THE EFFECTS OF HYPOCAPNIA ON MYOCARDIAL BLOOD FLOW AND METABOLISM

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

SUMMARY

Moderate hypocapnia (arterial carbon dioxide tension about 25 mm Hg) was produced in closed-chest anaesthetized dogs using two methods—firstly by increasing minute ventilatory volume, and secondly by withdrawing carbon dioxide gas which had been added to the inspired gas mixture during hyperventilation. Myocardial blood flow was measured by estimating the rate of clearance of radioactive xenon from the myocardium after its selective injection into one of the two main branches of the left coronary artery. Hypocapnia was associated with a highly significant reduction in myocardial blood flow and oxygen availability but myocardial oxygen extraction increased so that oxygen consumption by the myocardium was unaffected. Mean arterial blood pressure, heart rate and cardiac output did not change significantly. Hypocapnia caused an increase in systemic blood lactate level but myocardial consumption of glucose, lactate, pyruvate and non-esterified fatty acid was not significantly altered.

It is well established that the volume flow of blood through tissues may be profoundly influenced by alterations in the carbon dioxide tension of the blood; for example, cerebral blood flow is increased during hypercapnia and decreased during hypocapnia.

In the myocardium most recent studies indicate that hypercapnia is accompanied by an increase in blood flow (Feinberg, Gerola and Katz, 1960; Kittle, Aoki and Brown, 1965; Eberlein, 1966; Lochner, Hirche and Koike, 1967; Ledingham et al., 1970). However, reports of investigations on the effect of hypocapnia on myocardial blood flow have shown considerable disagreement. Feinberg, Gerola and Katz (1960) reported no change between control and hypocapnic flows but when an increased load was applied to the heart (in the form of a clamp on the aorta) flow during hypocapnia was apparently greater than during normocapnia. Rowe, Castillo and Crompton (1962) reported a slight but non-significant increase in flow during hypocapnia in anaesthetized dogs, while McArthur (1965) and Scheuer (1968) demonstrated a reduction in flow with hyperventilation. However, Scheuer's animals, which were vigorously hyperventilated, showed a mean fall in blood pressure of 49% which could possibly have accounted for much of the observed flow changes.

Since passive hyperventilation with the production of moderate degrees of hypocapnia is an accepted part of current anaesthetic practice, the study reported here was undertaken in an attempt to determine if such techniques are accompanied by changes in blood flow, oxygen consumption and certain aspects of substrate metabolism in the myocardium.

METHOD

Anaesthesia was induced in 11 healthy, adult, mongrel dogs (weight range 18–25 kg) with sodium thiopentone (15 mg/kg given intravenously). After endotracheal intubation, anaesthesia was maintained using trichloroethylene (0.5–1.0%) vaporized from a Tritec vaporizer (Cyprane Ltd, Keighley, Yorks.), the carrier gas being a mixture of nitrogen and oxygen, the proportions of which were adjusted to produce an arterial oxygen tension of about 100 mm Hg. Reflex movement was prevented by the intermittent intramuscular injection of 50-mg doses of suxamethonium chloride and ventilation was controlled using a Palmer respiratory pump. The minute volume of ventilation was adjusted to produce, for control measurements, an arterial carbon dioxide tension of about 40 mm Hg.

A no. 7 Sones catheter was introduced into the left common carotid artery in the neck and manipulated under radiographic control until its tip came to lie a few millimetres within the orifice of the left coronary artery or one of its two main branches and figure 1 shows a coronary angiogram taken during
the preparation of one of the animals. Other catheters were similarly manipulated into the
coronary sinus via the left external jugular vein,
and in 6 dogs into the pulmonary artery also via the
left external jugular vein, and in the remaining 5 dogs
into the right atrium via the right femoral vein. A
fourth catheter was positioned in the descending aorta
via the right femoral artery. These catheters were
thus available for sampling of arterial, coronary sinus
and mixed venous blood. Pressures were recorded
from the aorta and pulmonary artery or right atrium
using capacitance transducers (Elema Schonander
EMT 33 and 35 respectively). The electrocardiogram
(standard limb lead II) and the aortic pressure trace
were continuously visible on an oscilloscope and were
recorded during flow measurements on an ink-jet
recorder (Elema Schonander Mingograf 81) along
with the pulmonary artery or right atrial pressure
trace. Mean arterial pressure was obtained by integra-
tion. Heparin 25 mg was administered after the
positioning of the coronary arterial catheter and at 2-
hourly intervals thereafter. Mid-oesophageal tempera-
ture was measured using a copper-constantan thermo-
couple (Ellab).

