SODIUM ACETATE, AN ARTERIAL VASODILATOR: 
HAEMODYNAMIC CHARACTERISATION IN NORMAL DOGS

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Summary

Sodium acetate (SA) has been implicated in hypotensive episodes of haemodialysis because of its vasodilatory effects. The haemodynamic correlates of the changes in blood pressure, cardiac output (CO) and total peripheral resistance (TPR) are well known but the site of action of SA (i.e. arteriolar, venular or both) is not yet clarified. We thus studied the changes in CO, TPR and mean arterial pressure (MAP) induced by four graded doses of SA (0.034 to 0.300 mEq/kg/min) in seven normal dogs. To evaluate the site of vasodilation we also measured the changes in cardiopulmonary volume (CPV), mean pulmonary artery pressure (MPAP) and mean transit time (MTT). From control to the highest infusion rate, CO increased from 1.63±0.20 to 3.59±0.38L/min (p<0.001), TPR decreased from 78.2±11.3 to 36.4±4.8A.U. (p<0.001). MAP rose significantly from 107.2±4.0 to 116.5±8.5mmHg (p<0.05) and stroke volume was maintained (17.2±2.3 to 19.6±2.1ml, NS) in spite of the marked tachycardia observed (heart rate from 106.1±7.6 to 194.8±9.1bpm, p<0.001). This was associated with increases in MPAP (from 13.3±0.7 to 19.6±2.1mmHg, p<0.01) and CPV (from 195.0±21.3 to 224.4±24.3ml, p<0.01) and marked decrease in MTT (from 7.74±0.73 to 3.78±0.22sec, p<0.01). Our data show that marked increases in CO occur associated with vasodilation induced by SA and that MAP increases significantly; the decrease in MTT shows that hyperkinetic circulation is induced by the infusion. This may be due to a sympathetic reflex activity originated by the increase in CPV and MPAP. This haemodynamic pattern strongly suggests an arterial site of action of acetate as a vasodilator. Because MAP increased during infusion, a stimulatory effect of acetate itself must also be postulated to explain the hyperkinetic circulation observed.

Introduction

Hypotensive episodes during haemodialysis have been frequently attributed to the mass of sodium acetate buffer transferred to the patients [1,2]. Although the vasodilatory effects of this substance have been documented [3,4] the
comparative mode of action in the arteriolar and venular circulations, as well as its cardiac effects still remain to be fully described. Thus, in order to provide the characterisation of its haemodynamic effects we studied the pattern of vasodilation to graded doses of sodium acetate in normal dogs, using standard haemodynamic techniques.

Material and methods

We studied the haemodynamic responses of 10 normal mongrel dogs, anaesthetised with morphine (2mg/kg) and sodium pentobarbital (15mg/kg), to graded infusions of sodium acetate at the rates of 0.037, 0.075, 0.150 and 0.300mEq/kg/min, during 20 minutes at each dose. At the end of each period of infusion, haemodynamic measurements were performed. We used dye-dilution techniques in a Gilford cuvette densitometer for haemodynamic measurements and a Gould 2400S writing recorder with Statham pressure transducers for direct blood pressure recordings. To study the actions of sodium acetate in the systemic circulation, the following indices were obtained: heart rate (HR), mean arterial pressure (MAP), cardiac output (CO), total peripheral resistance (TPR) and mean transit time (MTT). Cardiopulmonary blood volume (CPV), obtained from the dye-dilution curve, and mean pulmonary artery pressure (MPAP), were determined to evaluate the actions of the drug in the pulmonary circulation. The ratio between cardiac output and the cardiopulmonary volume (CO/CPV) was determined and used as an index of cardiac performance.

**TABLE I. Changes in haemodynamic parameters induced by four graded doses of sodium acetate**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>0.037</th>
<th>0.075</th>
<th>0.150</th>
<th>0.300*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP</td>
<td>107.2±4.0</td>
<td>109.3±3.7</td>
<td>111.2±5.6</td>
<td>117.6±6.2</td>
<td>116.5±8.5</td>
</tr>
<tr>
<td>HR</td>
<td>106.1±7.6</td>
<td>135.2±8.9</td>
<td>150.4±11.7</td>
<td>178.3±13.3</td>
<td>194.8±9.1</td>
</tr>
<tr>
<td>CO</td>
<td>1.63±0.20</td>
<td>1.82±0.25</td>
<td>2.36±0.30</td>
<td>2.90±0.31</td>
<td>3.59±0.38</td>
</tr>
<tr>
<td>TPR</td>
<td>78.2±11.3</td>
<td>69.4±7.8</td>
<td>54.1±6.1</td>
<td>43.1±4.0</td>
<td>36.4±4.8</td>
</tr>
<tr>
<td>SV</td>
<td>17.2±2.3</td>
<td>15.1±2.3</td>
<td>18.1±2.6</td>
<td>17.7±2.3</td>
<td>19.6±2.1</td>
</tr>
<tr>
<td>MPAP</td>
<td>13.3±0.7</td>
<td>15.8±0.8</td>
<td>17.6±1.5</td>
<td>19.1±1.5</td>
<td>19.7±1.7</td>
</tr>
<tr>
<td>CPV</td>
<td>195.0±21.3</td>
<td>188.8±22.6</td>
<td>209.0±22.2</td>
<td>223.5±23.6</td>
<td>224.4±24.3</td>
</tr>
<tr>
<td>MTT</td>
<td>7.74±0.65</td>
<td>6.63±0.51</td>
<td>5.57±0.40</td>
<td>4.96±0.45</td>
<td>3.78±0.22</td>
</tr>
<tr>
<td>CO/CPV</td>
<td>8.33±0.73</td>
<td>9.66±0.82</td>
<td>11.37±0.86</td>
<td>13.33±0.95</td>
<td>16.22±1.02</td>
</tr>
</tbody>
</table>

