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Histological examinations of chief and parietal cells of the rat gastric glands after experimental administration of cephalexin and ethanol

The lack of data regarding the action of cephalexin on the cells of gastric glands inclined us to undertake this research.

Despite that the toxicity of cephalosporins is small (9), sporadically the damage of haematopoietic tissue and liver was noticed. Dyspeptic symptoms, nausea, vomiting and diarrhoea can occur after oral administration (3). Ethyl alcohol increases the toxic action of many drugs, but on the other hand, it decreases the absorption of oral beta-lactam antibiotics (1).

We decided to assess the influence of cephalexin administered separately and together with alcohol on chief and parietal cells.

MATERIAL AND METHODS

The experiment was carried out on rats inbreeding Wistar race males weighing about 200 g. The animals were divided into three experimental groups and one control group, including five animals each. Rats from the control group received standard granulated fodder and water *ad libitum*. In the experimental group I, rats received standard granulated fodder and 20% ethyl alcohol instead of water for 10 days. Rats from experimental group II received cephalexin (Lilly, Florence, Italy) in a single dose of 42 mg/24 h. This dose corresponded to tenfold minimal therapeutic dose in human. The drug was administered each day morning for ten days as suspension in 0.9% NaCl. Animals from experimental group III received cephalexin in the same way as animals from experimental group II. Moreover, instead of water they received 20% ethyl alcohol *ad libitum*. Each animal from experimental group I drank about 20 ml of alcohol and from experimental group III – about 15 ml of alcohol per 24 h. After 10 days animals were guillotined. Specimens taken from the greater curvature of the stomach were fixed with 10% formaldehyde, dehydrated in graded ethanol solutions, cleared in xylene and embedded in paraffin. Seven-mm thick paraffin slices were stained with hematoxylin and eosin and with hematoxylin and Kongo purple.

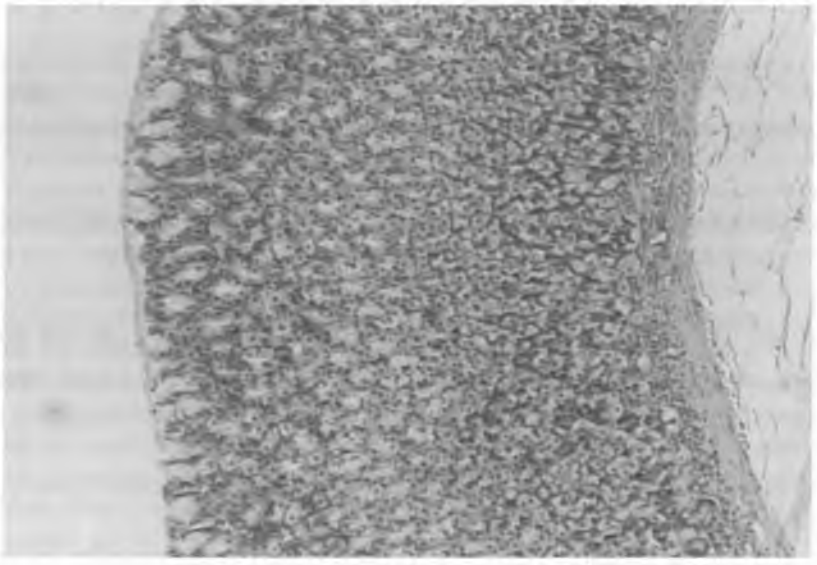

Fig. 1. The gastric mucous membrane of a rat from the control group. Basophilic chief cells are visible from the side of the submucous membrane, and the layer of mucous secretion – on a free surface. H+E staining. Magn. 100x

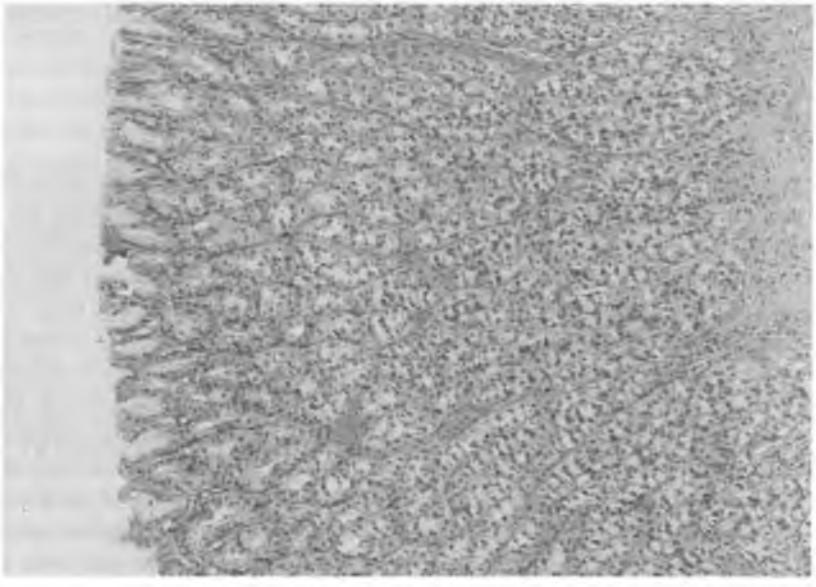

Fig. 2. The gastric mucous membrane of a rat from the experimental group I. Dilated interglandular blood vessels are visible. H+E staining. Magn. 100x