Myocardial blood flow was measured using a
method similar to that described by Ross and
associates (1964) and subsequently used by Rees and
associates (1966) and Vance, Parratt and Ledingham
(1971). This consisted of measuring the rate of
clearance from the myocardium of a small volume
(0.5–1.0 ml) of a solution of the radioactive isotope
xenon-133 which was injected into the coronary
arterial catheter and flushed into the coronary artery
with 3 ml heparinized saline. The clearance of the
isotope was measured using an Ekco GP scintillation
counter suspended over the precordial area. The output
from the counter passed to an Ekco ratemeter and
the clearance was recorded as a curve on a Servo-
scribe recorder (Kelvin Electronics) operating at a
paper speed of 120 mm/min. Figure 2 shows such a
curve, the greater part of which is exponential

\[
\text{myocardial blood flow} = \frac{(k \times 100)}{\rho}
\]

where \(\lambda\) is the partition coefficient of xenon-133
between myocardium and blood and is equal to 0.72
(Conn, 1961), \(\rho\) is the density of the myocardium
and is equal to 1.05 g/ml (Herd et al., 1962) and \(k\) is
the clearance rate constant log \(2/\tau_1\). The derivation
of the above equation is explained in the paper by
Ross and associates (1964).

Blood oxygen and carbon dioxide tensions and pH
were measured using appropriate, suitably calibrated
electrode systems (Radiometer, Copenhagen). Blood
glucose, lactate, pyruvate and non-esterified fatty acid
EFFECTS OF HYPOCAPNIA ON MYOCARDIAL BLOOD FLOW

(NEFA) concentrations were measured using standard laboratory methods. Haemoglobin concentration was measured using the cyanhaemoglobin method. Cardiac output was measured using indocyanine green dilution, the descending aortic blood being withdrawn through a cuvette densitometer (XC302, Waters Company, Rochester, Minnesota) after injection of the dye into the pulmonary artery or right atrium.

Blood oxygen content was calculated using the formula:

\[ O_2 \text{ content} = Hb \times 1.34 \times \% \text{ saturation} / 100 + (P_{O_2} \times 0.0031). \]

All blood-gas and pH measurements were corrected for any difference in temperature between the animals’ mid-oesophagus and the electrodes after an appropriate blood-gas factor had been applied to the \( P_{O_2} \) values to allow for the difference in measurement of \( P_{O_2} \) in gas and blood (McDowall, Ledingham and Tindal, 1968). Blood-oxygen saturation was calculated from the \( P_{O_2} \) values thus corrected, using the dog cursor on the Radiometer blood-gas calculator designed by Severinghaus (1966).

The satisfactory correlation between the above method of calculation of blood-oxygen content when compared with simultaneous estimations using the Van Slyke method is presented in the paper by Ledingham and associates (1970).

The following data were also derived:

- **Myocardial \( O_2 \) consumption (ml. min\(^{-1}\). lOOg\(^{-1}\))**
  \[ = \text{arterial-coronary sinus } O_2 \text{ content difference} / \text{myocardial blood flow (ml. min}\(^{-1}\). 100g\(^{-1}\}) \times 0.01 \]

- **Myocardial consumption of metabolic substrate**
  \[ = \text{arterial-coronary sinus concentration difference} / \text{myocardial blood flow (ml. min}\(^{-1}\). 100g\(^{-1}\}) \times 0.01 \]

- **Myocardial \( O_2 \) availability (ml. min\(^{-1}\). 100 g\(^{-1}\))**
  \[ = \text{arterial } O_2 \text{ content (ml/100 ml)} / \text{myocardial blood flow (ml. min}\(^{-1}\). 100 g\(^{-1}\}) \times 0.01 \]

- **Myocardial \( O_2 \) extraction (%)**
  \[ = (\text{arterial-coronary sinus } O_2 \text{ content difference}) / \text{arterial } O_2 \text{ content (ml/100 ml)} \times 100 \]

The experiments were carried out in five phases as follows:

1. **Control phase**: \( P_{CO_2} \) about 40 mm Hg.
2. **Hyperventilation by increasing tidal volume only**: \( P_{CO_2} \) about 25 mm Hg.
3. **As phase 2 with \( CO_2 \) gas added to the inspired gas mixture**: \( P_{CO_2} \) about 40 mm Hg.
4. **\( CO_2 \) gas removed**: \( P_{CO_2} \) about 25 mm Hg.
5. **Ventilation returned to control level**: \( P_{CO_2} \) about 40 mm Hg.

