RESEARCH PAPER

# Effects of pneumoperitoneum and of an alveolar recruitment maneuver followed by positive end-expiratory pressure on cardiopulmonary function in sheep anesthetized with isoflurane—fentanyl

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#### **Abstract**

**Objective** To investigate the effects of pneumoperitoneum alone or combined with an alveolar recruitment maneuver (ARM) followed by positive end-expiratory pressure (PEEP) on cardiopulmonary function in sheep.

**Study design** Prospective, randomized, crossover study.

Animals A total of nine adult sheep (36–52 kg).

Methods Sheep were administered three treatments (≥10-day intervals) during iso-flurane—fentanyl anesthesia and volume-controlled ventilation (tidal volume: 12 mL kg<sup>-1</sup>) with oxygen: CONTROL (no intervention); PNEUMO (120 minutes of CO<sub>2</sub> pneumoperitoneum); PNEUMO ARM/PEEP (PNEUMO protocol with an ARM instituted after 60 minutes of pneumoperitoneum). The ARM (5 cmH<sub>2</sub>O increases in PEEP of 1 minute duration until 20 cmH<sub>2</sub>O of PEEP) followed by 10 cmH<sub>2</sub>O of PEEP until the end of anesthesia. Cardiopulmonary data were recorded until 30 minutes after abdominal deflation.

**Results** PaO<sub>2</sub> was decreased from 435–462 mmHg (58.0–61.6 kPa) (range of mean values in CONTROL) to 377–397 mmHg (50.3–52.9 kPa) in PNEUMO (p < 0.05). Quasistatic compliance ( $C_{\text{qst}}$ , mL cmH<sub>2</sub>O<sup>-1</sup> kg<sup>-1</sup>) was decreased from 0.85–0.92 in CONTROL to 0.52–0.58 in

PNEUMO. PaO<sub>2</sub> increased from 383-385 mmHg (51.1-51.3 kPa) in PNEUMO to 429-444 mmHg (57.2-59.2 kPa) in PNEUMO 429-444 mmHg (57.2-59.2 kPa) in PNEUMO429-444 mmHg and 429-444 mmHg 429-444 mmHg. The increased from 429-444 mmHg and 429-444 mmHg and 429-444 mmHg 429-444 mmHg and increased from 429-444 mmHg. The increased from 429-444 mmHg and 429-444 mmHg and increased mean pulmonary artery pressure from 429-444 mmHg.

Conclusions and clinical relevance Abdominal deflation did not reverse the pulmonary function impairment associated with pneumoperitoneum. The ARM/PEEP improved respiratory compliance and reversed the oxygenation impairment induced by pneumoperitoneum with acceptable hemodynamic changes in healthy sheep.

**Keywords** alveolar recruitment maneuver, pneumoperitoneum, sheep.

#### Introduction

Anesthetized sheep may develop oxygenation impairment and increased alveolar-to-arterial oxygen gradient  $[P(A-a)O_2]$  owing to the presence of large areas of atelectasis in dependent lung regions

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(Hedenstierna et al. 1989). Changes in lung function in anesthetized sheep are similar with those observed in anesthetized humans because the development of atelectatic areas on computed tomography show a strong linear correlation with the degree of oxygenation impairment and intrapulmonary shunt fraction  $(\dot{O}_s/\dot{O}_t)$  in both species (Wolf et al. 2015).

Pneumoperitoneum for laparoscopic surgery is commonly used in humans and in dogs. Inflation of the abdomen in humans with carbon dioxide (CO<sub>2</sub>) for laparoscopic procedures results in decreased total respiratory compliance owing to a cranial displacement of the diaphragm, although arterial oxygenation may not be significantly impaired (Andersson et al. 2002; Sprung et al. 2002; Nguyen et al. 2004). However, lung function in anesthetized sheep and other ruminants may be more severely affected by pneumoperitoneum because progressive gas trapping within the rumen may further displace the diaphragm cranially and result in oxygenation impairment because of atelectasis (Fujimoto & Leneham 1985; Hedenstierna et al. 1989).

