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Oxygen delivery by mask improves the PaO_2 of pregnant ewes during short term anaesthesia for caesarean delivery of preterm lambs

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ABSTRACT

The aim of this study was to determine if oxygen supplementation improved the PaO_2 of pregnant ewes during short anaesthesia, when compared to a previous study where oxygen was not provided (Musk and Kemp, 2018). Twenty-six pregnant Merino cross ewes at 121–123 days of gestation were anaesthetised with intravenous midazolam and ketamine for subarachnoid administration of 60 mg of lignocaine and caesarean delivery of the preterm lamb. 100% oxygen was administered to the ewe by a face mask. Arterial blood samples were collected from the ewe immediately after delivery of the foetus. The ewes weighed 60.7 ± 5.5 kg and received 0.51 (0.47–0.58) mg/kg of midazolam and 10.3 (9.4–11.6) mg/kg of ketamine intravenously. The PaO_2 of ewes receiving oxygen by face mask was higher than previously reported [92.6 ± 44.0 mmHg compared to 45.2 ± 11.8 mmHg (Musk and Kemp, 2018) ($p = 0.0007$)]. Oxygen delivery by mask improved the PaO_2 of pregnant ewes during short term anaesthesia.

Pregnant sheep are a common model for investigations into the causes and consequences of preterm birth (Morrison et al., 2018) and some studies involve short term anaesthesia of the pregnant ewe for caesarean delivery of the preterm foetus (Maneenil et al., 2015; Schmidt et al., 2017). In the context of these studies endotracheal intubation of the ewe is not performed as fast and efficient delivery of the foetus is prioritised. Thus hypoxemia is likely to occur and is documented in pregnant ewes undergoing such procedures (Musk & Kemp, 2018). Given that the administration of 100% oxygen at 100 mL/kg/min or at 3 L/min created an inspired oxygen concentration (FIO_2) of approximately 90% and improved the PaO_2 of dogs (Ambros, Carrozzo & Jones, 2018; Wong, Uquillas, Hall, Dart & Dart, 2019) it is likely that a similar effect would occur in pregnant sheep.

The aim of this study was to determine whether 100% oxygen delivered by face mask improved the PaO_2 of pregnant sheep during short term anaesthesia for caesarean delivery of the preterm lamb when compared to an historical cohort.

Twenty-six pregnant singleton Merino ewes at 121–123 days of gestation were involved in this opportunistic study. Care and husbandry of the ewes was as previously described and in accordance with standard procedures for this AAALAC accredited facility (Musk & Kemp, 2018).

The study was performed on blood samples collected from animals enrolled in a study approved by the Animal Ethics Committee of the University of Western Australian in accordance with *The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* (AustralianGovernment, 2013). The ewes were anaesthetised as previously described (Musk & Kemp, 2018), with a combination of midazolam and ketamine administered by intravenous injection through a catheter in the cephalic vein. Following the induction of anaesthesia a subarachnoid injection of lidocaine (60 mg) was administered. Oxygen was delivered by facemask (100%, 3 L/min through a circle breathing system) throughout the procedure. Immediately after delivery of the foetus an off-the-needle arterial blood sample was collected from the ewe's radial artery and from the foetal umbilical vein. The ewe was then euthanased with an intravenous injection of pentobarbitone (160 mg/kg) and the foetus was involved in a project requiring short term mechanical ventilation and then euthanasia.

Blood samples were collected into heparinised syringes (RapidLyte Arterial Line draw Sampler, Siemens Healthcare Diagnostics Pty Ltd, Victoria, Australia) and analysed within 5 min (RapidLab 1265; Siemens Healthcare Diagnostics).

Data from the current study were tested for normality with a Shapiro-Wilk test and compared to data from a previous study (Musk & Kemp, 2018) with a *t*-test for parametric data and a Mann Whitney test for

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non-parametric data (GraphPad Prism 8.3.1, 2019). Normally distributed data are presented as mean (±SD) or mean ± SD (95% confidence interval); otherwise data are median (25–75 percentile). Statistical significance was set at $p < 0.05$.

