DEPRESSION OF HYPOXIC PULMONARY VASOCONSTRICTION BY SODIUM NITROPRUSSIDE AND NITROGLYCERINE


SUMMARY

The pulmonary vasoconstrictor response to the unilateral administration of 7% oxygen was studied in 10 anaesthetized dogs in which the lungs were mechanically ventilated. The distribution of blood flow between the two lungs was measured continuously by recording the radioactivity in the mixed expired gas from each lung during the infusion i.v. of xenon-133. Infusions of nitroglycerine and sodium nitroprusside which produced the same decrease in mean aortic pressure produced similar decreases in hypoxic pulmonary vasoconstriction. The reduction in arterial $P_{O_2}$ during unilateral hypoxia was greater when the hypoxic vasoconstrictor response was depressed by drugs than it was during the control periods, although mixed venous $P_{O_2}$ was unchanged. It is concluded that both drugs may cause hypoxaemia by increasing the blood flow to alveoli with a low ventilation/perfusion ratio.

Sodium nitroprusside (SNP) and nitroglycerine (NG) are used to treat arterial hypertension in patients undergoing coronary artery bypass surgery. However, both drugs reduce arterial oxygen tension (Wildsmith, Drummond and MacRae, 1975; Seltzer, Doto and Jacoby, 1976; Kopman et al., 1978). There appear to be three possible mechanisms which could decrease $P_{a_O_2}$.

First, the drug might produce a reduction in venous return caused by dilatation of capacitance vessels and so decrease cardiac output and mixed venous $P_{O_2}$ ($P_{m_{O_2}}$). In the presence of areas of lung with a low ventilation/perfusion ratio, the reduction in $P_{m_{O_2}}$ would cause a reduction in $P_{a_{O_2}}$, even though the proportion of blood flowing through such areas was unchanged (Sykes, Young and Robinson, 1965). A second explanation is that the drug might cause pulmonary vasodilatation and decrease pulmonary artery pressure. If there were underventilated alveoli in the dependent zones of the lung, the reduction in pulmonary artery pressure might decrease the flow to the normally ventilated portions of the lung and so increase the proportion of blood flowing through the underventilated alveoli even though the absolute flow through such alveoli was unchanged (Colley and Cheney, 1977; Colley, Cheney and Butler, 1977). The third possibility is that the proportion of blood flowing through underventilated lung zones might be increased by a drug-induced depression of the hypoxic vasoconstrictor mechanism which normally diverts flow away from areas of lung with a low alveolar $P_{O_2}$ (Hughes, 1975).

Studies in dogs indicate that SNP may depress this mechanism (Colley, Cheney and Hlastala, 1979; Hill, Sykes and Reyes, 1979). The present experiments were designed to compare the effects of NG and SNP on the pulmonary vasoconstrictor response to unilateral alveolar hypoxia.

METHODS

The experiments were performed on 10 dogs of varied breed (weight 16–24 kg). They were anaesthetized with thiopentone 20–30 mg kg$^{-1}$ i.v. supplemented by increments of pentobarbitone to a total of 20 mg kg$^{-1}$. The animals were placed supine in a V-shaped trough and the lungs ventilated mechanically. Pancuronium 2–4 mg was injected at intervals to ensure no spontaneous respiratory activity. These three drugs have been shown to have no effect on the hypoxic vasconstrictor response. Cannulae were inserted to the femoral vessels for pressure recording, blood sampling, dye injection and withdrawal, and infusion of xenon-133. Two catheters, one of the Swan–Ganz type, were passed into the pulmonary artery for blood sampling and simultaneous recording of pulmonary artery ($P_{PA}$)
and pulmonary wedge pressures \( (P_{PAW}) \) and a separate i.v. infusion line was established for fluid and drug administration. Tracheotomy was performed and a double-lumen tracheal divider passed (Seed and Sykes, 1972). After inflation of the cuff, accurate placement of the tube was checked by measurements of the tidal volume issuing from each lung. The absence of leaks was demonstrated by pressurizing each lung to +3.0 kPa whilst the opposite limb of the tube was connected to a tube placed under water. Each limb of the tube was then connected to a separate non-rebreathing valve and second-stage ventilator circuit which could be driven by the main ventilator at 15 b.p.m. (Reyes et al., 1979). The tidal volume to each lung was adjusted to produce equal end-tidal carbon dioxide concentrations of 4-4.5% and then kept constant during the experiment.