MAP=mean arterial pressure; HR=heart rate; CO=cardiac output; TPR=total peripheral resistance; SV=stroke volume; MPAP=mean pulmonary artery pressure; CPV=cardiopulmonary volume; MTT=mean transit time.

* mEq/kg/min

Analysis of variance was used to assess significance of the changes from control values. Results are expressed as mean ± standard error of the mean and are summarised in Table I.
Results

The infusions of sodium acetate induced dose-dependent changes in most of the haemodynamic variables studied. From control to the fourth dose, TPR decreased (from 78.2±11.3 to 36.4±4.8AU, p<0.001), CO increased (from 1.63±0.20 to 3.59±0.38L/min, p<0.001), and HR also increased (from 106.1±7.6 to 194.8±9.1bpm, p<0.001). Mean arterial pressure increased during the infusion (from 107.2±4.0 to 116.5±8.5mmHg, p<0.05), while SV did not change significantly (from 17.2±2.3 to 19.6±2.1ml, NS). We also noted a marked, dose-dependent decrease in MTT (from 7.74±0.65 to 3.78±0.22sec, p<0.001).

The cardiopulmonary volume increased significantly during the infusion (from 185.0±21.3 to 224.4±24.3ml, p<0.01) and so did MPAP (from 13.3±0.7 to 19.7±1.7mmHg, p<0.01). Also, CO/CPV increased significantly during the infusion (from 8.33±0.73 to 16.22±1.02, p<0.001). Haematocrit, however, did not change significantly during the experiments (see Table I).

Discussion

Our results clearly show that dose-dependent vasodilation was induced by the infusion of the graded doses of sodium acetate. This effect was accompanied by marked increases in CO and in heart rate. As a result, stroke volume did not decrease, but rather, it tended to increase with the drug. This is in accordance with previous reports suggesting an arteriolar site of action of sodium acetate in normal dogs [3]. In the present work we could document significant increases in MPAP and in CPV, associated with hyperkinetic circulation, as shown by the marked decreases observed in MTT. This pattern of action is indeed consistent with a predominantly arteriolar site of action of sodium acetate as a vasodilator with little effects, if any, on the venous circulation [5,6]. Because haematocrit did not significantly change during the infusion, it is reasonable to assume that the total blood volume was not affected [7] and thus the increased cardiopulmonary volume and pulmonary pressure must be attributed to shifts of blood from the periphery to the central circulation. In this case, the increases in CO observed during the experiments may be explained by reflex sympathetic activity elicited by distension of pressure and volume receptors of the pulmonary circulation. On the other hand, a venoconstrictor action of sodium acetate as suggested by Molnar et al [8] cannot be ruled out, since this effect also helps to explain the marked increases observed in cardiac output through increases in venous return.

We also noted marked shortening of MTT associated with increases, rather than decreases in MAP. Also, stroke volume was not decreased during the infusion as it might be expected because of the marked tachycardia induced by the drug. These facts strongly suggest that increased sympathetic support to the heart elicited by reflex activity may be a major determinant of the increased cardiac pump performance observed during the infusion of sodium acetate. This cardiostimulatory action was further documented by the significant increase observed in the CO/CPV ratio. However, the possibility still exists that this action may be related to a direct effect of acetate on the heart by providing
energy substrate [9]. This question can be resolved with appropriate sympathetic blockade studies to obviate reflex activity. Nevertheless, the overcompensation observed in MAP during sodium acetate infusion suggest that this latter mechanism can be at least in part involved in the overall response. Further investigation is also still necessary to clearly differentiate the haemodynamic effects of acetate from those of infused hyperosmolar sodium solutions.

References
3 Kirkendol PL, Robie NW, Gonzalez FM et al. Trans ASAIO 1978; 24: 714
4 Olinger GN, Werner PH, Bonchek LI. Ann Surg 1979; 190: 305
9 Ling CS, Lowenstein JM. J Clin Invest 1978; 62: 1029