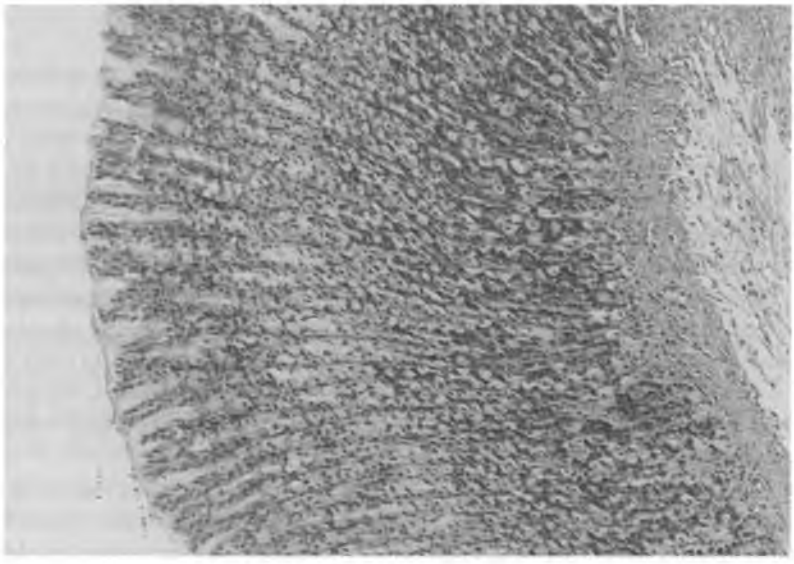

Fig. 3. The gastric mucous membrane of a rat from the experimental group II. The increased number of chief cells and their increased affinity for hematoxylin are visible. H+E staining. Magn. 100x

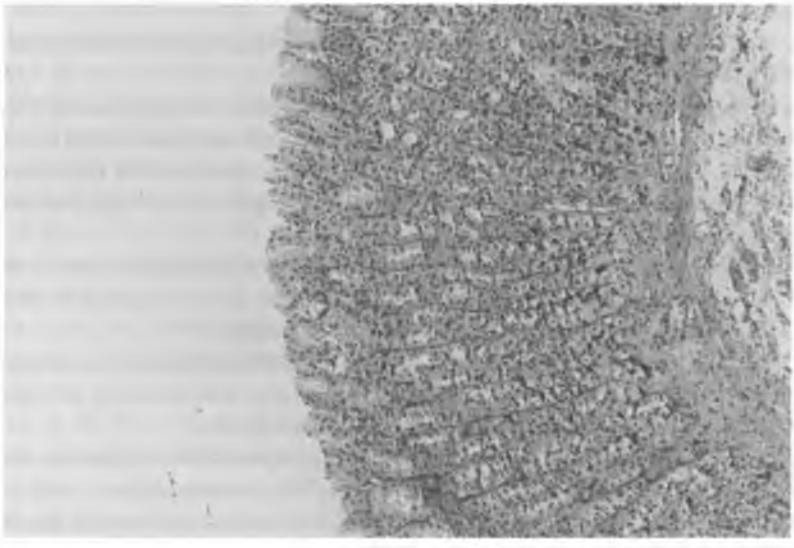

Fig. 4. The gastric mucous membrane of a rat from the experimental group III. Distinct narrowing of its thickness and atrophy of glandular cells, especially chief cells are visible. H+E staining. Magn. 100x

RESULTS AND DISCUSSION

A subtle proliferation of connective tissue from the side of the muscularis mucosae was revealed in the lamina propria of the gastric mucous membrane. The observed dilatation of periglandular blood vessels was connected with the decline in blood pressure and blood flow rate. The number of chief cells and their affinity of taking stain were smaller than in the control animals. A smaller affinity for hematoxylin can be connected with the decrease in the amount of ribosomal RNA. A consequence of this was the decreased activity of cells in the process of pepsinogen synthesis. Other authors (6, 8) revealed that ethanol decreases the gastric juice secretion in rats through the decline in the level of cAMP – the intracellular secretion regulator, due to the adenyl cyclase action. Ethanol administered in 5–7% concentration inhibits the peptic action of pepsin in the stomach and ethanol administered in 20% concentration completely inactivates the enzyme. Our results are similar to other authors' observations who revealed that ethanol causes the decline in number of ribosomes, the decrease of albumin synthesis (5), desaggregation of polyribosomes connected with endoplasmic reticulum (7) and proliferation of smooth endoplasmic reticulum in hepatocytes (2).