The distribution of pulmonary blood flow between the two lungs was measured continuously by infusing xenon-133 dissolved in 50-100 ml of normal saline at a rate of 1-2 mCi h\(^{-1}\) using a Braun continuous infusion pump. Approximately 95% of the xenon was evolved to the alveoli during its passage through the lungs and then washed out by the tidal ventilation.

The expired gas from each lung was passed through a fan-assisted mixing unit and the mixed expired gas then circulated through a glass coil situated within the collimator of a scintillation detector. The output from each detector was processed to yield a continuous record of the radioactivity issuing from each lung. Since tidal volumes were initially matched to the blood flow to each lung, the initial ratio of right/left (R/L) radioactivity was 1. When hypoxic vasoconstriction was induced in the left lung by ventilating it with hypoxic gas mixture, the radioactivity on that side decreased and the radioactivity on the opposite side increased. This caused an increased R/L ratio of radioactivity which reflected the magnitude of diversion of blood flow away from the hypoxic lung (Sykes, Hill et al., 1977). In this study, the percentage diversion was calculated from the equation:

\[
\text{\% diversion} = \frac{C_R - C_L}{C_i} \times 100
\]

where \( C_i \) = mean counts from both lungs during bilateral ventilation with oxygen; \( C_R, C_L \) = counts from right and left lungs during unilateral hypoxia.

Vascular and airway pressures were monitored continuously with Consolidated Dynamics strain gauges and a Devices M 19 heated stylus recorder. Oesophageal temperature was monitored with a thermistor probe and body temperature maintained at 37 ± 1 °C.

Cardiac output was determined in triplicate with indocyanine green dye using a calibrated Gilford system, the curves being analysed by the method of Simons and White (1976). Blood-gas tensions and pH measurements were made on two separate electrode systems (Radiometer ABL1 and the standard Radiometer system) which were calibrated with previously analysed gases and repeatedly checked with tonometered blood samples (Sykes et al., 1970; Selman and Tait, 1976).

The right lung was ventilated throughout with pure oxygen. The left lung was initially ventilated with oxygen and the hypoxic vasoconstrictor response elicited by switching the ventilating gas mixture to 7% oxygen in nitrogen. This gas mixture yields alveolar oxygen tensions in the mixed venous range.

The initial measurements of xenon count, cardiac output, vascular and airway pressures, end-tidal carbon dioxide concentration and blood-gases were made 20-30 min after stable conditions had been achieved with both lungs ventilated with oxygen. The ventilating gas to the left lung was then changed to 7% oxygen and a second set of measurements made 10-15 min later when vascular pressures and xenon counts were stable. Both lungs were again ventilated with oxygen and an infusion of the drug started. The dose rate was adjusted to produce a mean arterial pressure of 105-110 mm Hg, the lowest that could usually be achieved with NG, and a third set of measurements was made 10 min later. The drug infusion was continued and the left lung switched to 7% oxygen, the fourth set of measurements being made when conditions had stabilized after a further 10-15 min. The drug was then discontinued and both lungs ventilated with oxygen until the pressures had returned to pre-existing values. A fifth set of measurements on bilateral oxygen was made 30-40 min after discontinuing the drug and a sixth set 10-15 min after again ventilating the left lung with 7% oxygen. The fifth and sixth sets of measurements...
also served as control measurements for the second drug which was administered in a manner similar to the first. Hypoxic responses were obtained during the period of administration of the second drug and 30-40 min after withdrawing the drug. The order in which the SNP and NG were administered was varied in a random manner so that five animals received SNP as the first drug and five animals NG first. The results were subjected to an analysis of variance followed by t tests where indicated. The statistical analysis compared the effects of each drug with the controls before and after administration of the drug and also tested for the effect of time and sequence of drug administration. The drugs used in these studies were SNP (Roche) 0.01% (mean dose 9.1 mg, range 6.7-50 mg) and NG (Arnar-Stone Laboratories Inc.) 0.1% (mean dose 17.5 mg, range 10-40 mg).

