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RESEARCH PAPER

Comparison of different methods to calculate venous admixture in anaesthetized horses

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Abstract

Objective The aim of this study was to compare different methods to determine venous admixture ($\dot{Q}_s/\dot{Q}_t$) in anaesthetized horses. The first objective was to estimate $\dot{Q}_s/\dot{Q}_t$ using jugular venous blood oxygen content ($\dot{Q}_s/\dot{Q}_{t\ jugular}$), and a fixed value for the oxygen extraction (F-shunt). The second objective was to assess the influence of blood pressure and positioning on oxygen extraction. The third objective was to perform regression analysis between jugular and mixed venous blood oxygen tensions.

Study design Prospective, experimental trial.

Animals The study was performed with seven warmblood horses that were anaesthetized with detomidine, butorphanol, ketamine, diazepam and isoflurane in oxygen.

Methods Multiple simultaneous arterial, jugular venous and pulmonary arterial blood samples were taken under normotensive and hypotensive conditions in lateral and dorsal recumbency. Arterial, mixed venous, and end-capillary oxygen content were calculated.

Results A significant correlation between $\dot{Q}_s/\dot{Q}_t$ and $\dot{Q}_s/\dot{Q}_{t\ jugular}$ was found [intraclass correlation coefficient (ICC) = 0.68, $p < 0.001$], and Bland–Altman analysis showed a bias of −11.5% and wide limits of agreement (−27.7% to 4.6%). F-shunt significantly correlated with $\dot{Q}_s/\dot{Q}_t$ (ICC = 0.88, $p < 0.001$), and Bland–Altman analysis showed a lower bias (−1.97) and narrower limits of agreement (−13.8% to 9.9%). Positioning and blood pressure significantly influenced oxygen extraction. The regression formula was $Y = 0.80X + 2.61$ (where Y is the calculated mixed venous oxygen tension and X is the jugular venous oxygen tension) when outliers were excluded (ICC=0.82, $p < 0.001$).

Conclusions and clinical relevance This study shows that F-shunt provides reasonable estimates of $\dot{Q}_s/\dot{Q}_t$ but can possibly be improved by using simple algorithms without the need for pulmonary arterial catheterization. These algorithms use blood pressure- and positioning-dependent oxygen extraction and regression analysis between jugular venous and pulmonary arterial oxygen tension. Although promising, the validity of these algorithms needs to be determined in future studies.

Keywords anaesthesia, equine, oxygen content, $\dot{Q}_s/\dot{Q}_t$, venous admixture.

Introduction

Anaesthetized horses are at risk of developing hypoxaemia as a result of ventilation − perfusion ($\dot{V}/\dot{Q}$) mismatch, leading to venous admixture (Nyman et al. 1990). Furthermore, oxygen delivery to the peripheral tissues may be compromised as a result of decreases in cardiac output and arterial blood pressure during general anaesthesia (Steffey 2002; De Vries et al. 2009). The combination of hypoxaemia and decreases in cardiac output likely increases equine anaesthesia-related risk significantly (Hubbell and Muir 2015).

The gold standard for determining venous admixture ($\dot{Q}_s/\dot{Q}_t$) is calculation using the Berggren 'shunt equation': $\dot{Q}_s/\dot{Q}_t = \frac{(Cc'O2) - \text{arterial oxygen content } (CaO2)}{Cc'O2 - \text{mxedvenous oxygen content } (CmvO2)}$ (Berggren 1942). This 'shunt equation' requires pulmonary arterial (mixed venous) as well as peripheral arterial

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blood sampling, whereas pulmonary end-capillary blood oxygen content is calculated from inspiratory oxygen fraction (FIO_2) and arterial carbon dioxide tension ($PaCO_2$) using the alveolar gas equation. In experimental studies, this approach is feasible and is used to obtain the most accurate calculation of venous admixture in anaesthetized horses (Mosing et al. 2016). However, pulmonary artery catheterization is a more invasive procedure that requires more sophisticated equipment. In critically ill human patients, central venous blood samples have been used as a surrogate for mixed venous blood samples (Rivers et al. 2001). However, in human patients (Martin et al. 1992) and in canine experimental studies (Martin et al. 1985), central venous oxygen saturation may be similar to mixed venous oxygen saturation, but the correlation is not consistently high enough to allow simple substitution for mixed venous oxygen values.

