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

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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 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 haemoglobin 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 anaesthetized, 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 3.9 years of age and weighing ≈ 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.
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 intravascular administration was 3.7 ± 1.9 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.

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

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>5 min</th>
<th>15 min</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP Dobutamine</td>
<td>49 ± 7</td>
<td>63 ± 11</td>
<td>71 ± 9</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>(mmHg) Ephedrine</td>
<td>50 ± 5</td>
<td>57 ± 6</td>
<td>62 ± 7</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HR Dobutamine</td>
<td>38 ± 10</td>
<td>34 ± 9</td>
<td>34 ± 11</td>
<td>n.s.</td>
</tr>
<tr>
<td>(beats/min) Ephedrine</td>
<td>39 ± 9</td>
<td>34 ± 7</td>
<td>35 ± 10</td>
<td>n.s.</td>
</tr>
<tr>
<td>PCV Dobutamine</td>
<td>30 ± 6</td>
<td>32 ± 6</td>
<td>36 ± 7</td>
<td>0.0006</td>
</tr>
<tr>
<td>(%) Ephedrine</td>
<td>31 ± 4</td>
<td>31 ± 4</td>
<td>32 ± 4</td>
<td>n.s.</td>
</tr>
<tr>
<td>TP Dobutamine</td>
<td>6.0 ± 0.8</td>
<td>6.0 ± 0.7</td>
<td>5.9 ± 0.9</td>
<td>n.s.</td>
</tr>
<tr>
<td>(g/dL) Ephedrine</td>
<td>6.1 ± 0.5</td>
<td>5.9 ± 0.5</td>
<td>5.9 ± 0.4</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Values are mean ± 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.
REFERENCES