RESULTS

Control periods

The three sets of control values (C1, C2, and C3) on bilateral oxygen and unilateral hypoxia were grouped according to the sequence in which they were obtained. During bilateral ventilation with oxygen the only measurement which changed significantly during the experiment was PfXw. This increased from 2.6 mm Hg at C1 to 4.6 mm Hg at C3.

Unilateral ventilation with 7% oxygen resulted in significant reductions in PaO2, PvO2, and left lung end-tidal carbon dioxide concentration (FeCO2) and a significant increase in FeCO2 in the right (oxygenated) lung (table I). However, it produced no significant change in cardiac output, vascular and airway pressures, Pao2, base excess or haemoglobin concentration. Unilateral hypoxia reduced the proportion of blood flowing to the hypoxic lung, the magnitude of this response increasing with time.

Effect of drugs

The variables measured during the period of drug administration were compared with the means of the control values obtained before and after the infusion (table II).

During bilateral oxygen ventilation, NG produced significant reductions in cardiac output (Q), mean aortic pressure (Pao), Pf and Pfj. During the same conditions, SNP produced significant decreases in Pao, Pf and Pf and a significant increase in heart rate (HR). There were no significant changes in any of the other measured variables.

Pao, Pf and PaO2 were significantly reduced during unilateral hypoxia and NG administration compared with the means of the before and after control values during unilateral hypoxia. SNP produced significant reductions in Pao, Pf and PaO2, and a significant increase in HR compared with the means of unilateral hypoxia control measurements. During unilateral hypoxia, both drugs produced a similar degree of depression of

<table>
<thead>
<tr>
<th>Table I. Significant changes in measurements recorded during control periods. Results grouped according to the time sequence in which they were obtained (C1, C2 and C3). The left lung was subjected to hypoxia. The end-tidal carbon dioxide (FeCO2) comparisons were based on the average results from the three control periods</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>% Reduction in left lung blood flow</td>
</tr>
<tr>
<td>SD</td>
</tr>
<tr>
<td>PaO2 (kPa)</td>
</tr>
<tr>
<td>SD</td>
</tr>
<tr>
<td>PvO2 (kPa)</td>
</tr>
<tr>
<td>SD</td>
</tr>
<tr>
<td>FeCO2 (left) (%)</td>
</tr>
<tr>
<td>SD</td>
</tr>
<tr>
<td>FeCO2 (right) (%)</td>
</tr>
<tr>
<td>SD</td>
</tr>
</tbody>
</table>
TABLE II. Cardiorespiratory measurements (mean ± SD) at each stage of the experiment

