Effect of Neurotensin on Regional Intestinal Blood Flow in the Dog*


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Summary. The effect of various doses of synthetic neurotensin on regional blood flow in different tissue layers of the stomach, small bowel, colon, pancreas, brain, kidneys, adrenal gland, and heart of six dogs was studied using an isotope microsphere technique. Infusion of high doses (20, 40 pmol/kg·min⁻¹) of exogenous synthetic neurotensin caused an increase of blood flow in the "muscularis" of duodenum, jejunum, ileum, and colon. Neurotensin infused in a dose (2.5 pmol/kg·min⁻¹) raising neurotensin plasma levels to concentrations comparable to those observed after a meal caused an increase of blood flow in the muscular layer in ileum. Our results suggest that one of the physiologic actions of neurotensin may be the regulation of blood flow in the muscular layer of the ileum.

Key words: Neurotensin infusion – Neurotensin plasma levels – Intestinal blood flow – Microspheres

Neurotensin has been isolated from hypothalamus [5] and small intestinal mucosa [6, 10, 15]. Its physiologic role is unknown but in pharmacologic doses it increases vascular permeability, causes cyanosis, hypotension, and contraction as well as relaxation of smooth muscles [5, 8, 11]. It inhibits motor activity in the antral part of the stomach [5] and it inhibits gastric acid secretion [1]. Intravenous infusion of 12–71 pmol/kg·min⁻¹ produces slight hypotension, and initial vasodilatation in the small intestine determined by cannulation of a mesenteric vein [13]. Infusions of neurotensin resulting in plasma levels of the same order of magnitude as observed after a meal have been shown to inhibit gastric acid secretion, to delay gastric emptying [2], and to reduce lower esophageal sphincter pressure [16]. As several effects concern gastrointestinal motility we examined regional blood flow in muscular and mucosal layers in dogs using microspheres and exogenous neurotensin in a dose causing plasma levels comparable to the post-prandial state.

* Supported by the Deutsche Forschungsgemeinschaft Fe 127/4

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Material and Methods

The experiments were performed on six bastard dogs (25 ± 5 kg) anesthetized with sodium pentobarbital 30 mg/kg. The animals were ventilated by a respirator. The right femoral artery was cannulated to record arterial pressure (AP), the peptide was infused into the right femoral vein. The left femoral artery was used as reference arterial sample and as thermistor to measure cardiac output (CO). A catheter inserted into the left cardiac ventricle through the left brachial artery was used for the injection of the microspheres and to measure left ventricular pressure (LVP).

A Swan-Ganz catheter (Edward Laboratories, Santa Ana, CA, USA) was introduced via a jugular vein into the pulmonary artery to determine pulmonal arterial pressure (PAP). A second catheter in the same vein to the right atrium was used to determine CO by the thermo-dilution method.

Ninety minutes after induction of anesthesia 2.5, 20, and 40 pmol/kg·min⁻¹ synthetic neurotensin (Serva, Heidelberg, FRG) was infused i.v. Each infusion lasted approximately 13 min, thereafter normal saline solution was infused for 30 min. This 30 min interval served as basal period for the next infusion with neurotensin. The different doses (one without neurotensin as control) were given in randomized order.

Regional intestinal blood flow was evaluated by injection of 8–10 μm tracer microspheres (¹²⁵I, ¹³¹Ce, ⁸⁵Sr, ⁴⁶Sc, 3M Company) [4]. The microspheres (approximately 2–6 × 10⁶) were injected 10 min after the start of the neurotensin infusion.

AP, PAP, LVP, LV-dp/dt max. were determined during the experiment and simultaneously recorded on a multichannel oscillograph (Brush, Gould, Cleveland, OH). At the end of the experiment the dog was killed by an injection of potassium chloride. Mucosa and submucosa were isolated from muscularis and serosa in samples of stomach, duodenum, upper jejunum, lower ileum, and transverse colon. Mucosa and submucosa will be designed “mucosa”, muscularis and serosa as “muscularis” in our text. Brain, heart, kidneys, pancreas, and adrenal glands were cut in 0.5–2 g samples. Approximately ten tissue samples were taken from the different organs. Radioactivity in the tissue samples was determined with a gamma scintillation counter [4]. Radioactivity of all tissue samples ranged from 200–6,000 cpm/g in the “muscularis” from 200–800 and in the “mucosa” from 700–1,800 cpm/g.

Neurotensin plasma levels after infusion of synthetic neurotensin were determined in another series of six conscious dogs. After a basal period 2.5, 20, and 40 pmol/kg·min⁻¹ of synthetic neurotensin was infused i.v. The different doses were given in randomized order. Venous blood samples were taken at 10-min intervals from a vein of the other leg, 5 ml blood was collected in ice-cold polyester tubes containing 1,000 KIU Trasylof (Bayer, Leverkusen, FRG) and 250 IU heparin. After centrifugation at 4°C the plasma was stored at −20°C. In the feeding experiment six dogs received 40 g/kg commercial dog food (Latz) containing 9.8% protein, 4.3% fat, 0.4% calcium, 0.3% phosphor, 0.25% sodium. Blood was taken at 15-min intervals for determination of neurotensin and treated as described above. Neurotensin levels were determined in unextracted plasma by a radioimmunoassay kit for neurotensin (Immunonuclear, Stillwaters, MN, USA). For statistics the paired Student’s t-test was used.

Results

Total blood flow without neurotensin in the gut segments ranged from highest 0.590 ± 0.110 ml/g·min in the jejunum to lowest in stomach and colon 0.320 ± 0.040 and 0.440 ± 0.050 ml/g·min (M ± SEM). During control time and neurotensin infusion blood flow in heart, brain, kidneys, and adrenal glands did not change significantly (Table 1). 2.5 pmol/kg·min of neurotensin stimulated pancreatic blood flow from 0.59 ± 0.1 to 0.78 ± 0.2 ml/g·min. This rise was not significant due to a considerable standard error.