EFFECT OF SUBDIAPHRAGMATIC VAGOTOMY ON ZINC EXCRETION BY PANETH CELLS OF THE RAT SMALL INTESTINE UNDER FUNCTIONAL LOAD

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Recent clinical and experimental studies have shown that vagotomy gives rise to a variety of general metabolic disturbances, including disturbance of mineral metabolism [1, 5, 6, 10, 11]. In some of these investigations it was found that disturbance of the excretion of mineral components at the level of the intestinal wall is an important link in the pathogenesis of the disorders of mineral metabolism [7, 11]. As a rule, however, the authors cited recorded only general parameters of this process, whereas its fine cytophysiological mechanisms were ignored. It is clear that such an approach cannot yield sufficiently complete information on the pathogenesis of these disturbances or their structural basis. At the same time, the study of this aspect of the problem is of definite interest for a deeper understanding of the mechanism of nervous regulation of the excretory function of the intestine.

For the above reasons it was decided to undertake a morphological analysis of zinc excretion by the Paneth cells of the jejunum in intact and vogatomized rats under specific functional loading.

EXPERIMENTAL METHOD

Sixty male noninbred albino rats weighing 160-180 g were used; 29 of these animals underwent vagotomy, the rest served as controls. Zinc acetate in a dose of 50 mg/100 g body weight (the dose was chosen after a preliminary toxicologic experiment) was injected intraperitoneally into the experimental and control rats 7 days after the operation and 18 h after the last meal. Rats (experimental and control) were killed with ether vapor 45 min and 1.5, 3.5, 7, and 12 h after injection of the salt. Material (pieces of the proximal portion of the jejunum) was fixed in 70% alcohol saturated with H_2S. Zinc was detected histochemically in paraffin sections by Vogt's silver sulfide method in Shevchuk's modification [3]. The relative number of crypts containing Paneth cells with zinc-positive material (ZPM) was counted (per 50 crypts) in the preparation and expressed as a percentage. The number of Paneth cells was determined in 20 such crypts and expressed in absolute terms, for we know that the total number of cells in crypts of the jejunum is unchanged at this time after vagotomy [4]. The content of ZPM in the Paneth cells was estimated semiquantitatively and recorded on a four-point system. The quantity of ZPM which occupied the whole of a Paneth cell was assessed as 4 points, single granules in the apical part of the cell as 1 point, and intermediate forms as 2 and 3 points. To express the general level of zinc excretion quantitatively, the total number of Paneth cells per 100 crypts was calculated by multiplying the number (in %) of crypts containing Paneth cells with ZPM by the number of these Paneth cells per crypt. The numerical results were subjected to statistical analysis by Strelkov's method [2].

EXPERIMENTAL RESULTS

In intact rats the ZPM in the Paneth cells was in the form of circular granules of similar size localized in the apical part, which could merge into larger conglomerates and occupy the greater part of the cell or its entire volume. The number of crypts containing Paneth cells with ZPM before functional loading was 63.5%. The Paneth cells were mainly located in the lower third and at the bottom of the crypts and their mean number per crypt was 1.7. Of the total number of Paneth cells 13.3% contained a little ZPM (1 point), 37.3% contained a moderate amount (2 points), 45.5% a considerable amount (3 points), and 14.1% the maximal

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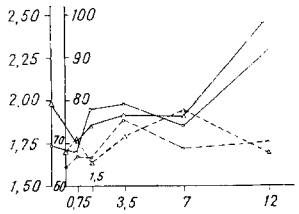

Fig. 1

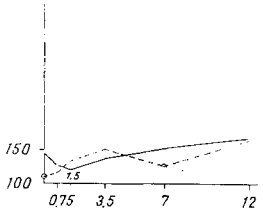

Fig. 2

Fig. 1. Changes in relative number of crypts containing Paneth cells with ZPM and number of Paneth cells per crypt in jejenum of intact and vagotomized rats after parenteral injection of zinc acetate. Abscissa, time after intraperitoneal injection of zinc acetate (in h); ordinate: A) relative number of crypts containing Paneth cells with ZPM (in %), B) number of Paneth cells per crypt (in absolute units). Circles — control, triangles — vagotomy.