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before drug</th>
<th>NG</th>
<th>After drug</th>
<th>C v. mean of A and E</th>
<th>D v. mean of B and F</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>Q (litre min⁻¹)</td>
<td>2.01 ± 0.69</td>
<td>1.90 ± 0.66</td>
<td>1.60 ± 0.44</td>
<td>1.85 ± 0.65</td>
<td>1.87 ± 0.52</td>
</tr>
<tr>
<td>P&lt;sub&gt;ao&lt;/sub&gt; (mm Hg)</td>
<td>143.0 ± 27.3</td>
<td>143.0</td>
<td>109.2 ± 17.4</td>
<td>115.7 ± 19.5</td>
<td>134.7 ± 13.1</td>
</tr>
<tr>
<td>P&lt;sub&gt;Pa&lt;/sub&gt; (mm Hg)</td>
<td>10.50 ± 1.58</td>
<td>12.25 ± 2.07</td>
<td>9.85 ± 1.60</td>
<td>12.40 ± 2.71</td>
<td>12.95 ± 2.83</td>
</tr>
<tr>
<td>P&lt;sub&gt;PaW&lt;/sub&gt; (mm Hg)</td>
<td>3.03 ± 1.47</td>
<td>4.05 ± 2.28</td>
<td>2.40 ± 1.56</td>
<td>2.45 ± 3.18</td>
<td>4.90 ± 2.55</td>
</tr>
<tr>
<td>HR (beat min⁻¹)</td>
<td>164.3 ± 39.1</td>
<td>165.7</td>
<td>187.9 ± 35.2</td>
<td>185.1 ± 27.4</td>
<td>179.3 ± 22.7</td>
</tr>
<tr>
<td>Pa&lt;sub&gt;O2&lt;/sub&gt; (kPa)</td>
<td>57.21 ± 8.04</td>
<td>18.96 ± 3.39</td>
<td>55.33 ± 11.39</td>
<td>14.09 ± 3.04</td>
<td>51.91 ± 15.52</td>
</tr>
<tr>
<td>P&lt;sub&gt;Vo&lt;/sub&gt; (kPa)</td>
<td>7.22 ± 1.11</td>
<td>5.98 ± 0.89</td>
<td>6.65 ± 1.01</td>
<td>5.62 ± 0.74</td>
<td>6.85 ± 1.06</td>
</tr>
<tr>
<td>Pa&lt;sub&gt;CO2&lt;/sub&gt; (kPa)</td>
<td>4.79 ± 0.49</td>
<td>4.81 ± 0.90</td>
<td>4.70 ± 0.50</td>
<td>4.79 ± 0.63</td>
<td>4.89 ± 0.57</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before drug</th>
<th>SNP</th>
<th>After drug</th>
<th>I v. mean of G and K</th>
<th>J v. mean of H and L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>G</td>
<td>H</td>
<td>I</td>
<td>J</td>
<td></td>
</tr>
<tr>
<td>Q (litre min⁻¹)</td>
<td>2.12 ± 0.69</td>
<td>1.94 ± 0.62</td>
<td>1.83 ± 0.61</td>
<td>2.16 ± 0.83</td>
<td>1.99 ± 0.61</td>
</tr>
<tr>
<td>P&lt;sub&gt;ao&lt;/sub&gt; (mm Hg)</td>
<td>133.5 ± 15.5</td>
<td>138.2</td>
<td>103.2 ± 14.8</td>
<td>107.4 ± 14.3</td>
<td>143.0 ± 24.3</td>
</tr>
<tr>
<td>P&lt;sub&gt;Pa&lt;/sub&gt; (mm Hg)</td>
<td>12.0 ± 2.58</td>
<td>13.40 ± 1.95</td>
<td>10.10 ± 2.99</td>
<td>11.27 ± 2.83</td>
<td>12.70 ± 3.36</td>
</tr>
<tr>
<td>P&lt;sub&gt;PaW&lt;/sub&gt; (mm Hg)</td>
<td>3.75 ± 2.93</td>
<td>4.51 ± 3.07</td>
<td>2.40 ± 2.39</td>
<td>2.65 ± 2.91</td>
<td>3.90 ± 2.01</td>
</tr>
<tr>
<td>HR (beat min⁻¹)</td>
<td>180.6 ± 22.1</td>
<td>185.6</td>
<td>195.9 ± 34.6</td>
<td>194.7 ± 34.1</td>
<td>159.2 ± 37.9</td>
</tr>
<tr>
<td>Pa&lt;sub&gt;O2&lt;/sub&gt; (kPa)</td>
<td>51.57 ± 15.87</td>
<td>16.41</td>
<td>54.09 ± 13.53</td>
<td>12.07 ± 2.84</td>
<td>54.13 ± 14.44</td>
</tr>
<tr>
<td>P&lt;sub&gt;Vo&lt;/sub&gt; (kPa)</td>
<td>7.0 ± 0.83</td>
<td>5.93 ± 0.61</td>
<td>6.89 ± 1.13</td>
<td>5.68 ± 1.04</td>
<td>6.84 ± 1.19</td>
</tr>
<tr>
<td>Pa&lt;sub&gt;CO2&lt;/sub&gt; (kPa)</td>
<td>4.89 ± 0.56</td>
<td>4.82 ± 0.61</td>
<td>4.78 ± 0.68</td>
<td>5.04 ± 0.56</td>
<td>4.98 ± 0.65</td>
</tr>
</tbody>
</table>

discussion

The study demonstrates that when NG and SNP were infused at dose rates which produced equal reductions in mean aortic pressure they produced similar degrees of depression of the pulmonary vasoconstrictor response to alveolar hypoxia. However, the slightly increased inhibition of the pulmonary vasoconstrictor response to alveolar hypoxia (table III). However, Pa<sub>O2</sub> during unilateral hypoxia was significantly less during SNP administration than during infusion of NG. This was probably because of the slightly greater inhibition of the hypoxic vasoconstrictor response by SNP.
TABLE III. Percentage decrease in blood flow in left lung in response to unilateral hypoxia

