>0.76</td>
<td>0.53</td>
<td>1.11</td>
<td>0.98</td>
</tr>
<tr>
<td>Pvo₂ (mmHg)</td>
<td></td>
<td>47.3</td>
<td>57.1*</td>
<td>58.8*</td>
<td>59.1*</td>
<td>60.1*</td>
<td>60.6*</td>
<td>60.6*</td>
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<tr>
<td>(mmHg)</td>
<td></td>
<td>4.3</td>
<td>[10.0]</td>
<td>[6.5]</td>
<td>[5.0]</td>
<td>[5.5]</td>
<td>[5.0]</td>
<td>[8.3]</td>
</tr>
<tr>
<td>SvO₂ (%)</td>
<td></td>
<td>64.4</td>
<td>78.8*</td>
<td>74.6*</td>
<td>76.8*</td>
<td>76.8*</td>
<td>78.1*</td>
<td>76.0*</td>
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<tr>
<td>(%)</td>
<td></td>
<td>[8.3]</td>
<td>[4.9]</td>
<td>[9.6]</td>
<td>[7.0]</td>
<td>[6.8]</td>
<td>[7.0]</td>
<td>[5.2]</td>
</tr>
<tr>
<td>Pvo₂ (mmHg)</td>
<td></td>
<td>38.8</td>
<td>43.3*</td>
<td>44.7*</td>
<td>44.8*</td>
<td>44.9*</td>
<td>44.1*</td>
<td>46.3*</td>
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<tr>
<td>(mmHg)</td>
<td></td>
<td>[3.7]</td>
<td>[3.7]</td>
<td>[3.9]</td>
<td>[4.0]</td>
<td>[3.3]</td>
<td>[2.8]</td>
<td>[2.8]</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol/L)</td>
<td></td>
<td>24.0</td>
<td>24.3</td>
<td>24.8</td>
<td>25.2</td>
<td>25.8*</td>
<td>25.6</td>
<td>26.2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[2.0]</td>
<td>[1.1]</td>
<td>[1.2]</td>
<td>[0.9]</td>
<td>[1.1]</td>
<td>[1.3]</td>
<td>[1.4]</td>
</tr>
</tbody>
</table>

*Significant difference when compared to T0 (\( P < 0.05 \)); HR: heart rate; SAP: systolic arterial pressure; f: respiratory rate; RT: rectal temperature; SpO₂: oxyhemoglobin saturation; SvO₂: venous oxyhemoglobin saturation; Pvo₂: venous carbon dioxide partial pressure; HCO₃⁻: bicarbonate concentration.

**RESULTS**

The lowest and highest doses of propofol required for induction of anesthesia that allowed orotracheal intubation were 5.26 and 7.5 mg/kg, respectively, and the mean dose was 6.53 ± 0.66 mg/kg. There was no occurrence of apnea after anesthetic induction. Intubation was performed without difficulty or occurrence of regurgitation; however, all sheep exhibited hypersalivation. Surgical procedures lasted 29 ± 0.5 min and were carried out without any complications, so additional bolus or adjustments on infusion rate of propofol were not necessary.

Data were normally distributed, so they are presented as means and standard deviations (Table 1). The HR was significantly higher at 10 min compared with basal values (\( P < 0.05 \)). No arrhythmias were detected during the anesthetic procedure. Systolic arterial pressure and \( f \) had no significant differences (\( P > 0.05 \)) and remained within the physiological range.
for the species. The RT decreased significantly from 20 min \((P < 0.05)\) until the end of measurements. According to the blood gas analysis, pH values were significantly lower from 10 min to 30 min, and at 60 min \((P < 0.05)\). There were increases in \(\text{PvO}_2\), \(\text{SvO}_2\), and \(\text{PvCO}_2\) from 10min of infusion \((P < 0.05)\), and in \(\text{HCO}_3^-\) at 40 min and 60 min in relation to baseline \((P < 0.05)\). Times to extubation, to achieve sternal recumbency, and to stand were \(4.00 \pm 1.41\), \(10.50 \pm 3.21\), and \(14.00 \pm 3.29\) min, respectively, and recovery was classified as good and developed without complications in all animals. The post-operative period occurred without problems.

**DISCUSSION**

The mean dose of propofol required to induce anesthesia in this study was within the range recommended for small ruminants without pretreatment, which may vary between 6.0 and 8.0 mg/kg [21]. In previous studies in sheep that were not given preanesthetic medication, the dose of 6.0 mg/kg propofol was used to induce anesthesia [1,13], whereas some authors have already described the use of lower doses of this anesthetic [17,18]. In goats premedicated with fentanyl or midazolam, the dose of propofol required was close to 4.0 mg/kg [6].

Authors have reported that increase, decrease or stability of HR could come from continuous infusion of propofol, owing its effects on myocardium and peripheral vasculature [10,20,23]. Likewise to what observed herein, the continuous infusion of propofol at rates between 0.05 and 0.45 mg/kg/min had not significantly affected HR in sheep and goats [1,5,17]. In this study, only healthy sheep were used; therefore, the sudden increase in HR only at 10min might be consequence of vagal blockade after anesthetic induction. Despite this, no arrhythmias were recorded during anesthetic procedure. Another reason for increase of HR at the first measurement would be the surgical stimulus, because propofol has little analgesic effect [20,21]. However, this supposition was refuted since lidocaine was injected at the site of surgery and promoted adequate analgesia, supported by absence of alterations in \(f\), SAP, and depth of anesthesia in response to surgical stimulus.

