EFFECT OF HYPOTENSION INDUCED WITH SODIUM NITROPRUSSIDE ON CANINE CORONARY ARTERIAL FLOW

J. P. Vance, D. M. Brown, G. Smith and J. Thorburn

SUMMARY

In seven dogs anaesthetized with pentobarbitone, coronary and pulmonary artery blood flows were measured using electromagnetic flow meters. The infusion of a 0.01% solution of sodium nitroprusside caused an initial small increase in mean coronary artery flow which returned to control as the arterial pressure decreased. No changes were noted in cardiac output nor were further changes observed in coronary flow. Heart rate was increased consistently during the hypotension and left ventricular dp/dt max was reduced as were coronary and total peripheral resistances. There were no significant changes in myocardial or total body oxygen extraction or consumption.

Arterial pressure is an important factor in determining the blood flow through any vascular bed. Since the arterial pressure in the coronary vascular bed is virtually identical with aortic pressure, factors which influence aortic pressure might be expected to affect flow in the coronary vasculature. This has been shown to be the case in haemorrhagic hypotension (Ledingham et al., 1971) and hypotension induced with halothane (Smith et al., 1974).

This investigation was carried out to determine if decreases in the arterial pressure produced by the infusion of sodium nitroprusside had an effect on coronary arterial flow.

METHODS

Seven healthy adult dogs (six greyhounds and one other) whose weights ranged between 25 and 31 kg were anaesthetized with pentobarbitone sodium 30 mg kg\(^{-1}\) i.v. Endotracheal intubation was performed once neuromuscular blockade had been achieved with suxamethonium 50 mg i.v. or i.m. Ventilation of the lungs was controlled (Palmer large animal ventilator) and the minute volume was adjusted to provide Pa\(_{\text{CO}_2}\) of approx. 5.3 kPa. The mixture of the ventilating gas (nitrogen in oxygen) was adjusted to produce Pa\(_{\text{O}_2}\) of approx. 13.3 kPa. During the investigation suxamethonium 50 mg i.m. was given as required to abolish reflex movement (usually about every 45 min).

With the animal in the right lateral position, catheters were inserted under radiographic control, into the coronary sinus via the left internal jugular vein and into the right atrium via the right femoral vein. A third catheter was passed via the right femoral artery, into the descending thoracic aorta. The right atrial and aortic catheters were connected to appropriate transducers for pressure recording. A copper–constantan thermocouple was passed into the oesophagus to the level of the heart and e.c.g. limb leads were attached by needle electrodes.

A left thoracotomy was performed and a short segment (1–2 cm) of either the circumflex or the anterior descending branch of the left coronary artery was dissected. A 2.0-mm or 2.5-mm flow transducer (Statham SP7515) was applied to the cleared segment of artery so that a close fit was obtained. The pulmonary artery was separated from the arch of the aorta by carefully dividing the ligamentum arteriosum and attached connective tissue. An 18-mm flow transducer (Statham SP7516–019) was applied to the pulmonary artery and in all animals a close fit was obtained. The two flow transducers were connected to flow meters with a non-occlusive zero facility (Statham SP2202). Thus flow could be measured simultaneously in a major coronary artery and in the pulmonary artery (cardiac output). In four of the animals a rigid catheter (Cournand type) was inserted into the left ventricle via the left common carotid artery for measurement of the maximum rate of increase of left ventricular pressure (l.v. dp/dt max). The Cournand catheter was connected to an Elema–Schonander transducer (EMT 34), the signal from which was differentiated electronically to give dp/dt max. The frequency response of this system was assessed in
and found to be satisfactory up to 25 Hz. During the measurement of dp/dt max, frequencies in excess of 20 Hz were filtered electronically. Positive end-expiratory pressure (PEEP) of 5 cm H\textsubscript{2}O was applied to the expiratory limb of the ventilator tubing to minimize pulmonary collapse and the exposed thoracic tissues were kept moist with swabs soaked in physiological saline.

