

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

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Summary

The effect of mesenteric ischaemia on the levels of neurotensin, vaso-active intestinal polypeptide and gastrin in portal venous blood and in the peripheral circulation was studied in two groups of 7 and 6 baboons (*Papio ursinus*). In peripheral blood a decreasing trend in levels of neurotensin was observed, while 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.

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As the major site of neurotensin (NT) production is in the terminal ileum,¹ it could be postulated that mesenteric ischaemia would bring about its reduction in the portal venous blood and possibly in the peripheral circulation. One of the properties of NT is inhibition of pentagastrin-stimulated secretion of gastrin acid.² Gastrin originates mainly in the stomach, duodenum and pancreas and, theoretically, its secretion should not be affected by mesenteric ischaemia alone, although its serum level could rise because of a suppressed NT secretion in mesenteric ischaemia. Vaso-active intestinal polypeptide (VIP) has a wide distribution throughout the gastro-intestinal tract³ and several factors cause its release into the portal venous blood, including mesenteric ischaemia.⁴ 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.

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 studies 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 peripheral venous 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 anaesthetic sustained for 6 hours. A fasting sample of blood was taken 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 continuously measured 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 marked ischaemia of the whole of the small intestine except for a few centimetres of proximal jejunum, the caecum and colon as far as the splenic flexure. Venous samples were taken as before, with the last specimen taken 6 hours after the introduction 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 (20 000 KIU aprotinin/ml) was placed in commercial heparin blood tubes. Blood was added (5 ml) and mixed and the plasma was separated by centrifugation at room temperature. The plasma samples were stored at -20°C. After brief 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 ml 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.

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TABLE I. SERUM LEVELS (pmol/l) OF NT, VIP AND GASTRIN (MEAN ± SD IN GROUP I ANIMALS)

Sample No.	NT		VIP		Gastrin	
	Control	Experiment	Control	Experiment	Control	Experiment
1	12,3 ± 11,9	14,5 ± 10,9	4,8 ± 0,5	4,5 ± 1,0	4,4 ± 1,1	4,0 ± 1,5
2	14,3 ± 15,2	12,8 ± 11,2	4,3 ± 0,5	4,3 ± 1,3	3,7 ± 1,5	4,4 ± 3,1
3	13,3 ± 14,6	11,3 ± 13,8	4,0 ± 0,0	4,5 ± 0,6	5,7 ± 3,4	3,0 ± 0,7
4	10,0 ± 15,5	7,8 ± 7,5	4,3 ± 0,5	4,3 ± 1,5	5,1 ± 3,7	2,5 ± 0,3
5	11,8 ± 12,9	9,0 ± 8,0	4,0 ± 0,8	4,5 ± 1,7	6,4 ± 1,3	4,2 ± 1,2
6	12,3 ± 13,2	9,8 ± 10,2	4,3 ± 1,0	4,8 ± 1,0	6,4 ± 2,7	3,4 ± 1,3

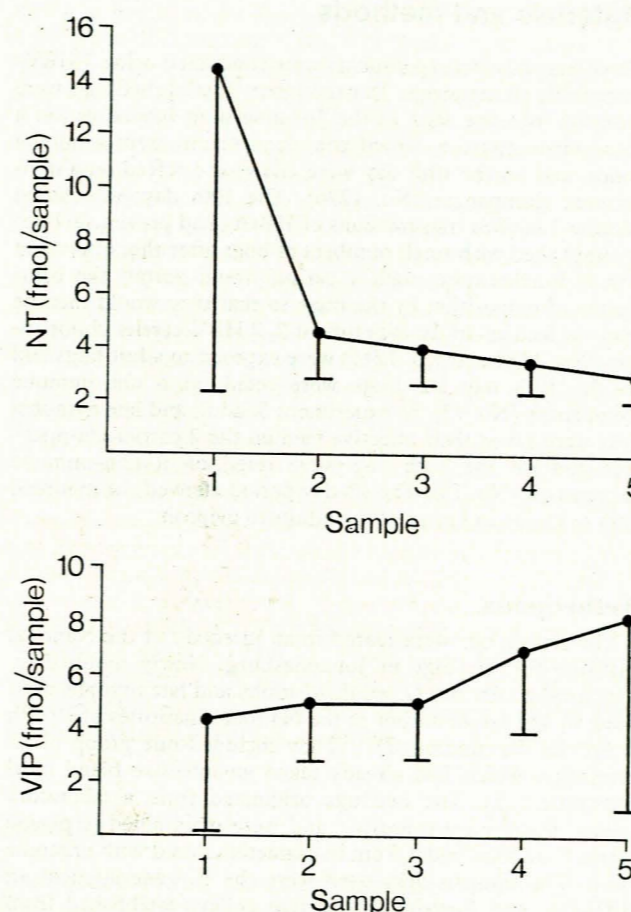


Fig. 1. Neurotensin levels in portal venous blood in group II animals (above). VIP levels in portal venous blood in group II animals (below).

The average volume of the intravenous infusion and urinary output and the pH changes in group II animals were similar to the animals in group I. Fig. 1 shows the changes in the portal venous blood serum levels before and after induction of mesenteric ischaemia. An initial decline in mean NT levels and an increasing trend in mean VIP levels was seen. Gastrin levels were unchanged (data not shown).

Discussion

In spite of the advent of special serological tests,⁵ early angiography⁶ and the awareness of this condition in the differential diagnosis of the acute abdomen in elderly patients, the prognosis 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 pilot 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,⁷ 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.⁶ The mean NT levels in the peripheral venous 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 theoretical possibility that diminished NT output in mesenteric ischaemia could precipitate a rise in gastrin levels through pH changes in the lumen of the stomach. Since gastric pH tended towards the alkaline in controls and in the animals with mesenteric ischaemia, these changes are probably nonspecific.

In this group of animals the small sample size precluded a statistical analysis of the results. We would suggest that an extended study of a larger number of animals would increase the probability of a statistically significant conclusion regarding the diagnostic potential for measurements of levels of these hormones in the peripheral blood in mesenteric ischaemia. At present it takes up to 48 hours to analyse these gut hormones, but it is anticipated that more rapid analysis will be possible in the future. The sampling of portal venous blood through a percutaneous transhepatic route cannot be considered feasible as a future special investigation in the diagnosis of early mesenteric ischaemia.

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