GASTRIN RESPONSE IN RATS DIFFERING IN SUSCEPTIBILITY TO GASTRIC MUCOSAL INJURY IN STRESS INDUCED BY IMMOBILIZATION AND COLD

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Morphological changes in the gastric mucosa in response to the action of the same stressor are known to vary over a wide range: from the absence of visible damage to multiple ulcers with perforations, including erosions and solitary ulcers. Since an important role in ulcerogenesis is played by gastrin, which has a trophic and protective action on the mucosa [1, 3], it was decided to investigate correlation between the character of the response to gastrin and acid and the visible morphological changes in the gastric mucosa associated with stress.

EXPERIMENTAL METHOD

Experiments were carried out on 72 noninbred male rats weighing 150-180 g, deprived of food for 24 h but allowed free access to water. The control consisted of 30 animals, and another 42 animals were subjected to immobilization-cold stress by crowding them in perforated constraining cages and keeping the latter in a refrigerator at 2-5°C for 5 h. The animals were then killed by decapitation, blood was collected in order to obtain serum pieces of the antrum and duodenum were excised and quickly placed on a slide kept on ice. The mucous membranes were scraped off the pieces with a coverslip, weighed, and homogenized with a pestle in 5 ml of distilled water for 3 min. The resulting samples of extracts of the antral and duodenal mucosa and the samples of serum were kept until required for analysis in the frozen form (at −18°C).

The gastrin concentration was determined by radioimmunoassay using kits from Sorin (France). The gastrin content in the mucosa was calculated per gram wet weight of tissue. The stomach was excised and divided along the greater curvature, the pH on the surface of the fundal mucosa of the stomach was measured with a glass electrode, after which the stomach was drawn onto a glass hemisphere by its serous surface and the mucosa examined under a magnifying glass in transmitted light.

The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

In eight rats (19%) subjected to stress, just as in the controls, no visible pathological changes were found in the mucosa. In 15 (36%) multiple petechial hemorrhagic erosions were noted, in seven (17%) there were solitary ulcers in the fundal region 1-3.5 mm long (on average 2.1 ± 0.7 mm), and in a further 12 (28%) there were multiple ulcers numbering 2-6 (average 3.5 ± 0.5), and with a total length of 1.5-11 mm (average 4.5 ± 0.9 mm).

The blood serum gastrin concentration in the control rats was 68 ± 4 pg/ml, in the antral mucosa 103 ± 26 ng/g wet weight of tissue, and in the duodenal mucosa 11.4 ± 1.0 ng/g wet weight of tissue; the pH on the surface of the fundal mucosa was 3.6 ± 0.2. In rats resistant to the damaging action of the stressor, the poststress serum gastrin concentration

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was 29% below the control (48 ± 4 pg/ml, $p < 0.02$), and the gastrin concentration in the antrum was indistinguishable (97 ± 25 ng/g) from the control (97 ± 25 ng/g), whereas in the duodenum it showed a tendency to rise (15.0 ± 2.1 ng/g, $p > 0.1$); the pH also exceeded the control level a little (4.1 ± 0.4, $p > 0.2$). In rats with erosions, post-stress hypogastrinemia still occurred (58 ± 3 pg/ml, $p < 0.05$), but it was less marked (15%), and at the same time the tendency for the gastrin concentration in the antrum to fall was strengthened (68 ± 17 ng/g, $p > 0.2$) and a definite fall in its value (by 42%) was observed in the duodenum (6.6 ± 0.7 ng/g, $p < 0.001$), and the pH was the same as in the control (3.4 ± 16). The parameters studied in rats with single and multiple ulcers did not differ significantly, so that they were pooled for statistical analysis. Absence of post-stress hypogastrinemia (67 ± 5 pg/ml) was found in these animals, together with a sharp fall in the tissue gastrin concentration of the antrum (6.8 ± 0.2 ng/g, reduction by 93%) and duodenum (5.1 ± 0.3 ng/g, a fall of 55%, $p < 0.001$), whereas the pH under these circumstances was significantly reduced (2.7 ± 0.08, $p < 0.001$).

These experiments showed correlation between the character of the gastrin response, the visible morphological changes in the fundal mucosa, and the pH on its surface during stress. In the chosen experimental design, when parameters of the experimental rats were compared after stress and in the control rats, not exposed to stress, it is impossible to give an unequivocal answer to the question whether the values of the parameters were the result of individual (more accurately, group) stress reactions, or whether they had been of that kind initially (before stress), i.e., that they are due to individual (group) characteristics of the animals.

If it is accepted that the parameters of the control rats correspond to those of the experimental rats before stress, the following conclusion can be drawn: the fundal mucosa of the stomach remains visibly intact, and whereas in response to the action of the stressor the gastrin concentration in the antral and duodenal mucosa was unchanged or increased a little, in the serum, on the other hand, it was significantly reduced. In other words, the impression is created that during stress the gastrin depot is not exhausted as a result of reduced release of gastrin into the blood. On the other hand, the fundal mucosa is ulcerated, if during stress the gastrin depot, especially in the antral mucosa, is exhausted, in which case one of the channels of leakage of gastrin is the blood. If leakage of gastrin into the blood and exhaustion of its depots are only of a very slight degree, mainly erosions develop, i.e., less profound morphological injuries of the mucosa. It can be tentatively suggested that in the case of absence of visible damage to the mucosa during stress, the flow of gastrin from mucosa into lumen predominates over its flow from mucosa into blood vessels, and under those circumstances the optimal conditions are created for gastrin to exert its trophic action on the fundal mucosa of the stomach. Conversely, in cases when the flow of gastrin in the second direction predominates, its protective action on the stomach is not exhibited.

The alternative interpretation is based on the assumption that the initial gastrin content in the tissue depots and blood of rats is subject to considerable individual variation, and that this correlates with the broad spectrum of morphological changes in the mucosa in response to a stressor. Consequently, for rats, whose mucosa is resistant to the damaging action of the stressor, a higher gastrin concentration in the antral-duodenal mucosa and a lower concentration in the blood compared with rats affected by stress-induced ulceration are characteristic. Analysis of the scatter of the data in the control rats shows that at intermediate levels of gastrin, there is an intermediate degree of severity of stress-induced damage, namely erosions.

Correlation between the poststress morphological state of the fundal mucosa and the pH on its surface deserves special discussion. Although in rats with ulcers the pH was significantly lower than in the rest, both experimental and control animals, the acid factor could hardly play an essential role in ulcerogenesis, for its magnitude did not exceed the limits established in the extradigestive period, namely 2.1-5.3 [2], not to mention the fact that it was much less acid than during digestion.

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