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EFFECT OF NORADRENALIN ON RESISTIVE AND CAPACITIVE FUNCTION OF THE GASTRIC VESSELS

E. I. Svirskaya and V. A. Makovskaya

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KEY WORDS: resistive and capacitive function; perfusion pressure; venous outflow; noradrenalin

Of all the different parts of the gastrointestinal tract, the stomach is that which has received the least study from the standpoint of adrenergic control of its interlinked vascular functions [3, 5], for most research on this problem has been done on the small intestine [1, 3, 4, 6]. Progress in the elucidation of humoral regulation of the gastric vessels has largely been impeded by the multicomponent nature of its blood supply and the consequent difficulty in using perfusion techniques to study its vascular functions [3]. Such research as has been published so far on this question [6, 7, 9, 10] has been distinguished by the contradictory and fragmentary nature of the results.

The aim of this investigation was to develop a physiologically adequate method of perfusing the vascular bed of the stomach and of studying the effect of noradrenalin on the resistive and capacitive functions of its vessels.

EXPERIMENTAL METHOD

Experiments were carried out on 15 male and female cats weighing 3-5 kg. The stomach was isolated in situ from other parts of the gastrointestinal tract by ligating it proximally at the esophageal level and distally on the boundary with the hepatoduodenal ligament. Collateral vessels and also parts of the omentum along the greater and lesser curvature of the stomach were ligated. The left gastric and gastroepiploic arteries and the right gastric vein were left intact, whereas the right gastric and gastroepiploic arteries and the right gastroepiploic and gastrosplenic veins were ligated. Heparin (1000 U/kg) was used to prevent clotting. The stomach, isolated hemodynamically in this manner, was perfused by the method described previously [3, 5]. Blood was taken from the animal's left femoral artery and reinjected into the left gastric artery by means of a constant delivery pump. Venous blood from the right gastric vein was directed through a catheter inserted into it into the extracorporeal venous reservoir, from which it was returned to the femoral vein by the second channel of the pump at constant volume, equal to the perfusion volume. The pressure of the venous outflow was set, on the basis of data in the literature [2], at 8 mm Hg. The volume velocity of perfusion in these experiments averaged 25 ml/min/100 g with a perfusion pressure of 100-110 mm Hg. Considering that the volume blood flow in the gastric vessels agreed with values in the literature [2, 6], it can be considered that under the conditions of hemodynamic isolation, no significant changes took place in its blood supply. In each experiment the completeness of blocking of anastomoses between the hemodynamically isolated vascular bed of the stomach and other abdominal organs was monitored.

Laboratory of Physiology and Pathology of the Circulation, Department of Physiology of Visceral Systems. Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR B. I. Tkachenko.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 109, No. 6, pp. 525-527, June, 1990. Original article submitted May 30, 1989.

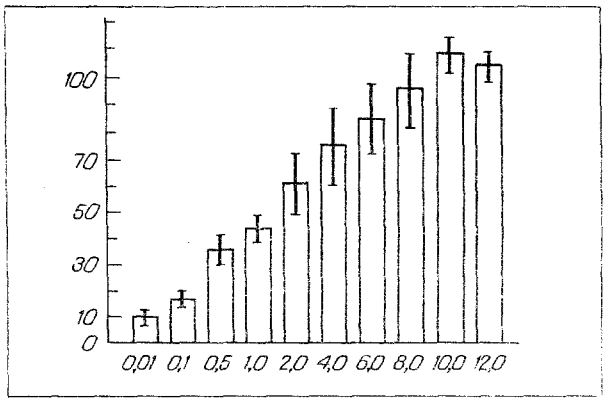

Fig. 1. Dose-dependence of changes in perfusion pressure in gastric vessels during exposure to noradrenalin. Abscissa, doses of noradrenalin (in μg); ordinate, increase of perfusion pressure (in per cent of initial level – Δpp%).

