J. vet. Pharmacol. Therap. **21**, 497–499, 1998. SHORT COMMUNICATION

The effects of dobutamine and ephedrine on packed cell volume, total protein, heart rate, and blood pressure in anaesthetized horses

P. W. HELLYER
A. E. WAGNER
K. R. MAMA &
J. S. GAYNOR

Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80523, USA

(Paper received 24 July 1998; accepted for publication 1 September 1998)

INTRODUCTION

Anaesthetized horses frequently require treatment for arterial hypotension (Donaldson, 1988). The administration of inotropic drugs, such as dobutamine or ephedrine, is one of the primary methods used to restore acceptable blood pressure in anaesthetized horses. The haemodynamic effects of dobutamine, a catecholamine with direct acting β_1-, β_2-, and α-adrenoceptor agonist activity (Ruffolo & Messick, 1985; Vernon *et al.*, 1992), have been well characterized in the anaesthetized horse (Swanson *et al.*, 1985). Dobutamine (2.5–5.0 μg/kg/min) increased oxygen delivery in ponies (Gasthuys *et al.*, 1991) and horses (Dyson & Pascoe, 1990; Wertz *et al.*, 1992) partly by increasing cardiac output and partly by increasing haemoglobin concentration. Anaesthetized horses administered dobutamine (> 1.5 μg/kg/min) may develop reflex decreases in heart rate or a number of atrial and ventricular arrhythmias (Swanson *et al.*, 1985; Donaldson, 1988; Light & Hellyer, 1993).

Ephedrine is a nonselective synthetic catecholamine that acts directly and indirectly (through the release of noradrenaline) on α-and β-adrenergic receptors (Stoelting, 1987). The haemodynamic effects of ephedrine has been investigated in anaesthetized dogs (Wagner *et al.*, 1993) and horses (Grandy *et al.*, 1989). Ephedrine increased cardiac output with no changes in heart rate or rhythm (Grandy *et al.*, 1989). Whereas a high dose of ephedrine (0.25 mg/kg, intravenously (i.v.)) increased ha emoglobin concentration in dogs (Wagner *et al.*, 1993), the effects of ephedrine on packed cell volume (PCV) has not been reported in clinically anaesthetized horses. The objectives of this study were to determine the effects of dobutamine and ephedrine on heart rate, blood pressure, PCV and total plasma protein (TP) in clinically anesthetized, hypotensive horses.

Data were collected from 41 client-owned horses which were anaesthetized at the Colorado State University Veterinary Teaching Hospital for a variety of surgical procedures. The anaesthetic protocol was tailored to the individual animal and was not standardized. Horses were sedated with xylazine and anaesthesia induced with guaifenesin or diazepam followed by ketamine or thiopental. Anaesthesia was maintained with either halothane or isoflurane in oxygen administered to effect. A balanced electrolyte solution (Normosol-R, Abbott Laboratories, North Chicago, IL) was administered at a rate of ≈ 10 mL/kg/h, intravenously. Arterial blood pressure was measured with a catheter percutaneously placed in the facial, transverse facial, or greater metatarsal artery and connected to a calibrated strain gauge transducer (Code Transducer, Aragon Medicals, Athens, TX). Zero pressure was considered to be the point of the shoulder with the horse in dorsal recumbency, and the sternum in lateral recumbency. Horses with arterial hypotension (mean arterial pressure < 65 mmHg) were administered either ephedrine (Ephedrine sulfate, Abbott Laboratories, North Chicago, IL) (0.06 mg/kg, i.v., 1–2 boluses) or dobutamine (Abbott Laboratories, North Chicago, IL) (1–4 μg/kg/min, i.v.) after obtaining baseline measurements of heart rate, mean arterial pressure, PCV and TP. Blood samples for the determination of PCV and TP were obtained percutaneously from a peripheral vein or the indwelling arterial catheter ($n = 1$). The selection of inotrope to treat hypotension was left up to the discretion of the individual anaesthetist managing the case. Heart rate, mean arterial pressure, PCV and TP were obtained at 5 and 15 min after beginning inotrope administration. The effect of treatment (dobutamine, ephedrine) over time on measured parameters was analysed using a two-way ANOVA for repeated measures. If differences were significant, a Bonferroni/Dunn test was used for specific time comparisons. $P < 0.05$ was considered statistically significant. The effects of ephedrine and dobutamine on measured parameters were not compared to each other as there was no attempt made to administer equivalent inotropic doses of the two drugs. Data are presented as mean ± standard deviation.

