THE EFFECT OF ACUTE PORTACAVAL SHUNTING IN DOGS ON CEREBRAL AND PERIPHERAL BLOOD FLOW AND METABOLISM

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SUMMARY

1. Changes in brain and hind-limb blood flow and metabolism have been studied in six dogs before and after the acute shunting of portal vein blood into the systemic circulation.

2. An initial increase in brain blood flow, oxygen and glucose consumption was found.

3. More prolonged shunting caused a fall in flow and in oxygen and glucose utilization by the brain.

4. Although peripheral blood flow and oxygen consumption were reduced by shunting glucose consumption was increased throughout the period of shunting.

5. The possible mechanisms of these changes is discussed, together with their relevance to the causation of encephalopathy in patients after portacaval shunts.

Key words: portacaval shunting, cerebral blood flow, peripheral blood flow, cerebral metabolism, peripheral metabolism, encephalopathy.

After portacaval anastomosis in man there is an increase in cardiac output with a corresponding increase in blood flow in a variety of peripheral vascular beds (Foda, Badawi & Salah, 1964; Delaney, Goodale, Cheng & Wangensteen, 1965; Gitlin, Grahame, Kreel & Sherlock, 1968).

In patients who have no neurological or psychological disturbances there is a large increase in cerebral blood flow (Bianchi Porro, Maiolo & Della Porta, 1969) but in those patients who have well-marked neurological and psychological stigmata of portacaval encephalopathy, cerebral blood flow is reduced (Fazekas, Ticktin, Ehrmantraut & Alman, 1956; Posner & Plum, 1960; James, Sampson, Nashat, Williams & Garassini, 1969).

According to Bianchi Porro et al. (1969) those patients with an increase in cerebral blood flow usually also had an increase in brain oxygen and glucose consumption. On the other hand, where there was a decrease in cerebral blood flow, although brain glucose consumption was normal, cerebral oxygen utilization was severely decreased (James et al., 1969). It is pos-

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sible that small concentrations of toxic substances absorbed from the gut may cause increased cerebral blood flow and metabolism, but produce a fall in higher concentrations.

To test this hypothesis the changes in metabolism and blood flow, in the brain and the periphery, after portacaval shunting and high protein loading, have been studied in dogs. Although it is likely that the toxic substances absorbed from the gut are protein breakdown products, since their exact nature is unknown, changes in blood ammonia concentration have been followed as an index of hepatic by-pass.

**METHODS**

A single experiment was performed on each of six mongrel dogs, mean weight 13.2 kg ± 1.4 (SD). The animals were anaesthetized with sodium pentobarbitone (25 mg/kg) and ventilated at constant rate and depth throughout the experiment. End-tidal CO₂ concentration was measured continuously by means of a Beckmann infra-red gas analyser.

A catheter, 7.5 mm in diameter, was inserted into the hepatic portal vein via the splenic vein and a similar catheter was inserted into the inferior vena cava. Shunting of blood from the hepatic portal vein into the inferior vena cava was carried out using a perfusion pump, at maximum rates of between 40 and 50 ml of blood/min. To prevent clotting all dogs were given heparin (10,000 i.u.) intravenously. A pressure manometer was incorporated between the portal vein catheter and the perfusion pump so that any obstruction of the catheter during the shunting procedure could be recognized immediately and corrected.

The tip of a rubber tube (12.5 mm in diameter) was placed in the duodenum via a gastrostomy. Through this tube a specially prepared protein digest was given 10 min before the beginning of the first control period. The digest was prepared by mixing approx. 100 g of meat homogenate with 5 g of chymotrypsin, bringing to pH 8.5 with solid sodium bicarbonate and incubating at 38°C for 12 h before use.

Cortical blood flow was measured by intracarotid injection of ⁸³Krrypton (Ingvar & Lassen, 1962). The left common carotid artery was catheterized via the left superior thyroid artery. Craniotomy and removal of the dura were carried out in the conventional manner. Radioactivity was measured with a small Geiger counter placed over the left parietal region. The radioactive gas, dissolved in saline, was injected into the carotid artery over approx. 1 min so that a constant amount of radioactivity was registered over the left parietal region for 45 s. Cortical blood flow was then obtained from the analysis of the first 100 s of the ensuing decay curve as suggested by Ingvar & Lassen (1962).