The blood-gas tensions and pH were measured with suitably calibrated electrodes (Instrumentation Laboratories, I.L. 182) and corrected for any temperature difference between the animal's mid-oesophagus and the electrode. The haemoglobin concentration was measured using a co-oximeter (Instrumentation Laboratories, I.L. 213). Arterial hypotension was produced by the infusion of a 0.01% solution of sodium nitroprusside in physiological saline into a fore-leg vein. In each animal the arterial pressure was decreased to four different values—100-90 mm Hg, 90-80 mm Hg, 80-70 mm Hg and 70-60 mm Hg. The rate of infusion necessary to attain the required hypotension varied according to the sensitivity of the animal to nitroprusside, the range being 0.5-1.6 ml min\textsuperscript{-1} (0.05-0.16 mg min\textsuperscript{-1}). These infusion rates were slowed appropriately when the desired hypotension was achieved. The mean duration of infusion was 11 min and the mean duration of stable hypotension was 7.2 min. The arterial pressure was allowed to return to its control value between each period of hypotension and the order in which the various levels of hypotension were attained was randomized. On cessation of the infusion, all values returned to control values within 4 min except for the heart rate, which took up to 10 min to return to control.

Blood oxygen saturation was calculated from \( P_{O_2} \), taking into account pH and temperature. Blood oxygen content was then calculated as follows:

\[
O_2 \text{ content (ml dl}^{-1}) = Hb \ (g \text{ dl}^{-1}) \times 1.36 \times \frac{\% \text{ saturation}}{100} + P_{O_2} \ (kPa) \times 0.0232
\]

This method of oxygen content calculation as used in this laboratory has been shown to correlate satisfactorily with the direct method of Van-Slyke (Ledingham et al., 1971).

The following data were derived:

Myocardial \( O_2 \) consumption (ml min\textsuperscript{-1})
\[
= (C_{aO_2} - C_{csO_2}) \ (ml \text{ dl}^{-1}) \times \text{coronary flow (ml min}^{-1}) \times 1/100
\]

Total body \( O_2 \) consumption (ml min\textsuperscript{-1})
\[
= (C_{aO_2} - C_{vwO_2}) \ (ml \text{ dl}^{-1}) \times \text{CO (litre min}^{-1}) \times 10
\]

Myocardial \( O_2 \) extraction (%)
\[
= \frac{(C_{aO_2} - C_{csO_2}) \ (ml \text{ dl}^{-1})}{C_{aO_2} \ (ml \text{ dl}^{-1})} \times 100
\]

Total \( O_2 \) extraction (%)
\[
= \frac{(C_{aO_2} - C_{vwO_2}) \ (ml \text{ dl}^{-1})}{C_{aO_2} \ (ml \text{ dl}^{-1})} \times 100
\]

Coronary artery resistance (units) =
\[
\frac{\text{arterial pressure} - \text{right atrial pressure (mm Hg)}}{\text{coronary flow (ml min}^{-1})} \times 10
\]

Total peripheral resistance (units) =
\[
\frac{\text{arterial pressure} - \text{right atrial pressure (mm Hg)}}{\text{CO (litre min}^{-1})} \times 10
\]

where \( C_{aO_2} \) = arterial oxygen content; \( C_{csO_2} \) = coronary sinus oxygen content; \( C_{vwO_2} \) = mixed venous oxygen content; \( CO \) = cardiac output.

It is assumed for the above calculations that coronary sinus blood was representative of the venous effluent of the area perfused by the artery whose flow was measured and that right atrial blood may be regarded as mixed venous.

In order to confirm the accuracy of the flow measuring system, in one animal a branch of the left femoral artery of appropriate size was dissected out. A cannula was inserted into the vessel which was then ligated distally and the 2.0-mm flow transducer attached proximally with a gate clamp still more proximally. The blood from the vessel was drained through the cannula into a graduated measuring cylinder over timed periods of 0.5 or 1 min. Absolute flow could thus be compared with mean flow measured by the meter and the flow rate varied by means of the gate clamp.

The changes produced during each hypotensive period were compared with the control values obtained immediately before. Comparisons were made using a Student's \( t \) test for paired data and the \( P \) values are stated where significant changes took place (\( P<0.05 \)).

RESULTS

The comparison between the flows measured by collection over timed periods and the flows measured by the meter are presented in figure 1. A satisfactory
correlation was demonstrated \((r = 0.99, y = 1.134x - 9.00)\).

The initial response noted on the infusion of nitroprusside solution was a small but consistent increase in mean coronary arterial blood flow which returned to its control value as the arterial pressure decreased.

Subsequently, the most striking feature was that, despite an average decrease in mean arterial pressure of up to about 50\%, the mean coronary artery flow and the cardiac output were not altered significantly (table I). Coronary artery resistance and total peripheral resistance both decreased progressively as the arterial pressure decreased and they did so in a manner which was similar in magnitude. There was a significant increase in heart rate during each period of hypotension and this became proportionately higher as the arterial pressure became less.