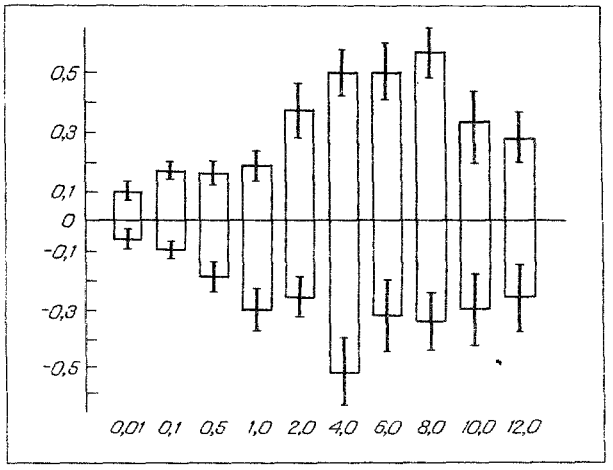

Fig. 2. Qualitative and quantitative changes in venous outflow from gastric vessels (ordinate, ΔVO, in ml) on injection of noradrenalin (NA) into them. Numbers below are doses of NA (in μg). Above abscissa – increase, below abcissa – decrease in venous outflow.

Changes in the resistive function of the gastric vessels were judged by changes in perfusion pressure in the arterial catheter, which were expressed in per cent of the initial level. While the volume of blood supplied to the arterial bed of the test region by one channel of the pump and the intake of blood from the extracorporeal reservoir by the second channel, having exactly the same throughput as the first pump, was maintained constant, changes in the blood level in the reservoir, measured in milliliters, reflected changes in the capacity of the vascular bed (the capacitive function). The systemic blood pressure was measured in the femoral artery. The perfusion, venous, and systemic arterial pressure and changes in the blood level in the extracorporeal reservoir were recorded by means of electromanometers with mechanical to electrical transducers (manufactured by the experimental production workshops, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR), on an N-327/5 ink-writing instrument. The motor function of the stomach was judged by changes in the intraventricular pressure, recorded graphically by a balloon method [8].

Noradrenalin was injected in one stage into the inlet pipe of the pump in increasing doses (from 0.01 to 12 μg) in 0.1 ml physiological saline. The results were subjected to statistical analysis by the Fisher–Student test.

EXPERIMENTAL RESULTS

The investigation showed that noradrenalin, in increasing doses from 0.01 to 2 μg, injected into the gastric vessels caused a significant and dose-dependent increase of perfusion pressure in all experiments (Fig. 1). When large doses of this substance were injected, the tendency for the constrictor response of the arteries to increase was preserved, but this dependence was not significant compared with the preceding dose. The minimal increase of perfusion pressure in the gastric vessels in these experiments corresponded to a dose of 0.01 μg noradrenalin and was 9.8 ± 3.2% of the initial level; the maximal increase, with a dose of 10 μg, was 108.2 ± 6.6%.

Comparison of the results of these experiments on the stomach with data in the literature for the small intestine, as part of the digestive tract physiologically similar to the stomach, showed [1, 3] that with a volume blood flow of 23-26 ml/min/100 g, injection of noradrenalin into vessels of the small intestine in a dose of 0.01 μg caused the perfusion pressure to rise by 1.89 ± 0.69% of its initial level (110-115 mm Hg), whereas injection of a dose of 10 μg led to an increase of 118.43 ± 16.94%. It can accordingly be concluded that the reactivity of the gastric vessels is higher than that of the corresponding vessels of the small intestine, for with an approximately equal volume blood flow and initial level of perfusion pressure, changes in the latter in response to injection of a threshold dose of noradrenalin (0.01 μg) [3] into the gastric vessels, was always greater than in the vessels of the small intestine, but the maximal response of the vessels of these parts of the digestive tract to a dose of 10 μg was virtually identical.

Whereas the perfusion pressure in the gastric vessels in response to injection of noradrenalin was increased in all experiments, the venous outflow in most cases was reduced (86.7%), although it could also be increased (14.3%). The minimal increase in venous outflow from vessels of the stomach in these experiments in response to injection of noradrenalin, as is clear from Fig. 2, corresponded to a dose of 0.01 μg and amounted to 0.102 ± 0.032 ml; the maximal increase corresponded to a dose of 8 μg and was 0.54 ± 0.12 ml. However, in a study of the dose–effect relationship, flattening out of the response on a plateau began with 2 μg. The minimal reduction of the venous outflow was observed with noradrenalin in a dose of 0.01 μg and amounted to 0.06 ± 0.032 ml, and with an increase in the dose to 1.0 μg, it also increased. The maximal decrease in venous outflow, which was 0.515 ± 0.12 ml, corresponded to a dose of noradrenalin of 4 μg. In the case of larger doses (up to 12 μg) the decrease was smaller. When studying the small intestine, several workers [1, 3, 4] also demonstrated that both an increase or a decrease in the capacity of its capacitive bed for catecholamines could take place. Meanwhile the relationship between these responses, in per cent, in the stomach and small intestine, differed. The increase in venous outflow in response to injection of noradrenalin was observed in the small intestine in 63.8% of cases, a decrease in 36.2%; in other words, reduction of the venous outflow was observed more often in the vascular bed of the stomach, whereas an increase was observed less often than in the small intestine.

