EFFECT OF VITAMIN E ON THE PARIETAL pH PROFILE OF THE ALIMENTARY TRACT OF INTACT AND VAGOTOMIZED RATS

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Much experimental evidence has been obtained to show that subdiaphragmatic vagotomy leads to the development of neurodystrophic changes in the digestive organs [3]. At the same time, a similar operation (truncal or selective vagotomy) is widely used in surgical practice for the treatment of duodenal ulcer. Consequently, the search for pathogenetic approaches to the pharmacotherapy of complications developing after operations accompanied by division of the vagus nerves or their branches is of undoubted interest for medical practice. Experiments have shown that α-tocopherol acetate appreciably improves certain parameters of mitochondrial and microsomal function and morphology in the rat liver, disturbed as a result of vagotomy [2, 4]. However, considering that peptic ulcer (especially duodenal) is accompanied by gastric hypersecretion, and the therapeutic effect of vagotomy is due to a lasting inhibition of this function of the stomach, the effect of vitamin E on the level of gastric acid production is of great interest.

For this purpose, in the investigation described below the effect of α-tocopherol acetate on the parietal pH of the alimentary tract was studied in intact and vagotomized rats.

EXPERIMENTAL METHOD

Experiments were carried out on 85 male albino rats weighing 190-230 g. In the experiments of series I α-tocopherol acetate was injected intramuscularly (5% oily solution, 1 mg/kg body weight) into intact animals for 7, 15, and 30 days. In series II a similar procedure was undertaken on vagotomized rats (starting from the 1st day after bilateral subdiaphragmatic truncal vagotomy). Intact rats and rats undergoing the operation, but not receiving the vitamin at the corresponding times, served as the control. At the end of the course of injections and 24 h after the last meal, the parietal pH (PpH) was determined under urethane anesthesia (150 mg/100 g body weight) in the experimental and control animals, in the body of the stomach, duodenum, jejunum, ileum, cecum, and rectum by means of a fine pH-probe and pH-meter (pH-340) by the method described in [7]. To determine PpH in the rectum the probe was inserted per rectum to a depth of 3-5 cm; in the other cases the probe was passed as far as the required segment through an opening made 3-7 cm from the measuring point. PpH gradients in the alimentary tract were described quantitatively by calculating the coefficient E — the ratio between the value of PpH in the proximal portion and the corresponding value in the distal portion, between which the gradient was determined. The results of the measurements were subjected to statistical analysis by Strelkov's method.

EXPERIMENTAL RESULTS

As the results show (Table 1), a proximal-distal PpH gradient exists in the alimentary tract of intact rats and is characterized by the presence of two local drops of Pph — gastroduodenal (from acid to weakly alkaline, E = 0.47 ± 0.02) and ileocecal (from weakly alkaline to alkaline, E = 0.87 ± 0.01). A marked change in structure of the PpH profile of the gastrointestinal tract was observed 7 days after vagotomy: As a result of an increase in PpH in the stomach and a decrease in the duodenum the gastroduodenal gradient disappeared (E = 1.004 ± 0.06) and the absolute values of PpH fell in the ileum and cecum (the physiological gradient

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TABLE 1. Effect of Vitamin E on PpH Profile of Alimentary Tract of Intact and Vagotomized Rats

Experimental conditions	Stomach	Duodenum	Jejunum	Ileum	Cecum	Rectum
			Intact animals			
Control	5,78±0,21	7,89±0,14	8,11±0,08	8,80±0,06	10,05±0,08	8,57±0,22
Injection of vitamin E:						
7 days	4,69±0,09**	8,02±0,08	8,09±0,09	8,78±0,08	10,21±0,08	8,53±0,06
14 days	5,36±0,20	7,99±0,09	8,22±0,06	8,72±0,08	10,07±0,17	8,27±0,92
30 days	5,77±0,24	8,12±0,11	8,38±0,09	8,45±0,09	9,96±0,18	8,60±0,04
			Vagotomized animals			
Vagotomy 4 days	7,20±0,18*	7,17±0,14	7,84±0,08	8,35±0,01*	9,79±0,19*	8,39±0,15
Vagotomy 7 days + vitamin E	6,01±0,21**	7,45±0,13	7,97±0,10	8,18±0,07*	9,79±0,10	8,30±0,13
Vagotomy 14 days	5,91±0,14	7,70±0,20	8,19±0,09	8,59±0,10	10,0±0,18	7,89±0,41
Vagotomy 14 days + vitamin E	5,75±0,14	7,53±0,17	8,16±0,05	8,55±0,06	10,44±0,13	7,75±0,17
Vigotomy 30 days	5,95±0,19	7,57±0,11	7,68±0,11	8,52±0,09	10,1±0,19	8,95±0,16
Vagotomy 30 days + vitamin E	5,81±0,17	8,25±0,09	7,93±0,09	8,47±0,09	9,95±0,21	8,59±0,07

Legend. *) Statistically significant ($P < 0.05$) deviations from control, **) statistically significant ($P < 0.05$) differences between intact (or vagotomized) rats not receiving vitamin E and analogous groups of animals receiving vitamin E.

between them still remained). No appreciable changes in the PpH profile of the alimentary tract compared with the control could be found 14 and 30 days after the operation.