Percentage changes in hind limb flow were measured with an electromagnetic flowmeter placed around the right femoral artery. The size of the probe was such that a tight fit was obtained without causing constriction of the vessel.

The left femoral artery was cannulated with a polyethylene catheter and mean arterial blood pressure was continuously recorded with a Statham P23 AC transducer. Arterial blood samples were obtained from the same source.

Samples for oxygen and glucose contents, pH, P₁CO₂ and P₁O₂ were taken from the superior sagittal sinus and right femoral vein as well as from the left femoral artery, thus enabling changes in brain and hind limb oxygen and glucose consumptions to be obtained.

Oxygen content was measured with an oxygen electrode (Linden, Ledsome & Norman, 1965) and glucose with glucose oxidase (Morley, Dawson & Monks, 1968).
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Appropriate radiometer electrodes were used for pH, $Pa,CO_2$ and $Pa,O_2$ and the values were corrected for changes in ambient temperature according to the nomogram of Severinghaus, Stupfel & Bradley (1956). Blood ammonia was estimated by the method of McCullough (1967).

The control period began an hour after all operative procedures were completed. Readings were taken at the end of two control periods of 20 min. Portacaval shunting was then carried out for a period of 1 h, during which readings were taken every 20 min. All measurements were repeated 20 min after the shunt had been turned off.

Since the electromagnetic flowmeter recorded only percentage changes in hind limb flow all values of brain and peripheral blood flow, oxygen and glucose consumptions have been expressed as a percentage of the first control values. The absolute values (mean $\pm$ SEM) from which percentage changes have been calculated are as follows:

- Mean cortical blood flow $= 108 \pm 10$ ml min$^{-1}$ 100 g$^{-1}$
- Mean cortical oxygen consumption $= 8.5 \pm 1.5$ ml min$^{-1}$ 100 g$^{-1}$
- Mean cortical glucose consumption $= 22 \pm 6$ mg min$^{-1}$ 100 g$^{-1}$

RESULTS AND DISCUSSION

Shunting, which produced a progressive rise in blood ammonia, lowered the mean arterial pressure (Table 1). There was a progressive increase in arterial pH in spite of the constant ventilation. The fall in blood pressure was only partly corrected after the shunt had been concluded.

After 20 min of portacaval shunting (Table 1) there was a significant increase in cerebral blood flow, and oxygen and glucose consumptions. These had fallen by 40 min. In contrast, the peripheral changes were a sustained increase in glucose consumption, but a fall of blood flow and oxygen consumption. The circulatory factors changed by 31% at most. The most striking effect of shunting blood from the portal vein into the inferior vena cava was the great increase in glucose consumption by both the brain and the hind limb. However, whereas the increase in cerebral glucose consumption was transient, the increase in glucose consumption by the hind limb was sustained.