An alternative method to determine venous admixture is to assume a fixed arterial to mixed venous oxygen content difference [$C(a-v)O_2$] of 3.5 mL dL^{-1}, thus negating the need for a pulmonary artery catheter. This estimate has become known as 'F-shunt' and has shown reasonable to good agreement with venous admixture calculations based on mixed venous blood samples in humans (Wandrup 1995), anaesthetized sheep (Araos et al. 2012) and horses (Briganti et al. 2015). However, the assumption of a fixed oxygen extraction ignores the possibility of changes in oxygen extraction as a result of changes in tissue perfusion and the state of cellular metabolism. If oxygen delivery decreases, oxygen extraction may increase in order to maintain aerobic conditions in the peripheral tissues (McLellan & Walsh 2004). In human patients with septic shock, oxygen extraction may be very low because of the inability of the tissues to extract and/or utilize oxygen. Therefore, during tissue hypoperfusion and/or in critically ill patients, assuming a fixed arterial to mixed venous oxygen content difference to calculate venous admixture may produce inaccurate results (Park et al. 2015).

The aim of this study was to improve the estimation of $\dot{Q}_s/\dot{Q}_t$ in anaesthetized horses, without the need for mixed venous blood sampling. The first objective was to compare the correlation between venous admixture ($\dot{Q}_s/\dot{Q}_t$) with venous admixture estimated from jugular venous blood oxygen content values ($\dot{Q}_s/\dot{Q}_{t\ jugular}$), and with venous admixture estimated from a fixed value for the arterio-venous oxygen content difference (F-shunt). The second objective was to calculate arterio-venous oxygen content differences during states of arterial normo- and hypotension and during lateral and dorsal recumbency. The third objective was to calculate regression formulas describing the relationship between jugular venous oxygen tension ($PjvO_2$) and pulmonary arterial mixed venous oxygen tension ($P\bar{v}O_2$). These new algorithms should then be tested in a new data set to determine their accuracy to estimate $\dot{Q}_s/\dot{Q}_t$.

Materials and methods

Study design

The study was designed as a prospective experimental trial and was performed with seven healthy (American Society of Anesthesiologists status I) warmblood horses (Table 1) anaesthetized for an unrelated nonrecovery procedure. The study was approved by the institutional ethics committee on animal experimentation, in accordance with Dutch national legislation on experimental animal use (2013. III.01.012).

Anaesthesia

Horses were premedicated with detomidine intravenous (IV) 0.01 mg kg^{-1} (Domosedan; Orion Pharma, Finland) and butorphanol IV 0.02 mg/kg (Dolorex; MSD Animal Health, The Netherlands). The jugular vein was catheterized with an IV catheter (Intraflon; Q2 12 gauge, 80 mm). General anaesthesia was induced with ketamine 2.2 mg kg^{-1} IV (Narketan; Vetoquinol, The Netherlands) and diazepam 0.05 mg/kg IV (Diazepam; Centrafarm, The Netherlands), and the trachea was intubated with a cuffed endotracheal tube (internal diameter 26 mm). Horses were connected to a large animal circle (BDO Medipass, The Netherlands) and mechanically ventilated (Smith; BDO Medipass). Anaesthesia was maintained with an end-tidal isoflurane ($F_E'Iso$) concentration of 1.2−1.4% (Isoflo; AST Farma, The Netherlands) in oxygen supplemented with a detomidine constant rate infusion (CRI; 0.01 mg kg^{-1} $hour^{-1}$). During anaesthesia, normotension was maintained by a crystalloid infusion (Ringers; 5−10 mL kg^{-1} $hour^{-1}$) Q3 and a dobutamine CRI (Dobutamine; Hameln Pharma, Germany; 1−5 μg kg^{-1} $minute^{-1}$ to effect) to maintain mean arterial pressure (MAP) above 70 mmHg. Hypotension was induced by increasing isoflurane concentration towards 2−2.4% $F_E'Iso$ and Q4 cessation of dobutamine CRI. Monitoring of

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