Dobutamine was administered to 28 horses which were 6.0 ± 4.8 years of age and weighing ≈ 443 ± 99 kg. Dobutamine was administered at a rate of ≈ 1–2 μg/kg/min ($n = 24$) and 2–4 μg/kg/min ($n = 4$). Ephedrine was administered to 13 horses which were 3.3 ± 3.9 years of age and weighing ≈ 399 ± 128 kg. Table 1 shows that dobutamine and ephedrine significantly increased mean arterial pressure at 5 min as compared to baseline. Dobutamine further increased mean arterial pressure at 15 min as compared to baseline and 5 min.

Table 1. Clinical use of dobutamine and ephedrine in anaesthetized horses

		Baseline	5 min	15 min	ANOVA
MAP	Dobutamine	49 ± 7^a	63 ± 11^b	71 ± 9^c	< 0.0001
(mmHg)	Ephedrine	50 ± 5^a	57 ± 6^b	62 ± 7^b	< 0.0001
HR	Dobutamine	38 ± 10^a	34 ± 9^a	34 ± 11^a	n.s.
(beats/min)	Ephedrine	39 ± 9^a	34 ± 7^a	35 ± 10^a	n.s.
PCV	Dobutamine	30 ± 6^a	32 ± 6^a	36 ± 7^b	0.0006
(%)	Ephedrine	31 ± 4^a	31 ± 4^a	32 ± 4^a	n.s.
TP	Dobutamine	6.0 ± 0.8^a	6.0 ± 0.7^a	5.9 ± 0.9^a	n.s.
(g/dL)	Ephedrine	6.1 ± 0.5^a	5.9 ± 0.5^a	5.9 ± 0.4^a	n.s.

Values are mean $\pm$ SD. Within each row, values with the same superscript are not different from one another. Dobutamine ($n = 28$) was administered as a constant rate infusion (1–4 μg/kg/min) and ephedrine ($n = 13$) was administered as one or two boluses (0.06 mg/kg, i.v.). MAP = mean arterial pressure, HR = heart rate, PCV = packed cell volume, TP = total plasma protein. n.s. = not statistically significant.

Heart rate tended to decrease following dobutamine and ephedrine; however, changes were not significant with either treatment. No arrhythmias were noted with either treatment. Dobutamine significantly increased PCV at 15 min as compared to baseline. Anaesthetic induction drug (ketamine or thiopental) did not significantly affect the change in PCV (data not shown). PCV did not change significantly after ephedrine administration. TP did not change significantly with either treatment. The mean volume of intravenous crystalloid fluids administered during the 15 min after inotrope administration was 3.7 ± 1.9 and 5.4 ± 3.6 mL/kg, for dobutamine and ephedrine treated horses, respectively. The mean volume of crystalloid fluids administered did not differ significantly between dobutamine and ephedrine treated horses.

The doses of dobutamine and ephedrine used in this study are standard doses used at Colorado State University to treat hypotension in horses. Our results demonstrate that dobutamine, but not ephedrine, increased PCV at 15 min when administered in clinically useful doses to anaesthetized horses. The induction of general anaesthesia may decrease PCV compared to values obtained in conscious horses by two separate, but related mechanisms (Jain, 1986; Wagner *et al.*, 1993). Inhibition of α-adrenergic receptors by anaesthetic drugs may cause vasodilation and splenic sequestration of red blood cells. Secondly, a reduction in intravascular hydrostatic pressure may allow extravascular fluids to shift to the intravascular space, thereby diluting the red blood cells. The mechanism for the increase in PCV observed in this clinical study with dobutamine was not determined, but is consistent with our clinical impressions, and the results of previous studies in horses (Dyson & Pascoe, 1990; Gasthuys *et al.*, 1991; Wertz *et al.*, 1992). Excitement, exercise, stress, and epinephrine may significantly increase PCV in horses secondary to splenic contraction (Jain, 1986). Dobutamine exerts α-adrenergic activity and has been shown to cause splenic contraction (Fuchs *et al.*, 1980). Although ephedrine also exerts α-adrenergic activity (Stoelting, 1987), the dose used in this study may have been insufficient to cause splenic contraction. Dobutamine-induced increases in cardiac output may have increased intravascular hydrostatic pressure, thereby shifting fluid out of the vasculature and increasing PCV. Although we did not measure cardiac output, dobutamine has been shown to increase cardiac output and arterial pressure in a dose-dependent manner in horses (Swanson *et al.*, 1985). As TP did not change with the administration of dobutamine, it is likely that the PCV increased as a result of splenic contraction rather than as a result of fluid shifts out of the vasculature. Although ephedrine may cause splenic contraction with a concomitant increase in PCV (Davies & Withrington, 1973), and has been shown to increase PCV in anaesthetized dogs (Wagner *et al.*, 1993), the i.v. dose required to do so in anaesthetized dogs (0.25 mg/kg) was much higher than the dose used in this study (0.06 mg/kg).

