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RESEARCH PAPER

Influence of detomidine and xylazine on spleen dimensions and on splenic response to epinephrine infusion in healthy adult horses

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Abstract

Objective To compare the changes in splenic length and thickness and in packed cell volume (PCV) following detomidine or xylazine administration and subsequent epinephrine infusion. Hypothesis: Spleen relaxation occurs following xylazine or detomidine administration and interferes with subsequent splenic contractile response to epinephrine.

Study design Randomized non-blinded crossover experimental study.

Animals 6 healthy adult mares.

Methods The mares received an intravenous (IV) epinephrine infusion (1 μg kg^{-1} $minute^{-1}$ over 5 minutes) one hour after IV administration of detomidine (0.01 mg kg^{-1}), xylazine (0.5 mg kg^{-1}) or no drug (control), with a withdrawal period of at least 7 days between experiments. The splenic length measured in two different axes, the splenic thickness, and the PCV were measured prior to sedation (T0), 30 minutes later, and at 5-minute intervals from the start of the epinephrine infusion (T1) until T1 + 40 minutes. Changes from base-line and between treatments were compared using a two-way ANOVA for repeated measures. Significance was set at $p < 0.05$.

Results Splenic length was significantly increased and PCV was significantly decreased after detomidine administration compared to baseline. Epinephrine infusion resulted in a significant decrease in splenic length and thickness, and a significant increase in PCV, irrespective of prior treatment with detomidine or xylazine.

Conclusions Detomidine administration was followed by a sonographically detectable increase of splenic length. Neither detomidine nor xylazine interfered with the ability of the spleen to contract following subsequent administration of an epinephrine infusion given one hour later.

Clinical relevance Previous sedation with alpha-2 agonists does not preclude the efficiency of epinephrine as a medical treatment of left dorsal displacement of the large colon, but further investigations are required with other drug doses and different time intervals between administrations.

Keywords detomidine, epinephrine, spleen, ultrasound, xylazine.

Introduction

Administration of alpha-adrenergic agents to promote splenic contraction is a common procedure in the medical treatment of left dorsal displacement of

the large colon (LDDLC) in adult horses (Hardy et al. 2000; Lindegaard et al. 2011). The smooth muscle fibers embedded in the spleen capsule have the property to contract in response to elevated catecholamine concentrations (Tablin & Weiss 1983) or alpha adrenergic agonist drugs, with subsequent reduction of the splenic size and increase in the packed cell volume (PCV) (Snow 1979; Hardy et al. 1994; Venner et al. 2001). Splenic contraction results in an enlargement of the space between the spleen and the abdominal wall, thus increasing the likelihood of the left colon to move back into its natural position.

Phenylephrine, a specific alpha-1 adrenergic agonist, is the drug most commonly recommended for this indication (Hardy et al. 2000; Lindegaard et al. 2011), but it is currently not available in an injectable form for veterinary use in many countries. Epinephrine (adrenaline) is a mixed alpha-1, alpha-2 and beta adrenergic agonist used widely in cardiovascular resuscitation and is accessible to veterinary practitioners. The efficiency of epinephrine infusion to promote splenic contraction in standing adult horses has been established (Snow 1979; Venner et al. 2001).

It is also common for horses suffering from LDDLC to be treated with alpha-2 adrenergic agonists such as xylazine and detomidine, primarily for their sedative and analgesic properties. Alpha-2 agonists prevent the liberation of noradrenergic neurotransmitters from the pre-synaptic neurons in the central nervous system and, to a lesser extent, activate peripheral alpha adrenergic receptors (Virtanen & MacDonald 1985; Cavalli et al. 2002; Daunt & Steffey 2002). They produce a dose-related and biphasic cardiovascular response with transient initial vasoconstriction and hypertension resulting from the activation of peripheral alpha receptors (Posner & Burns 2009), followed by a prolonged phase of reduced blood pressure (Gasthuys et al. 1990; Wagner et al. 1991). Heart rate and sympathetic tone remain low, and in the latter stages of the drug effect, peripheral vascular resistance decreases (Posner & Burns 2009).

Administration of xylazine or detomidine is followed by a decrease in PCV (Gasthuys et al. 1990; Wagner et al. 1991), the mechanism of which is not fully elucidated. A fluid shift from the extravascular compartment to the intravascular space may occur as alpha-2 agonists stimulate the secretion of atrial natriuretic factor (Daunt & Steffey 2002; Talukder & Hikasa 2009). This effect may result in a relative increase of plasma volume and a relative drop of PCV. An increased erythrocyte pool in the splenic vascular bed has also been mentioned as explanation for the decrease in PCV (Gasthuys et al. 1990; Wagner et al. 1991; Nunez et al. 2004; Lording 2008), given the fact that variations in spleen volume and sympathetic tone are the main causes of rapid changes in PCV in horses (Torten & Schalm 1964; Lording 2008). In a study of Navas et al. (2009), the splenic volume, extrapolated from ultrasonographic measurements, was slightly increased after detomidine administration but the difference was not significant. To our knowledge, the changes in direct splenic measurement following alpha-2 agonist administration in horses have not been studied.

Acepromazine (0.3 mg kg^{-1}) injected intramuscularly can prevent the increase in PCV following subsequent epinephrine infusion (Snow 1979), but a similar interaction of alpha-2 agonists with epinephrine is not documented.

The objective of the present study was to measure and compare the changes in splenic length and thickness, and changes in PCV following detomidine or xylazine administration and subsequent epinephrine infusion in healthy adult horses. We hypothesized that sonographically detectable splenic relaxation occurs following sedation with alpha-2 agonists, and interferes with either the amplitude or duration of the splenic contraction induced by epinephrine. This would be of clinical relevance in the medical management of LDDLC.

Materials and Methods

Animals

The experimental procedures were carried out under institutional ethical authorization (n°6935D), in compliance with the local guiding principles for the care and use of laboratory animals and conformed to the guidelines of the Guide for the Care and Use of Laboratory Animals (National Academies Press, Washington D, 2011).

Six healthy adult mares of mixed breed, aged 5–18 years (mean 10 years) and weighing 500–620 kg were used in this study. The mares belonged to the veterinary teaching hospital. They were regularly vaccinated and dewormed and were clinically healthy with no history of prior abdominal disease. They were housed in a paddock with free access to grass hay, and were used for teaching