Haemoglobin was estimated at the commencement of each phase. The duration of phases 1, 2, 3 and 4 was 20–30 min, while phase 5 was slightly longer (25–35 min).

Two sets of measurements of myocardial blood flow, haemodynamic data, arterial, coronary sinus and mixed venous blood gases and pH were made during each of the five phases. Along with the second of each of these sets of measurements, blood samples were withdrawn from the aorta and coronary sinus for estimation of blood glucose, lactate, pyruvate and NEFA. In total, the above samples required the withdrawal of some 60 ml of blood during each phase and this was replaced with Dextran 110 in 0.9% saline with the result that there was an increasing haemodilution throughout the experiment.

**RESULTS**

The results are presented in tables or figures which show the control phase measurements and those made in the subsequent four phases of the experiments. All results which refer to the group of animals are expressed as mean ± standard error of the mean (SEM). The data referred to as mixed venous include that from pulmonary artery and right atrial samples taken together, although the theoretical inaccuracy of right atrial samples in this respect is appreciated. The Student t-test for unpaired data was applied to each variable between succeeding phases of the experiment and the results of this test are quoted where significant changes took place (i.e. \( P<0.05 \)).

The blood-gas and pH changes occurring throughout the experiment are seen in table I. The changes in coronary sinus and mixed venous \( P_{CO_2} \) and pH paralleled those of the arterial blood.

Although the arterial oxygen tension remained stable throughout the procedure, there were considerable falls in coronary sinus \( P_{O_2} \) during hypocapnia, suggesting an increased oxygen extraction by the myocardium when \( P_{CO_2} \) is reduced and this is confirmed in a later table. A similar but less striking pattern is seen in mixed venous \( P_{O_2} \).

The myocardial blood flow and important systemic haemodynamic data are set out in table II. Significant reductions in myocardial blood flow occurred when hypocapnia was produced. Although a slight fall in arterial blood pressure occurred and was sustained...
TABLE I. \( \text{Pco}_2, \text{Po}_2 \) and pH changes in arterial, coronary sinus and mixed venous blood. (Mean±SEM, 11 dogs.)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hyperventilation</th>
<th>Hyperventilation + CO(_2)</th>
<th>CO(_2) off</th>
<th>Normoventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial ( \text{Pco}_2 ) (mm Hg)</td>
<td>40.7</td>
<td>24.9</td>
<td>41.8</td>
<td>25.1</td>
<td>40.7</td>
</tr>
<tr>
<td></td>
<td>±0.7</td>
<td>±0.4</td>
<td>±0.6</td>
<td>±0.6</td>
<td>±1.0</td>
</tr>
<tr>
<td></td>
<td>±0.012</td>
<td>±0.006</td>
<td>±0.012</td>
<td>±0.008</td>
<td>±0.005</td>
</tr>
<tr>
<td>Arterial ( \text{Po}_2 ) (mm Hg)</td>
<td>100.8</td>
<td>105.8</td>
<td>97.4</td>
<td>101.0</td>
<td>102.4</td>
</tr>
<tr>
<td></td>
<td>±1.7</td>
<td>±1.9</td>
<td>±2.0</td>
<td>±1.9</td>
<td>±1.7</td>
</tr>
<tr>
<td>Coronary sinus ( \text{Pco}_2 ) (mm Hg)</td>
<td>32.9</td>
<td>25.2</td>
<td>33.8</td>
<td>22.8</td>
<td>30.9</td>
</tr>
<tr>
<td></td>
<td>±0.7</td>
<td>±0.9</td>
<td>±0.9</td>
<td>±0.9</td>
<td>±0.9</td>
</tr>
<tr>
<td>Coronary sinus ( \text{Po}_2 ) (mm Hg)</td>
<td>55.2</td>
<td>48.4</td>
<td>50.1</td>
<td>41.6</td>
<td>45.2</td>
</tr>
<tr>
<td></td>
<td>±1.5</td>
<td>±1.7</td>
<td>±1.0</td>
<td>±0.9</td>
<td>±1.3</td>
</tr>
<tr>
<td>Coronary sinus pH</td>
<td>7.278</td>
<td>7.380</td>
<td>7.254</td>
<td>7.277</td>
<td>7.275</td>
</tr>
<tr>
<td></td>
<td>±0.007</td>
<td>±0.005</td>
<td>±0.014</td>
<td>±0.010</td>
<td>±0.008</td>
</tr>
<tr>
<td>Mixed venous ( \text{Pco}_2 ) (mm Hg)</td>
<td>47.6</td>
<td>33.4</td>
<td>49.6</td>
<td>34.5</td>
<td>46.7</td>
</tr>
<tr>
<td></td>
<td>±0.7</td>
<td>±0.5</td>
<td>±0.7</td>
<td>±1.2</td>
<td>±0.7</td>
</tr>
<tr>
<td>Mixed venous pH</td>
<td>7.296</td>
<td>7.402</td>
<td>7.268</td>
<td>7.408</td>
<td>7.302</td>
</tr>
<tr>
<td></td>
<td>±0.007</td>
<td>±0.006</td>
<td>±0.012</td>
<td>±0.009</td>
<td>±0.002</td>
</tr>
</tbody>
</table>