Fig. 2. Dynamics of total number of Paneth cells containing ZPM in jejunum of intact and vagotomized rats after parenteral injection of zinc acetate. Abscissa, time after interaperitoneal injection of zinc acetate (in h); ordinate, total number of Paneth cells containing ZPM per 100 crypts (in absolute units).

amount (4 points). The number of crypts containing Paneth cells with ZPM did not change significantly between 0 and 1.5 h after injection of zinc acetate, and after 3.5 h it was increased, after 7 h it showed a small decrease, and thereafter it remained initially until the end of the period of study (12 h; Fig. 1). The number of Paneth cells in the early period after loading was very slightly reduced, after 1.5 h it rose sharply, it remained at this level until 3.5 h, and then it fell gradually until 7 h, almost reaching the initial level, and this was followed by another increase. The qualitative composition of the Paneth cells population under these conditions changed as follows: After 0.75 h the number of these cells with a low zinc content increased on account of a decrease in the relative number of cells with the high and maximal content of ZPM (compared with the initial level), at the expense of the decrease in the number of Paneth cells with low and moderate ZPM content. The relative number of Paneth cells with the maximal ZPM content was increased after 3.5 h on account of the decrease in the number of cells with low and high ZPM content (compared with the previous period). After 7 h the picture of the qualitative composition was similar with that in the animals in the initial state. After 12 h the relative number of Paneth cells with the maximal ZPM content increased on account of a decrease in the number of cells with low and moderate ZPM content.

The general level of zinc excretion by the small intestine after parenteral loading in intact rats was thus fluctuating in its time course: increased between 0 and 3.5 h, reduced after 7 h, and increased again after 12 h (Fig. 2).

The number of crypts containing Paneth cells with ZPM was almost unchanged in the vagotomized rats. The mean number of Paneth cells per crypt was appreciably greater than in intact animals (2.2 compared with 1.73 in the control). The qualitative composition of the Paneth cell population showed a decrease in the relative number of them with low and moderate ZPM content and an increase in the relative number of cells with high and maximal ZPM content. The number of crypts containing ZPM in the Paneth cells 0.75 h after injection of zinc salt showed a very small increase above the initial level, after 1.5 h it fell almost to the

initial level, and thereafter it gradually increased until 7 h, after which it fell again to its initial value (Fig. 1). The qualitative composition of the Paneth cell population changed as follows: The number of cells with low and moderate ZPM content increased sharply 0.75 h after loading, whereas the number of cells with a high ZPM content decreased, and no cells with the maximal ZPM content were found whatsoever. After 1.5 h the number of cells with a moderate ZPM content and, in particular, the number with a low content were increased. After 3.5 h most cells had the maximal ZPM content, the number of cells with a high ZPM content was a little lower, and cells with a low content had disappeared completely. The number of Paneth cells with the maximal ZPM content showed a small decrease after 7 h and a few cells with the low ZPM content appeared, the number of cells with moderate and high content remaining unchanged. After 12 h the relative number of cells with maximal ZPM content was increased, and this was accompanied by a decrease in the number of cells with low, moderate, and high ZPM content.

The dynamics of the general level of zinc excretion by the small intestine in the vagotomized rats was characterized by a monomodal curve with a minimum 1.5 h after functional loading; the initial level was regained after 7 h, and exceeded after 12 h (Fig. 2).

The fact will be noted that between 0 and 0.75 h and between 3.5 and 7 h after loading, although the number of Paneth cells in the crypt remained unchanged or showed a decrease, the number of crypts containing Paneth cells with ZPM increased. This discovery suggests that the level of excretion in the small intestine can vary not only on account of an increase in the number of Paneth cells in the crypt, but also by the activation of reserve crypts not playing the role of excretory structures in a state of relative physiological rest. These two mechanisms (cell- and crypt-based) can function simultaneously or successively. Comparison of the kinetics of the resultant zinc excretion index in the small intestine (the total number of Paneth cells with ZPM per 100 crypts) in the control and experimental rats leads to the conclusion that vagotomy distorts the dynamics of this process: In the experimental animals there is initially a more rapid discharge of zinc by the Paneth cells (in which the initial content was greater), but this was followed (1.5-12 h) by slow accumulation of zinc in the Paneth cells. Meanwhile in the control rats, Paneth cells in the small intestine are able to accumulate the excess of zinc, to get rid of it, and then to begin storing it again.

Comparison of the results with those obtained by other workers who studied the excretory function of the intestine shows that vagotomy leads to a decrease in the excretion of certain mineral components from the body through a fall in the level of their excretion by the intestine at certain times after the operation (in the case of iron and copper 19 days after vagotomy [1, 6]).

Consequently, the process of zinc excretion by the Paneth cells of the small intestine of the rats after parenteral loading is characterized by a fluctuating time course: Initially zinc is accumulated (3.5 h), this is followed by its partial excretion (7 h), after which accumulation is again observed. Subdiaphragmatic vagotomy distorts the dynamics of zinc excretion: initial discharge (1.5 h) is followed by slow accumulation.

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