Myocardial oxygen consumption did not change significantly and as the blood flow was unchanged the oxygen extraction by the myocardium was unchanged also. Similar comments apply to total body oxygen consumption and extraction.

Table II shows the changes which occurred in \(dp/dt_{\text{max}}\) in four individual dogs. There was a consistent reduction in \(dp/dt_{\text{max}}\) during all levels of hypotension and the reduction was progressively greater as the decrease in arterial pressure became greater.

Apart from the increase in heart rate, no animal showed any electrocardiographic changes during the periods of hypotension.

**TABLE I. Changes in haemodynamic variables and oxygen consumption at four levels of hypotension produced by infusion of a 0.01\% solution of sodium nitroprusside (seven dogs, mean ± SEM)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hypotension</th>
<th>Control</th>
<th>Hypotension</th>
<th>Control</th>
<th>Hypotension</th>
<th>Control</th>
<th>Hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean aortic pressure</strong></td>
<td>122 ± 2</td>
<td>92 ± 0.9</td>
<td>126 ± 3</td>
<td>83 ± 1</td>
<td>124 ± 4</td>
<td>72 ± 0.9</td>
<td>121 ± 2.5</td>
<td>62.3 ± 1.2</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heart rate (beat min(^{-1}))</strong></td>
<td>189 ± 11</td>
<td>236 ± 16</td>
<td>198 ± 16</td>
<td>227 ± 9</td>
<td>179 ± 15</td>
<td>227 ± 16</td>
<td>179 ± 16</td>
<td>221 ± 19</td>
</tr>
<tr>
<td></td>
<td>((P &lt; 0.01))</td>
<td>((P &lt; 0.025))</td>
<td>((P &lt; 0.001))</td>
<td>((P &lt; 0.001))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean coronary artery flow</strong></td>
<td>55 ± 14</td>
<td>53 ± 9</td>
<td>46 ± 6</td>
<td>47 ± 7</td>
<td>48 ± 6</td>
<td>42 ± 7</td>
<td>43 ± 6</td>
<td>40 ± 6</td>
</tr>
<tr>
<td>(ml min(^{-1}))</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Coronary artery resistance</strong></td>
<td>27.1 ± 3.0</td>
<td>20.3 ± 3.2</td>
<td>28.8 ± 2.8</td>
<td>20.4 ± 3.3</td>
<td>28.2 ± 3.6</td>
<td>19.4 ± 3.1</td>
<td>30.2 ± 3.1</td>
<td>15.9 ± 2.6</td>
</tr>
<tr>
<td>(units)</td>
<td>((P &lt; 0.05))</td>
<td>((P &lt; 0.01))</td>
<td>((P &lt; 0.01))</td>
<td>((P &lt; 0.01))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac output (litre min(^{-1}))</strong></td>
<td>5.11 ± 0.46</td>
<td>5.24 ± 0.35</td>
<td>5.2 ± 0.4</td>
<td>4.9 ± 0.3</td>
<td>5.18 ± 0.29</td>
<td>4.8 ± 0.28</td>
<td>5.16 ± 0.28</td>
<td>5.11 ± 0.26</td>
</tr>
<tr>
<td></td>
<td>((P &lt; 0.005))</td>
<td>((P &lt; 0.005))</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total peripheral resistance</strong></td>
<td>246 ± 21</td>
<td>177 ± 13</td>
<td>240 ± 21</td>
<td>170 ± 13</td>
<td>241 ± 19</td>
<td>146 ± 9</td>
<td>233 ± 12</td>
<td>118 ± 10</td>
</tr>
<tr>
<td>(units)</td>
<td>((P &lt; 0.005))</td>
<td>((P &lt; 0.005))</td>
<td>((P &lt; 0.001))</td>
<td>((P &lt; 0.001))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Myocardial O(_2) consumption (ml min(^{-1}))</strong></td>
<td>4.0 ± 1.7</td>
<td>3.8 ± 0.7</td>
<td>4.1 ± 0.8</td>
<td>3.9 ± 0.6</td>
<td>4.2 ± 0.5</td>
<td>3.9 ± 0.5</td>
<td>3.9 ± 0.7</td>
<td>3.7 ± 0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Myocardial O(_2) extraction (%)</strong></td>
<td>35.1 ± 4</td>
<td>32.3 ± 4</td>
<td>35.4 ± 3</td>
<td>32.3 ± 3</td>
<td>34.7 ± 3</td>
<td>32 ± 3</td>
<td>30.7 ± 3</td>
<td>28.7 ± 4</td>
</tr>
<tr>
<td><strong>Total O(_2) consumption (ml min(^{-1}))</strong></td>
<td>164 ± 25</td>
<td>156 ± 27</td>
<td>178 ± 23</td>
<td>160 ± 20</td>
<td>145 ± 19</td>
<td>159 ± 19</td>
<td>156 ± 15</td>
<td>164 ± 24</td>
</tr>
<tr>
<td><strong>Total O(_2) extraction (%)</strong></td>
<td>14.1 ± 2</td>
<td>12.2 ± 2</td>
<td>13.7 ± 2</td>
<td>13.0 ± 1</td>
<td>11.2 ± 1</td>
<td>12.8 ± 1</td>
<td>12.1 ± 1</td>
<td>14.1 ± 2</td>
</tr>
</tbody>
</table>
Table II. Changes in dp/dt max (mm Hg s⁻¹) in four individual dogs during periods of hypotension produced by the infusion of sodium nitroprusside