These changes in peripheral glucose consumption were not paralleled by similar changes in peripheral oxygen consumption, nor was the initial increase in brain oxygen utilization as great as the increase in brain glucose utilization. It is obvious, therefore, that under these circumstances not all glucose was metabolized aerobically. The increase in glucose utilization may result in increased glutamine synthesis, or in increased formation of pyruvic acid and lactic acid which may contribute to the acidosis. Both abnormalities have been described in patients with chronic liver disease (Bessman & Bessman, 1955; Eichenholz, 1965). The cause of this large increase in glucose utilization by the brain and by the periphery is unclear. However, many amines have similar effects on cerebral metabolism, when administered intravenously, causing moderate increases in oxygen consumption and very much larger increases in glucose consumption (MacDonell, Xanalatos, Hall & James, 1971; Xanalatos & James, 1972). Although there is an initial increase in oxygen consumption, this metabolic effect becomes attenuated and even reversed if an acidosis is induced during the catecholamine infusion. It is known that many sympathomimetic amines absorbed from the gut escape breakdown by the liver during portacaval shunting (Kowalski & Ablemann, 1953). The fact that blood ammonia is raised
<table>
<thead>
<tr>
<th></th>
<th>First control period</th>
<th>Second control period</th>
<th>Portacaval shunt on for:</th>
<th>Shunt off 20 min</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>20 min</td>
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<tr>
<td>Cerebral blood flow</td>
<td>As 100%</td>
<td>98 ± 2</td>
<td>120 ± 6**</td>
<td>98 ± 5</td>
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<tr>
<td>Brain oxygen consumption</td>
<td>As 100%</td>
<td>101 ± 1</td>
<td>127 ± 4**</td>
<td>111 ± 10</td>
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<tr>
<td>Brain glucose consumption</td>
<td>As 100%</td>
<td>96 ± 3</td>
<td>163 ± 29**</td>
<td>103 ± 7</td>
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<tr>
<td>Peripheral blood flow</td>
<td>As 100%</td>
<td>100 ± 2</td>
<td>81 ± 10</td>
<td>89 ± 8</td>
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<tr>
<td>Peripheral oxygen consumption</td>
<td>As 100%</td>
<td>96 ± 4</td>
<td>82 ± 10</td>
<td>111 ± 19</td>
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<tr>
<td>Peripheral glucose consumption</td>
<td>As 100%</td>
<td>96 ± 10</td>
<td>209 ± 38**</td>
<td>77 ± 16</td>
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<tr>
<td>Blood NH₃ (μg of N/l)</td>
<td>116 ± 10</td>
<td>115 ± 10</td>
<td>180 ± 16**</td>
<td>120 ± 15</td>
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<tr>
<td>Mean arterial blood pressure (mmHg)</td>
<td>120 ± 10</td>
<td>124 ± 8</td>
<td>100 ± 7*</td>
<td>85 ± 12*</td>
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<td>Arterial [H⁺] (nmol/l)</td>
<td>62 ± 5</td>
<td>62 ± 5</td>
<td>85 ± 7</td>
<td>69 ± 10</td>
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<tr>
<td>PaCO₂ (mmHg)</td>
<td>45 ± 2</td>
<td>46 ± 2</td>
<td>45 ± 1</td>
<td>43 ± 2</td>
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* Significant decrease from control values at 5% level; ** significant increase from control values at 5% level.
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as a result of portacaval shunting in these experiments and in patients with portosystemic encephalopathy does not necessarily mean that the ammonia is the cause of the observed metabolic disturbances.

During these present experiments when the portacaval shunt was first turned on there was an increase in cerebral oxygen consumption. With continued shunting a marked metabolic acidosis occurred. This was accompanied by a decrease in brain oxygen utilization. As soon as the shunt was turned off the hydrogen ion concentration returned towards control values and oxygen consumption by the brain increased.

The decrease in brain oxygen utilization may have been caused or accentuated by the metabolic acidosis. These animals had some degree of metabolic acidosis in the control periods and even before all operative procedures. Further, they were unable to hyperventilate to correct this abnormality as they were ventilated at a constant rate. In patients with liver disease there is direct and indirect evidence of an intracellular acidosis (Bittar, 1964) even though plasma analyses suggest alkalosis. Total body potassium is often low in patients with liver disease (Casey, Summerskill & Orvis, 1965), and this would obscure the acidosis through a shift of hydrogen ions from the extracellular fluid space into the cells.

In patients without neurological disturbances after portacaval anastomosis there is an increase in cerebral blood flow and in brain oxygen and glucose consumption. Such changes occurred in dogs during the first stage of acute portacaval shunting when the blood ammonia and hydrogen ion concentration were still relatively low.

Later, with larger increases in blood ammonia, and with increased hydrogen concentration the dogs showed a decrease of brain blood flow and metabolism similar to that in patients in whom the neurological and psychological stigmata of portacaval encephalopathy are well marked.

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REFERENCES


