Neurotensin, vaso-active intestinal polypeptide and gastrin levels in plasma and portal venous blood in experimental mesenteric ischaemia

L. C. J. VAN RENBURG, G. MORRISON, R. DE BEER, A. F. STRACHAN

Summary

The effect of mesenteric ischaemia on the levels of neurotensin, vaso-active intestinal polypeptide and gastrin in baboons was studied in two groups of 7 and 6 baboons (Papio ursinus). In portal venous blood a decreasing trend in levels of neurotensin was observed, whereas vaso-active intestinal polypeptide and gastrin levels were unchanged. There was a similar trend in neurotensin levels in portal venous blood, together with an increasing trend in levels of vaso-active intestinal polypeptide. Gastrin levels were unchanged. Further investigation of these apparent trends in a larger number of animals is warranted.

Subjects and methods

Adult baboons (Papio ursinus) with an average weight of 16 kg were divided into two groups. In group I peripheral serum levels of NT, VIP and gastrin were measured. After these observations a decision was made to measure the hormone levels in portal venous serum (group II).

Group I

This group comprised 7 animals and each acted as its own control. Anaesthesia was induced (after a 10-hour fast) with ketamine hydrochloride 100 mg intravenously and sustained with hourly intravenous doses of pentobarbitone sodium 6% (m/v) 4.25 mg/kg/h. A nasogastric tube was passed, a peritoneal line for infusion of Ringer's lactate introduced, and a urinary catheter inserted. Venous samples were taken from an indwelling catheter in the femoral vein. A midline abdominal incision was made as a sham procedure and the anastomosis sustained for 6 hours. A fasting sample of blood was taken from the portal vein. This was followed by samples at induction of anaesthesia, on the completion of the laparotomy incision, within the 1st hour and then 2-hourly, with the 6th and last sample 6 hours after the laparotomy incision. Gastric pH was measured continuously with a pH probe positioned in the antrum of the stomach.

Three weeks later the baboons underwent re-operation. The superior mesenteric artery was isolated for the injection of microspheres. Debrisan beadlets 1 g (dextranomer beads 0.1 - 0.3 mm diameter), suspended in 2 ml saline, were injected and the artery ligated. This produced a reduction in the portal venous blood, including mesenteric ischaemia. A preliminary study was carried out to establish whether serum levels of NT, VIP and gastrin in the peripheral and portal venous blood changed in mesenteric ischaemia in the experimental animal.

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Table 1: Serum levels (pmol/l) of NT, VIP and Gastrin (Mean ± SD in Group I Animals)

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Control</th>
<th>Experiment</th>
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<tbody>
<tr>
<td>NT</td>
<td>Control</td>
<td>Experiment</td>
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<tr>
<td>VIP</td>
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<td>Gastrin</td>
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Discussion

In spite of the advent of special neurotrophic tests,1 early angiography2 and the awareness of this condition in the differential diagnosis of the acute abdomen in elderly patients, the diagnosis of mesenteric ischaemia is generally poor because of a delayed diagnosis. With increasing knowledge of gut hormones and the availability of diagnostic kits, it was postulated that changing levels of NT and VIP might be seen in mesenteric ischaemia. In these experiments (using a small number of animals) no changes could be demonstrated in the peripheral blood levels of these hormones. As it has been shown experimentally that VIP is extracted by the liver,3 it was not surprising to find no significant alterations in peripheral VIP levels, although a trend of increasing levels occurred in portal venous blood. Our findings are in keeping with other reports that VIP levels rise in the portal venous blood in mesenteric ischaemia.4 The mean levels in NT in the peripheral serum samples in group I showed a decreasing trend, which was also seen in the portal venous blood levels in group II; a finding which was anticipated. The high degree of variability and small size effect in NT measurements (Table I) indicates that much larger sample sizes will be necessary in order to reach statistical significance. The apparent trend in NT levels can then be verified. Gastrin levels remained unchanged in spite of the acute mesenteric ischaemia. As the major site of neurotensin (NT) production is in the proximal jejunum, the caecum and colon as the spleenic flexure. Venous samples were taken as before, with the exception of the specimen taken 6 hours after the induction of mesenteric ischaemia. For hormonal assay, all the samples were prepared in the following manner before despatch to the Francis Fraser Laboratories at Hammersmith Hospital, London: 200 μl sterile Trasylol (20000 KIU aprotinin/00) was placed in commercial heparin blood tubes. Blood was added (5 00) and mixed and the plasma was separated by centrifugation at room temperature. The plasma samples were stored at -20°C. After thawing, 1 ml aliquot samples were placed into freeze-drier tubes. After freeze-drying the aliquots were sealed under dry nitrogen for despatch.

Group II

In this group of 6 animals blood was taken from the portal vein for the measurement of NT, VIP and gastrin. The pre-operative preparation and anaesthesia was similar to that carried out in the animals in group I. After opening the abdomen, the superior mesenteric vessels and portal vein were exposed. A small mesenteric venous branch of the upper jejunum was chosen for the insertion of a thin polythene catheter into the portal vein in such a fashion that the portal venous blood flow was not interfered with. Two samples of blood were taken before the introduction of mesenteric ischaemia and then at 2-hourly intervals until the termination of the experiment after 6 hours.

Results

With continuous pH monitoring, it was found that the pH changed from an average low level of 1.9 to an average high of 6.6. Gastric output was no more than an average of 4 ml/h. The average volume of Ringer's lactate infused was 100 ml/h and the urinary output ranged between 150 and 350 ml over 6 hours. The serum levels of NT, VIP and gastrin are shown in Table I. There was no difference between the control animals and the animals with mesenteric ischaemia.