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RESEARCH PAPER

Effect of ephedrine and phenylephrine on cardiopulmonary parameters in horses undergoing elective surgery

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Abstract

Objective To assess the cardiopulmonary effects of ephedrine and phenylephrine for management of isoflurane-induced hypotension in horses.

Study design Prospective randomized clinical study.

Animals Fourteen isoflurane-anesthetized horses undergoing digital palmar neurectomy.

Methods Ephedrine (EPH group; 0.02 mg kg^{-1} $minute^{-1}$; $n = 7$) or phenylephrine (PHE group; 0.002 mg kg^{-1} $minute^{-1}$; $n = 7$) was administered to all horses when mean arterial pressure (MAP) was <60 mmHg. The infusions were ended when the target MAP was achieved, corresponding to a 50% increase over the pre-infusion MAP (baseline). The horses were instrumented with an arterial catheter to measure blood pressure and allow the collection of blood for pH and blood-gas analysis and a Swan-Ganz catheter for measurement of cardiac output using thermodilution. Cardiopulmonary parameters were recorded at baseline and at 5, 30, 60 and 90 minutes after achieving the target MAP.

Results In both groups, the MAP and systemic vascular resistance (SVR) increased significantly at 5, 30, 60 and 90 minutes post infusion compared to baseline ($p < 0.05$). The EPH group had a significant increase in cardiac index (CI) and systemic oxygen delivery index at 5, 30, 60 and 90 minutes post infusion compared to baseline ($p < 0.05$) and compared to the PHE group ($p < 0.05$). The PHE group had significantly higher SVR and no decrease in oxygen extraction compared with the EPH group at 30, 60 and 90 minutes post infusion ($p < 0.05$). No significant differences in ventilatory parameters were observed between groups after the infusion.

Conclusions Ephedrine increased the MAP by increasing CI and SVR. Phenylephrine increased MAP by increasing SVR but cardiac index decreased. Ephedrine resulted in better tissue oxygenation than phenylephrine.

Clinical relevance Ephedrine would be preferable to phenylephrine to treat isoflurane-induced hypotension in horses since it increases blood flow and pressure.

Keywords anesthesia, arterial blood pressure, ephedrine, horses, phenylephrine.

Introduction

Inhalational anesthesia produces a dose-related cardiovascular depression in horses (Steffey & Howland 1980), resulting in arterial hypotension and impairment of skeletal muscle blood flow (Lee et al. 2002). These effects contribute significantly to the production of post-anesthetic myopathy which is

associated with anesthetic-related deaths and post-operative morbidity in this species (Johnston et al. 2002; Raisis 2005; Duke et al. 2006; Voulgaris & Hofmeister 2009). To prevent post-anesthetic myopathy, prevention of myocardial depression and maintenance of tissue blood flow are of major importance in the anesthetized horse (Raisis 2005). A reduction in anesthetic depth, high-volume fluid therapy and cardiovascular support with drugs to maintain a mean arterial pressure (MAP) above 70 mmHg have been recommended to achieve this goal (Richey et al. 1990; Raisis et al. 2000b; Driessen et al. 2006; Duke et al. 2006).

Dobutamine is the most commonly administered vasoactive agent used to treat hypotension during inhalation anesthesia in horses. This β-1 agonist improves myocardial contractility, which is the main cause of hypotension induced by halothane (Hellyer et al. 1991; Gehlen et al. 2006). In horses anesthetized with isoflurane, however, it has been suggested that myocardial contractility is better preserved compared to halothane and that decreased systemic vascular resistance (SVR) is the main cause for hypotension (Steffey & Howland 1980; Raisis et al. 2000a). In addition, isoflurane has been documented to cause less cardiovascular depression than halothane (Raisis et al. 2005; Blissitt et al. 2008). Therefore, it has been suggested that alpha-adrenergic drugs, such as ephedrine (EPH) and phenylephrine (PHE), may be helpful for improving MAP, cardiac output (CO) and intramuscular blood flow when isoflurane is used (Lee et al. 2002; Raisis 2005).

EPH is a synthetic, non-catecholamine, sympathomimetic amine that acts directly and indirectly (through the release of norepinephrine from sympathetic nerve endings) on alpha- and beta-adrenergic receptors (Daunt 1990; Egger et al. 2009). EPH is an inexpensive drug that produces a prolonged hemodynamic improvement from a single bolus dose and has been proven to improve intramuscular blood flow in horses anesthetized with halothane (Grandy et al. 1989; Lee et al. 2002). PHE is another synthetic vasoactive drug with alpha-1 adrenergic activity that has been reported to be effective in treating severe peripheral vasodilation in horses (Dugdale et al. 2007). When administered as a first-line vasopressor agent in humans with septic shock, PHE is effective in increasing the mean arterial pressure (MAP) without compromising gastrointestinal and hepatosplanchnic perfusion as compared with norepinephrine (Morelli et al. 2008). PHE has been used to induce splenic contraction in the treatment of nephrosplenic entrapment of the large colon (Hardy et al. 1994; Frederick et al. 2010; Lindegaard et al. 2011). Its hemodynamic effects in horses with inhalation agent-induced hypotension to our knowledge have not been published.

Although advantages have been described regarding the use of EPH and PHE in experimental studies in other species, there is still a paucity of information available on the cardiopulmonary effects of these drugs for treating isoflurane-induced hypotension in horses under clinical conditions (Grandy et al. 1989; Hardy et al. 1994; Lee et al. 2002; Frederick et al. 2010). Therefore, the aim of this study was to investigate the effects of EPH and PHE infusions on hemodynamic and oxygenation parameters in horses with isoflurane-induced hypotension. The hypothesis was that EPH and PHE would improve hemodynamics and tissue oxygen delivery, when administered to horses with hypotension during isoflurane anesthesia.

Materials and methods

Animals

This study was conducted in accordance with the guidelines of the Ethical Principles in Animal Research of our institution (protocol #2286). Informed consent was obtained from the owners before inclusion of their animals in the study. Fourteen client-owned, healthy horses, aged 2–8 years and weighing 410–520 kg, were used. Animals were included in the study if no clinical cardiopulmonary abnormalities were detected after a complete physical examination and hematological and biochemical tests were performed, if they were scheduled for palmar digital neurectomy surgery in dorsal recumbency, and if they had arterial hypotension during surgery (MAP < 60 mmHg).

Anesthesia

Food was withheld for 12 hours and water for 4 hours before anesthesia. A 14-gauge catheter was fixed in the left jugular vein for intravenous (IV) administration of drugs and fluids. Phenylbutazone and amikacin were administered before anesthesia and continued for 3 days after surgery. The horses were premedicated with romifidine (0.1 mg kg^{-1}, Sedivet; Boehringer Ingelheim Vetmedica, MO, USA) and, after 20 minutes, diazepam (0.05 mg kg^{-1},