An alveolar recruitment maneuver (ARM) is used during mechanical ventilation to open collapsed alveoli by temporary administration of a high inspiratory pressure (Lachmann 1992; Tusman et al. 1999). This procedure is followed by long-term application of positive end-expiratory pressure (PEEP) that is adjusted to maintain these alveoli open throughout the entire respiratory cycle. This strategy may increase arterial oxygen partial pressure (PaO<sub>2</sub>) and respiratory system compliance during pneumoperitoneum for laparoscopic gastric banding in obese human patients (Almarakbi et al. 2009).

The hypothesis for the present study was that  $CO_2$  pneumoperitoneum up to an intra-abdominal pressure of 15 mmHg would cause a negative effect on respiratory system compliance [decreased quasistatic compliance ( $C_{\rm qst}$ )] and decrease  $PaO_2$  by increasing  $\dot{Q}_{\rm s}/\dot{Q}_{\rm t}$ . In this scenario, an ARM consisting of stepwise increases in PEEP until 20 cmH<sub>2</sub>O followed by 10 cmH<sub>2</sub>O of PEEP during volume-controlled ventilation would reverse the oxygenation impairment and decreased  $C_{\rm qst}$  without causing excessive cardiovascular depression.

## **Materials and methods**

# Animals and study design

This study was approved by the Animal Care Committee of the São Paulo State University (No. 171/2015). A total of nine Santa Inês sheep (four females

and five males), 14–18 months old and weighing 36–52 kg were selected for the study. Animals were healthy determined by physical examination, complete blood cell count and fecal egg count within normal ranges before each experiment.

The animals were administered three treatments at intervals of 10 days in a prospective, randomized (www.randomizer.org) crossover design: 1) CON-TROL treatment, anesthesia maintained with conventional volume-controlled ventilation volume (V<sub>T</sub>) 12 mL kg<sup>-1</sup>] and zero end-expiratory pressure (ZEEP) with no intervention; 2) PNEUMO treatment, CO<sub>2</sub> pneumoperitoneum with a 15 mmHg intra-abdominal pressure for 120 minutes, with the same ventilation protocol used in CONTROL; and 3) treatment, PNEUMO<sub>ARM/PEEP</sub>  $CO_2$ peritoneum with a 15 mmHg intra-abdominal pressure, ventilation protocol used in CONTROL for 60 minutes, followed by an ARM and 10 cmH<sub>2</sub>O PEEP for another 60 minutes.

Supplementary data related to this article can be found online at <a href="http://dx.doi.org/10.1016/j.vaa.2016.05.017">http://dx.doi.org/10.1016/j.vaa.2016.05.017</a>

### Instrumentation and variables monitored

Food and water were withheld for 24 and 12 hours before anesthesia, respectively. A 20 gauge catheter was inserted into a cephalic vein for drug administration and infusion of lactated Ringer's solution (2 mL kg<sup>-1</sup> hour<sup>-1</sup>; JP Indústria Farmacêutica, SP, Brazil) during anesthesia. Ceftiofur (1.1 mg kg<sup>-1</sup>; Minoxel Plus; Elanco, SP, Brazil) was administered intramuscularly (IM) before anesthesia and at 24 and 48 hours after anesthesia. Animals were administered flunixin meglumine (1.1 mg kg<sup>-1</sup>; Banamine. MSD, SP, Brazil) intravenously (IV) and fentanyl (5 μg kg<sup>-1</sup>; Fentanest; Cristália Produtos Químicos e Farmacêuticos Ltda, SP, Brazil) IV followed 15 minutes later by induction of anesthesia with IV propofol (5.6 ± 0.9 mg kg<sup>-1</sup>; Propovan; Cristália Produtos Químicos e Farmacêuticos Ltda) titrated until orotracheal intubation could be performed. Animals were positioned in dorsal recumbency and anesthesia was maintained with isoflurane (Isoforine; Cristália Produtos Químicos e Farmacêuticos Ltda) in oxygen and an infusion of fentanyl (5  $\mu g kg^{-1}$ hour<sup>-1</sup>) IV using a syringe pump (Pump 11 Elite; Harvard Apparatus, MA, USA). Inspired O2 fraction (FIO<sub>2</sub>) was monitored by a paramagnetic cell, whereas end-expired isoflurane fraction (Fe'Iso) and end-expired CO<sub>2</sub> partial pressure (PE'CO<sub>2</sub>) were

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