Injection of α-tocopherol acetate into intact rats for 7 days caused a decrease in PpH in the stomach and some increase in its value in the duodenum, and this was accompanied by a fall in the gastroduodenal gradient ($E = 0.58 \pm 0.01$). No significant deviations of PpH were found in these experiments in other parts of the alimentary tract. Injection of vitamin E for 14 and 30 days caused no significant modification of the proximal-distal PpH gradient of the gastrointestinal tract in intact rats. A course of vitamin therapy for 7 days gave an effect on vagotomized animals similar to that on intact rats receiving the vitamin for the same period: a fall of PpH in the stomach (almost to the initial level in intact animals) and a very small rise in the duodenum, resulting in a decrease in the gastroduodenal gradient ($E = 0.81 \pm 0.05$). In other parts of the alimentary tract no changes in PpH were found. Injection of vitamin E into vagotomized rats for 14 and 30 days caused no appreciable change in the PpH profile of the gastrointestinal tract; only a tendency was noted for PpH to fall in the stomach and to rise in the duodenum (the latter change was observed after a 30-day course).

α-Tocopherol acetate thus causes appreciable (although of short duration) changes in the structure of the PpH profile in the proximal portion of the alimentary tract in both intact and vagotomized rats; the changes are manifested as a fall of PpH in the stomach and a rise in the duodenum. The fact that the increase in acidity in the stomach under these conditions is not "compensated" by any corresponding fall in PpH in the duodenum, as a result of which the gastroduodenal gradient — one of the most important physiological constants of the alimentary tract — changes, suggests that vitamin E has a profound influence on the mechanisms regulating the acid—base properties of the paramucosal layer of the this portion of the gastrointestinal tract. Meanwhile attention is drawn to the fact that the changes described above in PpH were observed only after a 7-day course of the vitamin and were not found after a 30-day course. This phenomenon, in all probability, can be explained as follows. Although there is no firm evidence of direct participation of free-radical oxidation reactions of lipids in HCl secretion by the parietal cells of the gastric glands, their involvement in this process seems very probable if regard is paid to the fact that reactions of this type do take place in all membranous structures of the cell and play an essential role in the determination of many of their properties [1]. It can be tentatively suggested that vitamin E, a powerful inhibitor of free-radical oxidation reactions, lowers the level of lipid peroxidation (LPO) in the membranous structures of the parietal cells, and in turn this leads to activation of their acid-producing activity. At the same time, we know [1] that the LPO system has the property of self-regulation and is equipped with a number of nonspecific mechanisms maintaining homeostatic control over this process, of which the most important is the mechanism changing the relative content of easily oxidized lipid fractions in the membrane. However,

a certain time is evidently necessary for this regulatory act to take place. In the case of destabilization of the LPO system in the parietal cells of the gastric glands of rats by α-tocopherol, this time is probably close to 1 week. After the system has gone over to a new level of function, further administration of the antiradical agent in the previous dose had no marked action on it. When discussing this hypothesis we cannot, of course, rule out the possibility that the effect of vitamin E on the acid-producing structures of the stomach may not necessarily be linked with its antioxidative properties, because this vitamin is a multiple-profile, polyfunctional biologically active substance [6, 14, 15]. Special attention must be paid to the fact that after vagotomy the gastric glands, now in a "depressed" state (the parietal pH is raised), preserve (at least partly) their ability to respond to injection of vitamin E by increasing their HCl secretion. Moreover, under these conditions they do not lose their ability to "extinguish" (at about the same rate as in intact rats) changes in this process induced by the vitamin. These observations suggest that although the number of parietal cells in the gastric glands decreases after vagotomy, and a combination of degenerative changes takes place in most of those which remain [9, 11], from the physiological point of view they cannot be considered to have completely lost their function. Further evidence of partial preservation of the ability of the degeneratively changed parietal cells to respond by activation of secretory activity to injection of vitamin E is given by the appearance of free HCl in the gastric juice of patients with histamine-resistant achlorhydria when treated with large doses of the vitamin [8].

In can thus be concluded from this investigation that α-tocopherol acetate has a slight and brief effect on the PpH profile in the proximal portion of the alimentary tract, manifested as a fall in pH of the paramucosal layer of the gastric mucosa in intact rats by 18.9% and in vagotomized rats by 16.6%, and an increase in the gastroduodenal gradient. The clearly defined antihypoxic properties of vitamin E, its stabilizing action on biological membranes, and its favorable effect on the microcirculation [5, 12, 13] suggest that administration of this vitamin has a promising place in the pharmacologic correction of postoperative complications in patients with duodenal ulcer treated by vagotomy. However, since vitamin E has potential ability to stimulate HCl secretion in the stomach, its administration must be accompanied by monitoring of the acidity of the gastric juice or PpH of the gastric mucosa.

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