Reduction in blood pressure after intravenous induction with propofol is proportional to elevation of drug plasma concentration, which is directly related to the rate of injection [23,24]. It have been demonstrated that in sheep, rapid intravenous injections of propofol resulted in drastic decreases in blood pressure due to high blood concentrations of drug immediately after injection [25]. Furthermore, as the rate of propofol administration has minimal effects on its brain concentration [14], the slow application performed in present study resulted in a smooth induction and probably prevented the occurrence of high arterial concentrations of propofol and the risk of hypotension. Despite of Correia et al. [3] and Andaluz et al. [1] had reported decrease of blood pressure during intravenous maintenance with propofol in pregnant ewes, our findings are similar to those described in more recent studies with these drugs undertaken on other small ruminants [5,6,17].

Unfortunately, arterial blood gases were not evaluated due to difficulty to obtain arterial samples of the animals studied. Nevertheless, by assessment of venous blood gases, \(f\) and \(\text{SpO}_2\) we could note that, despite these two latter parameters have remained stable herein, ventilatory function was somehow depressed because the progressive increase in \(\text{PvCO}_2\) developed mild hypercapnia. Likewise, it was reported moderate hypercapnia in pregnant ewes and goats anesthetized with propofol by continuous infusion, which resulted in respiratory acidosis [1,13,18]. Therefore, the continuous decrease in venous \(\text{pH}\) observed in this study may be due to possible decline in tidal volume (not evaluated), which may have hindered \(\text{CO}_2\) elimination and caused progressive elevation of \(\text{PvCO}_2\). It must be highlighted that although sheep have remained under spontaneous ventilation and in left lateral decubitus position, there was no respiratory acidemia; however, acute hypercapnia stimulates erythrocytes to release \(\text{HCO}_3^-\), which justify the parallel increase of this parameter [4].

Overall analysis of tissue oxygenation requires an evaluation of venous blood and, consequently, \(\text{PvO}_2\) and \(\text{SvO}_2\) are the most important parameters [4]. In dogs, it was showed that \(\text{PvO}_2\) decreased as cardiac output was declined [15]; therefore, serial measurements of this blood gas parameter are well acceptable to assess severity of tissue hypoperfusion, which may occur in arterial hypotension. Hence, maintenance of adequate values of SAP and \(\text{SpO}_2\), the latter as an effect of 100% oxygen supplementation, probably allowed appropriate perfusion and oxygenation...
ation of tissues, which were confirmed in analyzes of \( \text{PvO}_2 \) and \( \text{SvO}_2 \).

Propofol decreases body temperature probably due to peripheral vasodilation and depression of thermoregulatory centers [8]. In present study, reduction in RT is not solely related to these anesthetic effects, but also to the absence of heat source to maintain the temperature of animals. Dzikiti et al. [5] demonstrated that esophageal temperature of goats subjected to continuous infusion of propofol had not decreased more than 1.0\(^\circ\)C because of the use of thermal blankets.

Short periods of anesthetic recovery are desirable for ruminants because prolonged decubitus position increases the risk of tympany and hypoxemia, in addition to increased probability of regurgitation and aspiration of rumen content [18]. Also, longer and complicated recovery periods can be deleterious for success of carotid artery transposition, because animals may injury the site of surgery if they become agitated during this phase [9]. We observed that all sheep presented easy and rapid transition to alertness and became in stand position with little effort and minimal ataxia; thus, anesthesia with propofol certainly contributed to the success of this new technique of carotid transposition.

The influence of food and water deprivation on propofol recovery was previously studied in sheep underwent carotid artery transposition [17], and it was concluded that longer food withdrawal times (>48 h) did not affect recovery time; however, regurgitation is increased and quality of anesthesia is decreased. In our study, animals were fasted for 18 h and free access to water was allowed up to 6 h before anesthesia. So, the fasting regimen used herein may be responsible for the absence of regurgitation and good quality anesthetic recoveries.

Propofol is characterized by a high volume of distribution and a rapid rate of biotransformation and excretion [8,20]. Additionally, 30% of propofol applied in sheep can be eliminated by lungs during first pass [11]. Because of these characteristics, propofol (3 mg/kg, IV) seemed to promote shorter times and better recoveries than thiopental (8 mg/kg, IV) and ketamine (10 mg/kg, IV) in goats [18]. Lin et al. [13] reported that TIVA with propofol resulted in faster and better quality recoveries when compared with dissociatives and halogenated anesthetics in sheep. Similarly to this study, these same authors observed recovery times close to 14 min and classified the recovery period as good. Also, Vettorato et al. [22] compared isoflurane and sevoflurane in lambs and observed longer extubation and recovery times than those noted in this study.

CONCLUSION

Under the conditions adopted in this study, it was concluded that total intravenous anesthesia with propofol does not promote major changes in the physiological parameters evaluated. Furthermore, propofol provides short periods of anesthetic recovery without complications, and may be, therefore, considered safe and effective for carotid artery transposition in healthy sheep.

REFERENCES