Dobutamine and ephedrine both significantly increased arterial blood pressure without significant changes in heart rate in this study. At the doses used, dobutamine tended to increase mean arterial pressure to a greater extent than ephedrine. This study was not designed to compare equipotent doses of ephedrine and dobutamine; however, these results support our clinical impression that dobutamine is more efficacious than ephedrine at increasing arterial blood pressure in anaesthetized horses. Although heart rate changes were not statistically significant in this study, the changes observed were qualitatively similar to heart rate changes observed in horses administered higher doses of dobutamine (3, 5, 10 μg/kg/min) (Swanson *et al.*, 1985). It is possible that significant heart rate changes were not observed in our study either because of clinical variability between animals, or because the doses of dobutamine administered in our study were not high enough or were not administered for a long enough period of time to induce statistically significant changes in heart rate. Nevertheless, the clinician should be prepared for a decrease in heart rate when administering either ephedrine or dobutamine to anaesthetized horses. Changes in PCV may be important to monitor in an anaesthetized horse to aid in the assessment of hydration status and blood loss; therefore, factors such as inotrope used that may affect PCV, should also be taken into account. In summary, this clinical study demonstrated that dobutamine significantly increased PCV, but not TP, and both dobutamine and ephedrine increased arterial blood pressure with only a small decrease in heart rate. Further work is needed to determine the mechanism(s) responsible for the dobutamine-induced increase in PCV, and to determine if there is a dose-dependent increase in PCV with ephedrine in anaesthetized horses.

REFERENCES

Davies, B.N. & Withrington, P.G. (1973) The actions of drugs on the smooth muscle of the capsule and blood vessels of the spleen. *Pharmacological Review*, **25,** 373–413.

Donaldson, L.L. (1988) Retrospective assessment of dobutamine therapy for hypotension in anesthetized horses. *Veterinary Surgery*, **17,** 53–57.

Dyson, D.H. & Pascoe, P.J. (1990) Influence of preinduction methoxamine, lactated Ringer solution, or hypertonic saline solution infusion or post-induction dobutamine infusion on anesthetic-induced hypotension in horses. *American Journal of Veterinary Research*, **51,** 17–21.

Fuchs, R.M., Rutlen, D.L. & Powell, W.J. (1980) Effect of dobutamine on systemic capacity in the dog. *Circulation Research*, **46,** 133–138.

Gasthuys, F., de Moor, A. & Parmentier, D. (1991) Influence of dopamine and dobutamine on the cardiovascular depression during a standard halothane anaesthesia in dorsally recumbent, ventilated ponies. *Zentralblatt Fur Veterinarmedizin-Reihe A*, **38,** 494–500.

Grandy, J.L., Hodgson, D.S., Dunlop, C.I., Chapman, P.L. & Heath, R.B. (1989) Cardiopulmonary effects of ephedrine in halothane-anesthetized horses. *Journal of Veterinary Pharmacology and Therapeutics*, **12,** 389–396.

Jain, N.C. (1986) The horse: Normal hematology with comments on response to disease. In *Schalm's Veterinary Hematology*, 4th edn, pp. 140–177. Lea & Febiger, Philadelphia.

Light, G.S. & Hellyer, P.W. (1993) Effects of atropine on the arrhythmogenic dose of dobutamine in xylazine-thiamylal-halothane anesthetized horses. *American Journal of Veterinary Research*, **54,** 2099–2103.

Ruffolo, R.R. & Messick, K. (1985) Systemic hemodynamic effects of dopamine, (±) -dobutamine and the (+)- and (-)-enantiomers of dobutamine in anesthetized normotensive rats. *European Journal of Pharmacology*, **109,** 173–181.

Stoelting, R.K. (1987) Sympathomimetics. In *Pharmacology and Physiology in Anesthetic Practice*, pp. 251–268. J.B. Lippincott Company, Philadelphia.

Swanson, C.R., Muir, W.W., Bednarski, R.M., Skarda, R.T. & Hubbell, J.A.E. (1985) Hemodynamic responses in halothane-anesthetized horses given infusions of dopamine or dobutamine. *American Journal of Veterinary Research*, **46,** 365–370.

Vernon, D.D., Garrett, J.S., Banner, W. & Dean, J.M. (1992) Hemodynamic effects of dobutamine in an intact animal model. *Critical Care Medicine*, **20,** 1322–1329.

Wagner, A.E., Dunlop, C.I. & Chapman, P.L. (1993) Effects of ephedrine on cardiovascular function and oxygen delivery in isoflurane-anesthetized dogs. *American Journal of Veterinary Research*, **54,** 1917–1922.

Wertz, E.M., Dunlop, C.I., Wagner, A.E., Heath, R.B. & Chapman, P.L. (1992) Cardiovascular and oxygenation responses to dobutamine and dopamine in halothane-anesthetized horses (Abstract). *Veterinary Surgery*, **21,** 501.