The ewes weighed 60.7 ± 5.5 kg and were at 122.45 ± 0.96 days of gestation. There was no difference in the weight; gestational age; duration of anaesthesia; and the doses of midazolam and ketamine compared to the previous study (Table 1). The PaO_2 was higher in ewes that received oxygen by facemask. There were no differences in the pH, $PaCO_2$, base excess, haematocrit and haemoglobin concentrations. Blood glucose and lactate concentrations were higher in the current study (Table 1).

The administration of oxygen by facemask to pregnant ewes during short term anaesthesia prior to euthanasia increased the PaO_2 when compared to a previously studied cohort of pregnant ewes. This result supports the value of delivery of oxygen by facemask during such procedures.

The PaO_2 of the ewes was significantly higher when oxygen was administered by facemask but given that the inspired oxygen concentration may have been around 90% it is likely that there remains significant upper airway obstruction and ventilation/perfusion mismatch in these sheep. According to the alveolar gas equation an FIO_2 of 90% should be associated with a PaO_2 of approximately 450 mmHg (Conkin, 2016). The values measured in the current study indicate that while oxygen supplementation improves the PaO_2, other measures to optimise the delivery of oxygen to the lungs require consideration, such as endotracheal intubation and mechanical ventilation.

Other than the PaO_2 the only other differences were the blood glucose and lactate concentrations. Although the difference between these values was statistically significant the values were not considered clinically significant. The ewes were otherwise physiologically similar as the other parameters were comparable and within normal limits (Loughran, Kemp & Musk, 2017).

There are a number of limitations to this study: the comparison to an historical cohort is not ideal but given that the study was opportunistic and that the cohort of animals within the study year was standardised (i.e. oxygen was administered to all or none of the animals to avoid introducing variation to the investigations of the foetal lamb) and the weight, gestational age and anaesthetic protocol was comparable there remains value in the results; and the impact of the improved maternal PaO_2 on the foetus requires investigation.

In the specific context of this study using pregnant sheep for the rapid caesarean delivery of the preterm foetus the administration of oxygen by facemask resulted in a higher maternal PaO_2 when compared to pregnant sheep not receiving supplemental oxygen.

There was no specific funding for this opportunistic study.

Ethics statement

The study was performed on blood samples collected from animals enroled in a study approved by the Animal Ethics Committee of the University of Western Australian in accordance with *The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* (AustralianGovernment, 2013).

Table 1
Anaesthesia time, drug doses and maternal arterial blood gas analysis results. Data are presented as mean ± SD (95% confidence interval) or median (25–75 percentile).

	Without oxygen by mask[7] ($n = 15$)	With oxygen by mask ($n = 26$)	p value
Time to collection of blood samples (minutes)	8.7 ± 1.3 (7.9–9.4)	9.6 ± 2.5 (8.5–10.6)	0.239
Midazolam dose (mg/kg)	0.54 (0.5–0.64)	0.51 (0.47–0.58)	0.1619
Ketamine dose (mg/kg)	10.8 (9.9–12.8)	10.3 (9.4–11.6)	0.1798
Arterial blood analysis variables			
pH	7.36 ± 0.05 (7.32–7.39)	7.34 ± 0.08 (7.31–7.38)	0.606
$PaCO_2$ (mmHg)	43.3 ± 6.2 (39.8–46.7)	44.9 ± 8.2 (41.5–48.5)	0.498
PaO_2 (mmHg)	45.2 (41.1–53.4)	92.6 ± 44.0 (74–111.2)	0.0007*
Base excess (mmol/L)	−1.8 ± 1.5 (−2.6 - −0.9)	−1.7 ± 3.9 (−3.3 - −0.1)	0.953
Glucose (mmol/L)	2.9 ± 0.6 (2.6–3.3)	3.7 (3.4–4.8)	<0.0001*
Lactate (mmol/L)	2.0 ± 0.7 (1.6–2.4)	3.2 ± 1.1 (2.7–3.7)	0.001*
Haematocrit (%)	31.3 ± 1.9 (30.2–32.4)	30.9 ± 2.9 (29.7–32.2)	0.661
Haemoglobin (g/L)	106.8 ± 6.9 (103–110.6)	105.3 ± 9.9 (101.1–109.5)	0.610

* $p < 0.05$.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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