Parietal cells stained weaker like chief cells, and their diameter was smaller than in the control animals. An acidophillity of the parietal cells is connected mainly with the presence of mitochondria. Lieber et al. (4) report that ethanol damages ultrastructure of these organelles causing their deformity, swelling and changes of cristae system. Simultaneously changes in activity of the majority of enzymes appear (10).

After 10-day-long administration of cephalexin the number of chief cells increased distinctly and their stainability also increased. They filled the 2/3 of gland in many places. Such change is a typical functional change indicating the increased secretory activity because of the increase in number of rough endoplasmic reticulum membranes.

Similar increase in number of ribosomes was observed in pancreas after administration of this antibiotic (12, 13).

Parietal cells also showed increased stainability after cephalexin administration, which was connected with the increase in the number of mitochondria in these cells and consequently their activity. Also, Tune et al. (11) observed a stimulation of mitochondrial respiration after cephalosporins in the epithelium of the main part of nephrons. The authors observed degenerative changes in mitochondria only after administration of the high dose of the medicine.

In our experiment, we observed the most distinct changes in the stomach mucosa after the concomitant administration of ethanol and cephalexin. Despite that they were similar to the changes induced by ethanol itself, drug interaction caused their intensification.

A small number of chief and parietal cells was observed in the distinctly thinner mucous membrane. Both cell types showed weak stainability. This is an evidence of a small secretory activity and the presence of processes connected especially with ethanol metabolism (10).

The decreased thickness of the mucous membrane and consequently the decline in the number of glandular cells are connected with degenerative processes. The flattening of gastric pits, irregular surface of the mucous membrane in some places and fibroplasia near to the muscularis mucosae also occurred. However, functional changes (hyperemia of the mucous membrane, reduced secretory activity of cells) were revealed after administration of ethanol itself, the concomitant administration of ethanol and cephalexin undoubtedly caused damage of the mucous membrane evident as typical atrophy. Our observations confirm the righteousness of the undertaking of this research.

CONCLUSIONS

1. 10-day administration of 20% alcohol *ad libitum* causes in rats: a) hyperemia of the stomach mucous membrane, b) reduction of secretory activity of chief and parietal cells.

2. 10-day administration of cephalexin in the dose of 42 mg/kg/24 h causes: a) the increase of the amount of chief cells, b) the increase of the secretory activity of chief and parietal cells.

3. Concomitant administration of ethanol and cephalexin in the above doses intensifies toxicity of both chemicals and causes atrophical changes in the form of: a) the decrease of the mucous membrane thickness, b) the flattening of gastric pits and local damage of the mucous membrane surface, c) fibroplasia near to the muscularis mucosae.

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SUMMARY

The experiment was carried out on Wistar rat males weighting about 200 g. Animals from experimental group I received 20% ethanol for drinking (*ad libitum*), animals from experimental group II – cephalexin in the dose of 42 mg/24 h, animals from experimental group III – cephalexin and ethanol in mentioned doses. After 10 days animals were decapitated and specimens of the stomach were taken from the greater curvature. It was stated that 10-day administration of 20% ethanol causes hyperemia of the gastric mucous membrane and the decrease of secretory activity of the glands. On the contrary, cephalexin causes the increase of secretory activity of chief and parietal cells. Concomitant administration of ethanol and cephalexin damages the gastric mucous membrane causing its narrowing, flattening of gastric pits and atrophy of secretory cells in the glands.

Histologiczne badania komórek głównych i okładzinowych gruczołów właściwych żołądka szczura po doświadczalnym podawaniu cefaleksyny i etanolu

Badania wykonano na szczurach, samcach rasy Wistar o masie ciała ok. 200 g. Zwierzęta I grupy doświadczalnej otrzymywały 20% etanol do picia (*ad libitum*), zwierzęta II grupy doświadczalnej – cefaleksynę w dawce 42 mg/24h, zwierzęta III grupy doświadczalnej – cefaleksynę i etanol w wyżej wymienionych dawkach. Po 10 dniach zwierzęta dekapitowano i z okolicy krzywizny większej pobierano wycinki żołądka. Stwierdzono, że 10-dniowe podawanie 20% etanolu wywołuje przekrwienie błony śluzowej i obniżenie aktywności wydzielniczej gruczołów, natomiast cefaleksyna powoduje wzrost aktywności wydzielniczej komórek głównych i okładzinowych. Łączne podawanie etanolu i cefaleksyny uszkadza błonę śluzową żołądka, powodując jej zwężenie, spłycenie dołeczków i zanik komórek wydzielniczych w gruczołach.