Throughout the whole period of hyperventilation, this was not statistically significant. Blood pressure returned to control level on resumption of normoventilation. Cardiac output fell gradually throughout the course of the investigation but there were no significant alterations between the succeeding phases of the experiment.

Arterial oxygen content and myocardial oxygen availability, extraction and consumption changes throughout the experiment are seen in table II. The haemodilution previously mentioned resulted in a steady fall in haemoglobin concentration, the mean values being as follows (phases 1–5 respectively): 22.4, 21.7, 19.5, 18.5, and 18.1 (g/100 ml). Arterial oxygen content fell as a consequence of the falling haemoglobin concentration. This trend is also seen in the myocardial oxygen availability figures, but these are of course influenced by the blood flow changes. There was a highly significant increase in myocardial oxygen extraction during hypocapnia and, although oxygen consumption fell gradually, there were no significant changes between succeeding phases of the experiment.

Although in most of the experiments the phase of hyperventilation was maintained for only some 20–25 minutes, in two of the animals it was maintained for a
TABLE III. Effects of hypocapnia induced by two methods on arterial oxygen content and myocardial oxygen availability, extraction and consumption. (Mean ± SEM, 11 dogs.)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hyperventilation</th>
<th>Hyperventilation + CO₂</th>
<th>CO₂ off</th>
<th>Normoventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial oxygen</td>
<td>29.4 ± 0.9</td>
<td>28.5 ± 1.5</td>
<td>25.5 ± 0.7</td>
<td>23.6 ± 1.0</td>
<td>23.7 ± 1.0</td>
</tr>
<tr>
<td>content (ml/100 ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial oxygen</td>
<td>31.0 ± 1.4</td>
<td>24.2 ± 1.1</td>
<td>27.0 ± 1.0</td>
<td>18.0 ± 1.1</td>
<td>20.2 ± 1.5</td>
</tr>
<tr>
<td>availability</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.01</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>(ml. min⁻¹, 100g⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial oxygen</td>
<td>48.0 ± 2.0</td>
<td>58.0 ± 2.0</td>
<td>45.0 ± 2.0</td>
<td>63.0 ± 1.5</td>
<td>49.0 ± 1.0</td>
</tr>
<tr>
<td>extraction (%)</td>
<td>P &lt; 0.005</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.005</td>
<td></td>
</tr>
<tr>
<td>Myocardial oxygen</td>
<td>15.0 ± 1.0</td>
<td>14.1 ± 1.0</td>
<td>12.4 ± 1.0</td>
<td>11.3 ± 0.7</td>
<td>10.7 ± 1.1</td>
</tr>
<tr>
<td>consumption (ml. min⁻¹, 100g⁻¹)</td>
<td>± 1.0</td>
<td>± 1.0</td>
<td>± 0.5</td>
<td>± 0.7</td>
<td>± 1.1</td>
</tr>
</tbody>
</table>

Fig. 3. Illustrates from a single animal the sustained reduction in myocardial blood flow which accompanies a prolonged period of hypocapnia (about 2 hours in this case). The arterial blood pressure was virtually unaffected. A longer period with similar results in both cases. Results from one of these are illustrated in figure 3. Throughout the prolonged period of hyperventilation the myocardial blood flow remained at a reduced level but rose promptly again when the Pa₉O₂ was returned to normal by adding carbon dioxide gas.