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before NG</td>
<td>During NG</td>
<td>After NG</td>
<td>Before SNP</td>
<td>During SNP</td>
<td>After SNP</td>
</tr>
<tr>
<td>1</td>
<td>40.0</td>
<td>32.6</td>
<td>30.0</td>
<td>30.0</td>
<td>10.0</td>
<td>27.2</td>
</tr>
<tr>
<td>2</td>
<td>27.0</td>
<td>34.0</td>
<td>40.0</td>
<td>40.0</td>
<td>16.9</td>
<td>57.6</td>
</tr>
<tr>
<td>3</td>
<td>30.8</td>
<td>29.5</td>
<td>39.0</td>
<td>18.6</td>
<td>0.0</td>
<td>30.8</td>
</tr>
<tr>
<td>4</td>
<td>20.7</td>
<td>10.8</td>
<td>40.0</td>
<td>40.0</td>
<td>22.2</td>
<td>37.7</td>
</tr>
<tr>
<td>5</td>
<td>26.6</td>
<td>0.0</td>
<td>24.4</td>
<td>24.4</td>
<td>23.0</td>
<td>48.2</td>
</tr>
<tr>
<td>6</td>
<td>32.9</td>
<td>13.8</td>
<td>34.3</td>
<td>23.3</td>
<td>11.1</td>
<td>32.9</td>
</tr>
<tr>
<td>7</td>
<td>35.0</td>
<td>35.0</td>
<td>35.5</td>
<td>20.0</td>
<td>13.6</td>
<td>35.0</td>
</tr>
<tr>
<td>8</td>
<td>44.2</td>
<td>17.2</td>
<td>66.6</td>
<td>70.8</td>
<td>36.5</td>
<td>44.2</td>
</tr>
<tr>
<td>9</td>
<td>31.3</td>
<td>19.0</td>
<td>50.0</td>
<td>50.0</td>
<td>46.3</td>
<td>62.5</td>
</tr>
<tr>
<td>10</td>
<td>50.6</td>
<td>36.0</td>
<td>76.6</td>
<td>57.1</td>
<td>32.3</td>
<td>50.6</td>
</tr>
<tr>
<td>Mean</td>
<td>33.9</td>
<td>22.8</td>
<td>43.6</td>
<td>35.4</td>
<td>19.2</td>
<td>42.7</td>
</tr>
<tr>
<td>SD</td>
<td>±8.9</td>
<td>±12.4</td>
<td>±16.4</td>
<td>±20.6</td>
<td>±15.1</td>
<td>±11.9</td>
</tr>
</tbody>
</table>

Significance: P < 0.01

Response by SNP produced a significantly greater reduction in arterial $P_O_2$ during unilateral hypoxia, although the mean values of mixed venous $P_O_2$ were the same. These results were confirmed by the changes in end-tidal carbon dioxide which normally reflect changes in blood flow.

The unilateral ventilation hypoxia model used in this study may be criticized because it does not exactly simulate the underventilated or atelectatic areas of the lung.

The first criticism is that the alveolar $P_O_2$ ($P_{A_O_2}$) values during ventilation hypoxia might not be comparable to those in an underventilated area of lung. End-tidal gas samples and sampling of blood from the pulmonary veins draining a lung or lobe ventilated with 7–9% oxygen have confirmed that this gas mixture produces $P_{A_O_2}$ values in the range 5–6 kPa when pulmonary vasoconstriction is established and alveolar $P_{CO_2}$ ($P_{A_{CO_2}}$) is reduced.