Noradrenalin is known to inhibit motor activity and to reduce muscle tone of the stomach [6, 8]. It can accordingly be suggested that when the venous outflow is reduced, an extravascular factor participated in its changes. However, in the first place, during these experiments with intraarterial injection of noradrenalin, changes in perfusion pressure (latent period 1 sec) began to occur only 1-2 sec before changes in the venous outflow, whereas changes in the intragastric pressure occurred 10-12 sec later still. In the second place, changes in intragastric pressure were also dose-dependent, but reached their maximum with a dose of 12 μg noradrenalin, whereas the perfusion pressure and venous outflow reached their maximal values when smaller doses of noradrenalin were given (Figs. 1 and 2). These facts evidently rule out the possibility of an effect of an extravascular factor on the qualitative character of the vasomotor responses, although its effect on quantitative characteristics are diffcult at present to rule out.

The investigations thus showed that injection of increasing doses of noradrenalin into the gastric vessels gives rise to changes in the resistive and capacitive functions of these vessels. Changes in the resistive function took the form of a dose-dependent increase of perfusion pressure. The reactivity of the gastric vessels to noradrenalin was higher than that of the vessels of the small intestine. Changes in the venous outflow, characterizing the capacitive function of the gastric vessels, could vary in two ways: most often they were reduced, but they could also be increased. Moreover, the storing of blood in response to injection of noradrenalin was observed on a larger scale in the stomach than in the small intestine.

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EFFECT OF HIGH AND LOW DOSES OF VITAMINS A AND E ON FROG CARDIOMYOCYTE EXCITABILITY

N. K. Satybaldina and V. A. Frolov

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Lipid-soluble vitamins A (retinol) and E (tocopherol) are components of the natural antioxidant system of the cell. Vitamin A is known as a labilizer of lysosomal membranes, vitamin E (depending on its concentration) as a labilizer and stabilizer of these membranes [1-4].

The aim of this investigation was to study the electrophysiological characteristics of cardiomyocytes exposed to the action of a combination of these vitamins. It was assumed that, being lysosomotrophic, tocopherol and retinol ought to influence the properties of the cell membrane, and specifically its ionic permeability.

EXPERIMENTAL METHOD

Preparations of the isolated frog (*Rana temporaria*) heart were used. Transmembrane potentials of the ventricular myocardium were recorded intracellularly by means of "floating" microelectrodes: the resting potential (RP) and action potential (AP). Microelectrodes with a resistance of between 5 and 15 MΩ were filled with 3 M KCl. The preparation was incubated at room temperature in a bath containing Ringer's solution, pH 7.2-7.4. Daily for 2 weeks the frogs were given intraperitoneal injections of retinol (40 μg/ml) and tocopherol (400 μg/ml) simultaneously, or they were given smaller doses (1.5 and 16 μg/ml) in olive oil (not more than 0.3 ml). The necessary concentrations of the vitamins were obtained by diluting ampul preparations in sterile olive oil ex tempora in accordance with the USSR Pharmacopoeia (42-1087-77). In control experiments, intact frogs received injections of 0.3 ml of the solvent (sterile olive oil or 1 ml Ringer's solution) by the same schedule.

EXPERIMENTAL RESULTS

Table 1 shows that the RP level and parameters of AP after injection of 0.3 ml of olive oil did not differ from those after injection of 1 ml of Ringer's solution.

Department of Pathological Physiology, Patrice Lumumba Peoples' Friendship University, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR K. V. Sudakov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 109, No. 6, pp. 527-529, June, 1990. Original article submitted March 6, 1989.