<table>
<thead>
<tr>
<th>Dog</th>
<th>Control</th>
<th>100-90</th>
<th>Control</th>
<th>90-80</th>
<th>Control</th>
<th>80-70</th>
<th>Control</th>
<th>70-60</th>
<th>Control</th>
<th>60-50</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2300</td>
<td>2000</td>
<td>2400</td>
<td>2000</td>
<td>2400</td>
<td>1800</td>
<td>2200</td>
<td>1600</td>
<td>2300</td>
<td>1600</td>
</tr>
<tr>
<td>2</td>
<td>2400</td>
<td>1900</td>
<td>2400</td>
<td>1900</td>
<td>2500</td>
<td>1700</td>
<td>2500</td>
<td>1400</td>
<td>2300</td>
<td>1000</td>
</tr>
<tr>
<td>3</td>
<td>2400</td>
<td>2000</td>
<td>2500</td>
<td>2000</td>
<td>2300</td>
<td>1900</td>
<td>2100</td>
<td>2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3300</td>
<td>3000</td>
<td>3400</td>
<td>2800</td>
<td>3400</td>
<td>2200</td>
<td>3000</td>
<td>2000</td>
<td>3200</td>
<td>1800</td>
</tr>
</tbody>
</table>

DISCUSSION

Sodium nitroprusside has been used to produce deliberate hypotension as an adjunct to anaesthesia in many circumstances, as for example in neurosurgery (Siegel, Moraca and Green, 1971), major e.n.t. surgery (Wildsmith, Drummond and MacRae, 1975) and major orthopaedic surgery (Simpson, Bellamy and Cole, 1976). It produces hypotension by a direct vasodilator effect on the blood vessels themselves. As with every technique of hypotensive anaesthesia, there is concern about perfusion of vital tissues and several workers have attempted to assess the adequacy of myocardial oxygenation during hypotension produced by nitroprusside. Simpson, Bellamy and Cole (1976), using the rather crude method of electrocardiography, concluded that none of their patients suffered permanent myocardial ischaemia although some did show minor but transient changes in the ST-segments and T-waves. A study by Ross and Cole (1973) suggested that in four dogs anaesthetized with chloralose, coronary flow and cardiac output increased during hypotension induced with nitroprusside while Wang, Liu and Katz (1977) observed that nitroprusside decreased coronary flow. Increases in cardiac output have been recorded also during the infusion of nitroprusside on a background of nitrous oxide and halothane anaesthesia (Wildsmith et al., 1973).

The present study has shown that in the dog anaesthetized with a barbiturate, the i.v. infusion of sodium nitroprusside caused a transient and small increase in coronary blood flow which returned to control values as the animal became progressively hypotensive. Thereafter, the coronary flow did not alter significantly. This initial small increase in flow reflects probably the fact that the coronary arteries are the first to receive the drug and thus react to it before it affects the peripheral vasculature. Cardiac output showed no significant changes during the periods of hypotension. In those dogs in which it was measured there were consistent decreases in left ventricular dp/dt max, suggesting that myocardial contractility had decreased. Increases in the heart rate during the infusion of nitroprusside were a consistent feature and probably contributed to the maintenance of cardiac output and of myocardial oxygen extraction and consumption. Otherwise these latter might have been expected to decrease as the after-load of the heart was reduced during the periods of hypotension. There were marked decreases in both myocardial and total peripheral vascular resistances during hypotension and indeed this is the means by which nitroprusside produces its hypotensive action.