The second criticism is that the maintenance of constant ventilation when blood flow is reduced by alveolar hypoxia results in a reduction in $P_{A_{CO_2}}$, whereas $P_{A_{CO_2}}$ is normally increased in an underventilated area of lung. Since a reduction in $P_{A_{CO_2}}$ decreases the magnitude of the response to hypoxia, the greater reduction in $P_{A_{CO_2}}$ during the control periods would have tended to minimize the differences between the control hypoxic responses and those recorded during the period of drug administration. It is therefore likely that the decrease in pulmonary vasoconstriction recorded in the present experiments underestimated the effect of the drug. Other experiments have demonstrated that the maintenance of constant end-tidal $P_{CO_2}$ values does not alter the qualitative results (Sykes et al., 1975; Hurtig, Tait and Sykes, 1977).

The third criticism is that regional lung volume and tidal volume are maintained at normal values. It is not known how hypoxic vasoconstriction varies with lung volume, but it is now believed that most of the reduction in blood flow in atelectatic lungs is a result of hypoxic pulmonary vasoconstriction. This can be reversed by drug administration (Barer, 1966; Benumof, 1979). It seems unlikely, therefore, that the use of ventilation hypoxia will affect the qualitative effect produced by the drugs.

The model has a number of advantages. First, factors which may affect the pulmonary circulation, such as changes in pulmonary vascular pressures, acid–base balance and temperature, are applied equally to both lungs. Airway pressures are closely controlled and both cardiovascular and respiratory variables can be monitored during the experiment. Second, the radio-isotope method of measuring flow is accurate, utilizes relatively little radioactivity and provides a continuous measurement of blood flow (Sykes, Hill et al., 1977). This enables the response to be monitored visually so that other measurements can be correctly synchronized with the peak response. It is believed that the advantages outweigh the disadvantages and that this model provides a satisfactory method of studying the problem.

The decreased vasoconstriction in the hypoxic lung observed during the period of drug administration could have been produced by a generalized reduction in pulmonary vascular tone.
or by an inhibition of the pulmonary vasoconstrictor response to alveolar hypoxia. In the present experiments both drugs produced a small increase in pulmonary vascular resistance. However, both $P_{PA}$ and $P_{PAW}$ decreased, so that the apparent increase in resistance could have been caused by a reduction in the cross-sectional area of the perfused vascular bed. Mentzer and Nolan (1977a) demonstrated that NG caused vasodilatation in a left lower lobe perfusion preparation in new-born puppies and Kaplan, Dunbar and Jones (1976) found that infusion at a mean dose rate of 0.96 ug kg$^{-1}$ min$^{-1}$ reduced pulmonary vascular resistance in patients undergoing open-heart surgery. Since alveolar oxygen tensions were normal or increased during these studies, it seems reasonable to conclude that the drug can act as a pulmonary vasodilator. There is also evidence that SNP may produce pulmonary vasodilatation. For example, Stinson and others (1975) found that SNP reduced pulmonary vascular resistance in patients after open-heart surgery. However, Mentzer and Nolan (1977b), Colley, Cheney and Hlastala (1979), and Hill, Sykes and Reyes (1979) found no evidence of decreased pulmonary vascular resistance in dogs.

If a drug produces vasodilatation by reducing wall tension in the pulmonary arterioles, the effect will depend on the radius of the vessel. According to the Laplace relationship, $P = 2\tau/R$, a given reduction in wall tension should produce a proportionally larger increase in radius when the vessel is constricted than when it is dilated. The administration of a vasodilator drug might therefore result in redistribution of flow towards the previously vasoconstricted vascular bed.

There is, however, increasing evidence which indicates that many drugs have a direct action on the hypoxic vasoconstrictor mechanism. For example, in isolated lungs perfused at constant flow, drugs such as ether and trichloroethylene inhibit the pressor response to alveolar hypoxia without altering pulmonary vascular tone (Sykes et al., 1973; Hurtig, Tait and Sykes, 1977). Similar results have been obtained in the intact animal (Sykes et al., 1975; Sykes, Hurtig et al., 1977). Inhibition can also be produced by calcium antagonists (McMurtry et al., 1976) and by carbon monoxide (Miller and Hales, 1978). Furthermore, both pulmonary vaso-constrictor and -dilator drugs inhibit hypoxic pulmonary vasoconstric-