The absolute concentrations of glucose, lactate, pyruvate and NEFA in arterial and coronary sinus blood are shown in table IV. The onset of hyperventilation was accompanied by a significant increase in lactate concentration in arterial and coronary sinus blood. There were no significant changes in systemic levels of glucose or NEFA associated with Pa₉O₂ changes. At no time did the myocardium appear to utilize important quantities of glucose but there was consistent extraction of lactate, pyruvate and NEFA from the arterial blood by the myocardium and the mean per cent extraction of these substrates is shown in table V. Myocardial consumption of lactate, pyruvate and NEFA are shown in table VI. Hypocapnia was not associated with significant changes in consumption of these substrates.

DISCUSSION

The radioactive inert gas clearance method of measurement of tissue blood flow is now well established and the theory underlying its use is described by Conn (1962) and Zierler (1965) and its application to the myocardium is discussed by Herd and associates (1962) and Ross and associates (1964).

TABLE IV. Absolute concentrations of lactate, pyruvate, non-esterified fatty acid (NEFA) and glucose in arterial (Art) and coronary sinus (CS) blood. (Mean ± SEM, 11 dogs.)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hyperventilation</th>
<th>Hyperventilation + CO₂</th>
<th>CO₂ off</th>
<th>Normoventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate (mg/100 ml)</td>
<td>20.2 ± 1.7 P &lt; 0.025</td>
<td>27.2 ± 2.8</td>
<td>26.0 ± 4.7</td>
<td>20.9 ± 3.5</td>
<td>17.5 ± 1.7</td>
</tr>
<tr>
<td>Pyruvate (mg/100 ml)</td>
<td>12.4 ± 1.0 P &lt; 0.01</td>
<td>19.4 ± 2.3</td>
<td>18.0 ± 5.6</td>
<td>16.9 ± 3.0</td>
<td>15.8 ± 1.5</td>
</tr>
<tr>
<td>NEFA (m-equiv/L)</td>
<td>0.6 ± 0.1</td>
<td>1.5 ± 0.2</td>
<td>1.1 ± 0.1</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.2</td>
</tr>
<tr>
<td>Glucose (mg/100 ml)</td>
<td>0.89 ± 0.10</td>
<td>1.12 ± 0.11</td>
<td>0.99 ± 0.13</td>
<td>1.10 ± 0.17</td>
<td>1.15 ± 0.14</td>
</tr>
<tr>
<td>(mg/100 ml)</td>
<td>0.90 ± 0.11</td>
<td>0.84 ± 0.12</td>
<td>0.82 ± 0.15</td>
<td>0.90 ± 0.10</td>
<td>0.88 ± 0.11</td>
</tr>
<tr>
<td>Glucose (mg/100 ml)</td>
<td>89.0 ± 5.0</td>
<td>88.0 ± 6.0</td>
<td>88.0 ± 6.0</td>
<td>92.0 ± 7.0</td>
<td>94.0 ± 6.0</td>
</tr>
</tbody>
</table>

The radioactivity of inert gas clearance method of measurement of tissue blood flow is now well established and the theory underlying its use is described by Conn (1962) and Zierler (1965) and its application to the myocardium is discussed by Herd and associates (1962) and Ross and associates (1964).
TABLE V. Effects of hypocapnia on the mean per cent extraction by the myocardium from arterial blood of lactate, pyruvate and non-esterified fatty acid (NEFA).

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hyperventilation</th>
<th>Hyperventilation + CO₂</th>
<th>CO₂ off</th>
<th>Normoventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>36</td>
<td>28</td>
<td>38</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>Pyruvate</td>
<td>43</td>
<td>38</td>
<td>33</td>
<td>25</td>
<td>29</td>
</tr>
<tr>
<td>NEFA</td>
<td>23</td>
<td>28</td>
<td>18</td>
<td>15</td>
<td>13</td>
</tr>
</tbody>
</table>