Studies of the influence of nitroprusside on cardiac output have shown varying results. In patients with myocardial infarction, in whom there was left ventricular failure and a low cardiac index, Franciosa and others (1972) described an increase of cardiac output with an infusion of nitroprusside. However, in those patients in whom the cardiac index was normal after infarction, nitroprusside produced no change in cardiac output. A complex study by Adams and others (1974) in dogs anaesthetized with nitrous oxide and halothane suggested that cardiac output was unchanged during the infusion of nitroprusside and that left ventricular dp/dt max was reduced in a dose-dependent manner. Our study is in agreement with these latter findings.

This study showed that during hypotension induced with nitroprusside, the coronary flow was well maintained. This is in contrast to the situation in which hypotension was induced with halothane when coronary vasoconstriction occurred (Smith et al., 1974). Therefore, these findings would suggest that hypotension brought about by nitroprusside is inherently safer as regards myocardial perfusion. The fact that a major degree of coronary vasodilatation occurred during hypotension indicates that, at least at the lower values of arterial pressure, there may be little capacity for further vasodilatation, for example in response to haemorrhage. The importance of
NITROPRUSSIDE HYPOTENSION AND CORONARY ARTERY FLOW

keeping blood volume during induced hypo-
tension must be stressed.

ACKNOWLEDGEMENTS
Dr J. P. Vance was in receipt of a Scottish Home and Health Department grant which financed this work. The authors are also grateful to Dr I. McA. Ledingham for laboratory time and to his technical staff for technical help.

REFERENCES
prusside and trimethaphan. Anesthesiology, 46, 40.
Wildsmith, J. A. W., Drummond, G. B., and MacRae, W. R. (1975). Blood-gas changes during induced hypo-

EFFET DE L'HYPOTENSION PROVOQUEE PAR LE NITROPRUSSIATE DE SODIUM SUR LE DEBIT DE L'ARTEREE CORONARIE DES CHIENS

RESUME
On a mesure le debit sanguin de l'arteree pulmonaire et de l'arteree coronarie de sept chiens anesthesies au pento-
obarbital, en employant des demitmetres electromagnetiques. L'infusion d'une solution de nitroprussiate de
sodium a 0,01% a provoque une legere augmentation initiale du debit moyen de l'arteree coronarie, lequel est retourn aux valeurs temoins au fur et a mesure que la pression arterielle a diminue. On n'a remarque aucune variation dans le debit cardiaque et on n'a observe aucun autre changement dans le debit coronarie. La frequence cardiaque a augmentee d'une maniere continue pendant l'hypotension et la dp/dt maximale ventriculaire gauche a diminue tout comme les resistances peripheriques totale et coronarie. Il n'y a eu aucune variation importante dans la consommation ou l'extraction de l'oxygene du corps ou du myocarde.

DER EINFLUSS VON DURCH NITROPRUSSID-
NATRIUM HERBEIGEFUHRTER HYPOTONIE
AUF DEN HERZKRANZ ARTERIENFLUSS
IN HUNDEN

ZUSAMMENFASSUNG
In sieben, mit Pentobarbiton anasthesierten Hunden wurden die Herzkranz- und Lungenarterienflusse unter Verwendung von elektromagnetischen Strommussern gemessen. Die Infusion einer 0,01-prozentigen Losung von Nitroprussidnatrium verursachte eine anfangliche geringfugige Erhohung des mittleren Herzkranzarterien-

EFFECTO EJERCIDO POR HIPOTENSION
INDUCIDA POR NITROPRUSSIATO SODICO
SOBRE LA CIRCULACION ARTERIAL
CORONARIA CANINA

SUMARIO
Se midieron las circulaciones de sangre arterial pulmonar y coronaria en siete perros anestesiados con pentobarbitona, empleando para tal fin flujometros electromagneticos. La infusi6n de una soluci6n con 0,01% de nitroprussiato sodico provoc6 un pequeno aumento inicial en la circulaci6n arterial coronaria media, que volvi6 a su valor de control a medida que disminu6 la presi6n arterial. No se notaron cambios en la capacidad cardica ni se observaron cambios adicionales en la circulaci6n coronaria. Los latidos del corazon aumentaron consistentemente durante la hipotension y se redujo el dp/dt max ventricular izquierdo, asi como las resistencias coronaria y periferica total. No se produjeron cambios significativos en la extracci6n ni consumo del oxigeno miocardiaco ni total del cuerpo.