**REFERENCES**


SNP, NITROGLYCERINE AND HYPOXIC RESPONSE


DEPRESSION DE LA VASOCONSTRICTION PULMONAIRE HYPOXIQUE PAR LE NITROPRUSSIATE DE SOUDE ET LA NITROGLYCERINE

RESUME
La réaction vasoconstrictrice pulmonaire à l'administration unilatérale de 7% d'oxygène a été étudiée sur 10 chiens anesthésies, dont les poumons étaient ventilés mécaniquement. La répartition du débit sanguin entre les deux poumons a été mesurée continuellement par enregistrement de la radioactivité des mélanges de gaz expirés de chaque poumon pendant la perfusion intraveineuse de xénon-133. Les perfusions de nitroglycerine et de nitroprussiate de soude qui produisent la même diminution de la pression aortique moyenne ont provoqué des diminutions similaires dans la vasoconstriction pulmonaire hypoxique. La réduction de la $P_O_2$ artérielle pendant l'hypoxie unilatérale a été plus forte lorsque la réaction vasoconstrictrice hypoxique a été déprimée par des médicaments, qu'elle ne l'avait été pendant les périodes de contrôle,
bien que la $P_{O_2}$ veineuse mélangée soit demeurée sans change-
ment. On en a conclu que les deux médicaments peuvent
provoquer l'hypoxémie en augmentant le débit sanguin allant
aux alvéoles avec un faible rapport ventilation/perfusion.

**DÄMPFUNG DER HYPOXISCHEN
PULMONARGEFÄSSVERENGUNG DURCH
NATRIUMNITROPRUSSID UND NITROGLYZERIN**

**ZUSAMMENFASSUNG**

Die pulmonare Vasokonstriktorreaktion auf die einseitige
Verabreichung von 7% Sauerstoff wurde bei 10 anästhesierten
Hunden untersucht, deren Lungen mechanisch belüftet
wurden. Die Blutflussverteilung zwischen den beiden Lungen-
flügel wurde kontinuierlich gemessen, indem die Radio-
aktivität des ausgestemten Gasmischm es aus jeder Lunge
während einer Infusion von Xenon-133 (intravenös) auf-
gezeichnet wurde. Infusionen von Nitroglycerin und Natrium-
nitroprussid, die den gleichen Abfall des mittleren Aorten-
drucks hervorriefen, bewirkten auch eine ähnliche
Verringerung der pulmonaren hypoxischen Gefässverengung.
Die Reduzierung von arteriellem $P_{O_2}$ während unilateraler
Hypoxie war größer, wenn die hypoxische Vasokonstriktor-
reaktion durch Drogen gedämpft wurde, als sie während der
Kontrollperioden war, obwohl das gemischte venöse $P_{O_2}$
unverändert blieb. Daraus schliesst man, dass beide Drogen
Hypoxämie verursachen können, indem sie die Blutzufluhr zu
den Alveolen mit niedrigem Belüftungs/Durchströmungs-
Verhältnis erhöhen.

**DEPRESION DE LA VASOCONSTRICCION
HIPOXICA PULMONAR MEDIANTE
NITROGLICERINA Y NITROPRUSIATO DE SODIO**

**SUMARIO**

La respuesta vasoconstrictora pulmonar a la administración
unilateral de 7% de oxígeno se estudió en 10 perros
anestesiados en los que los pulmones se ventilaron por medios
mecánicos. La distribución del flujo sanguíneo entre los dos
pulmones se midió continuamente mediante el registro de la
radioactividad existente en el gas mezclado de espiración
procedente de cada uno de los pulmones, durante la infusión
intravenosa de xenon-133. Las infusiones de nitroglicerina y de
nitroprussiato de sodio que produjeron la misma disminución en
la presión aórtica media produjeron, así mismo, disminuciones
similares en la vasoconstricción hipoxica pulmonar. La reduc-
ción del $P_{O_2}$ arterial durante la hipoxia unilateral fue mayor
cuando la respuesta hipoxica vasoconstrictora se redujo
mediante drogas de lo que fue durante los periodos de control,
aunque el $P_{O_2}$ mezclado de carácter venoso permaneció inalte-
rado. La conclusión es, por lo tanto, que ambas drogas pueden
ocasionar hipoxemia al incrementar el flujo sanguíneo al alveolo
con una baja relación de ventilación/perfusión.