The study reported here shows that hyperventilation of a degree sufficient to produce a reduction in PaₐCO₂ from 40 mm Hg to 25 mm Hg is accompanied by a mean fall of 18% in myocardial blood flow, and furthermore that the fall in flow is not dependent on haemodynamic changes associated with hyperventilation since a mean flow reduction of 26% occurred when hypocapnia was produced by withdrawing carbon dioxide gas from the inspired gases of the hyperventilated animal. The demonstration that the reduction in flow is maintained as long as the PaₐCO₂ remains low is in contrast to the effect of hypercapnia where the elevation in blood flow tends to pass off even though the PaₐCO₂ remains elevated. Ledingham and associates (1970) suggest that there are two separate actions of hypercapnia (Paco₂ 90-100 mm Hg) on the heart, one which dilates the myocardial vessels and another which reduces the oxygen consumption by direct myocardial depression, either by a carbon dioxide or pH effect. Oxygen consumption of the myocardium was unaffected by hypocapnia. The reduction in mixed venous oxygen tension during hypocapnia indicates an increase in total body oxygen extraction at these times and this, taken in conjunction with the unchanged cardiac output, indicates an increase in total body oxygen consumption during hypocapnia. This suggestion accords with the results of several workers in both animal and human investigations, for example, Cain (1970) and Karetzky and Cain (1970).

The observation that myocardial blood flow did not return to control level during phase 5 is probably explained on the grounds that a certain amount of myocardial depression was occurring due to a prolonged period of anaesthesia. This suggestion is supported by the downward trend in myocardial oxygen consumption and in the consumption of lactate and pyruvate by the myocardium.

The systemic haemodynamic effects of the degree of hyperventilation and hypocapnia utilized in the present study were unremarkable. Hyperventilation caused a slight but non-significant fall in mean arterial pressure and a slight, but also non-significant, rise in heart rate. Most workers have reported a fall in blood pressure with hyperventilation but the majority of studies have attained lower carbon dioxide levels than those reached here, e.g. in Scheuer's study quoted above the mean Paco₂ during hyperventilation was 13.7 mm Hg, and Little and Smith (1964), who also showed falls in blood pressure, attained end expiratory Paco₂ levels of 14-15 mm Hg. Richardson, Wasserman and Patterson (1961) suggest that the magnitude of circulatory effects of hyperventilation is related to the extent of reduction of carbon dioxide levels and also to the rapidity with which these reduced levels are attained. Although cardiac output fell gradually throughout the period of this study, there were no significant changes between the succeeding phases of the study, again emphasizing the lack of systemic haemodynamic upset with this level of hyperventilation and hypocapnia in the healthy animal.

In a study of passive hyperventilation in conscious humans where the PaₐCO₂ was reduced to a mean level
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of 23.8 mm Hg (i.e. comparable to that of the present study), Cullen, Eger and Gregory (1969) also failed to demonstrate changes in cardiac output or heart rate and also in stroke volume or total peripheral vascular resistance, and similarly Marshall and associates (1971) showed that cardiac index was not significantly different during hypocapnia and normocapnia in anaesthetized humans. On the other hand, hypocapnia was accompanied by an increase in cardiac index in both of the above studies. These findings are presumably related to the findings of Leigh, J. M., Blackburn, J. P., Conway, C. M., Lindop, M. J., and Reitan, J. A. (1971, personal communication) who observed that myocardial contractility was increased during hypocapnia but unchanged during hyperventilation. Related to these observations by other workers, the present study shows that with moderate hypocapnia myocardial oxygen consumption was unaffected, although myocardial oxygen availability was reduced concomitantly with the reductions in blood flow. The maintenance of oxygen consumption is explained by the important increases in oxygen extracted by the myocardium when the blood flow is reduced.

The energy requirements of the myocardium are met largely by the metabolism of glucose, lactate, pyruvate and fatty acids, although other substrates such as ketone bodies and amino acids are utilized. Olson and Piatnok (1959) point out that in the fasting state the metabolism of carbohydrate lessens while fatty acids are preferred. This observation presumably accounts for the lack of glucose uptake by the heart in the present investigation since all the animals involved had fasted.

The arterial pH rise during hyperventilation is slightly greater than that which would be expected with the PaCO₂ changes observed. This is probably accounted for by the slight increase in systemic lactate level which occurred at this time. This small but significant rise in arterial blood lactate concentration is in keeping with the work of Papadopoulos and Keats (1959) who showed an increase in lactate levels with hyperventilation. They suggested that the increased levels of fixed acid occurring during hyperventilation were produced as a tissue response to respiratory alkalosis and not as a result of tissue hypoxia.

In the clinical context passive hyperventilation of the anaesthetized patient is widely used and is usually regarded as a procedure without ill effects. However, Flemma and Young (1964) showed that in dogs and in post-thoracotomy patients hyperventilation caused a fall in serum K+ and that certain patients on digitalis therapy developed cardiac arrhythmias, probably as a result of this fall in serum K+. The results of the study reported here suggest that with moderate degrees of hypocapnia, myocardial blood flow decreased while myocardial oxygen extraction increased so that myocardial oxygen consumption was maintained. Where myocardial blood flow may already be low and oxygen extraction increased, it would seem reasonable to avoid undue reductions in arterial carbon dioxide tension lest a situation be precipitated where the myocardium is unable to extract sufficient oxygen from the grossly reduced amount of blood flowing through it. These conditions have been shown to exist in the dog in haemorrhagic hypotension (Ledingham et al., 1971) and presumably occur in patients under similar circumstances. They probably also exist in patients with severe myocardial ischaemic disease. Further support for a more cautious approach to hypcapnia where there is pre-existing cardiovascular disease is provided by Pryse-Roberts and associates (1972). These workers describe a patient who, while hypocapnic during anaesthesia, developed electrocardiographic evidence of myocardial ischaemia which was abolished when normocapnia was reinstituted.

ACKNOWLEDGEMENTS

The authors are deeply grateful to Dr I. McA. Ledingham for the generous provision of valuable laboratory time and facilities and to Messrs I. Douglas, K. Gorman and R. Thomson, and Misses G. Doherty and A. Stewart, for skilled technical assistance.

REFERENCES


**Effets de la hypocalpnie sur l'irrigation sanguine et le metabolisme du myocarde**

**Sommaire**

Une hypocalpnie modérée (tension du gaz carbonique artériel de 25 mm Hg environ) a été engendrée chez des chiens anesthésiés et dont le thorax était fermé, en recouinant à deux méthodes: premièrement, en augmentant la ventilation minute et deuxièmement, en supprimant le gaz carbonique qui avait été ajouté au mélange gazeux inhalé durant la phase d'hyperventilation. Le débit sanguin myocardique a été mesuré en évaluant le taux de clairance du xénon radioactif, à partir du myocarde, après injection sélective dans l'une des deux principales branches de l'artère coronaire gauche. L'hypocalpnie s'est accompagnée d'une diminution hautement significative du débit sanguin myocardique et de l'apport d'oxygène, mais l'extraction de l'oxygène par le myocarde s'étant accrue, il est en résulté que la consommation d'oxygène du myocarde n'a pas été perturbée. La pression artérielle moyenne, la fréquence cardiaque et le débit cardiaque n'ont pas présenté de variations significatives. L'hypocalpnie a déterminé un accroissement des concentrations de lactate et de pyruvate dans le sang de la circulation générale, mais la consommation du myocarde en glucose, lactate, pyruvate et acides gras non estérifiés n'a pas été modifiée d'une manière significative.

**Ueber die Wirkung der Hypocapnie auf die Blutdurchströmung und den Stoffwechsel des Myocards**

**Zusammenfassung**


**Los efectos de la hipocapnia sobre el flujo sanguineo del miocardio y el metabolismo.**

**Resumen**

Se produjo una hipocapnia moderada (tensión parcial arterial del dióxido de carbono: 25 mm de Hg) en perros anestesiados con toloxiado, usando dos métodos: primero, aumentando el volumen minuto ventilatorio, en segundo lugar, por sustracción del dióxido
de carbono, que era añadido a la mezcla gaseosa inspirada durante la hiperventilación. El flujo sanguíneo miocárdico fue medido por estimación de la cuota de clearance del xenón radiactivo del miocardio, después de su inyección selectiva en una de las ramas principales de la arteria coronaria izquierda. La hipocapnia se asociaba con una reducción altamente significativa del flujo sanguíneo del miocardio y del oxígeno disponible, pero aumentaba la extracción de oxígeno por el miocardio, de modo que no se afectaba el consumo de oxígeno miocárdico. La presión sanguínea arterial media, frecuencia cardíaca y gasto cardíaco, no variaban de un modo importante. La hipocapnia causaba un aumento del nivel de lactato en la sangre sistémica, pero no se alteraba importantemente el consumo miocárdico de glucosa, lactato, piruvato y ácidos grasos no esterificados.

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