ACTION OF HYDROCORTISONE ON MITOTIC CYCLE OF PYLORIC EPITHELIAL CELLS OF THE MOUSE STOMACH

A. A. Avetisyan

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It was shown by the use of thymidine-H^3 that the mitotic cycle of mucus-forming cells (superficial epithelial and mucosal cells of the neck) of the pyloric glands of the mouse stomach lasts 13.5 h (G_1 + ½ M = 7.6 h S = 5.3 h, G_2 + ½ M = 0.6 h). After administration of a physiological dose of hydrocortisone (0.1 mg) the duration of the mitotic cycle of these cells increased by 6.7 h (G_1 + ½ M = 11.6 h, S = 7.8 h, G_2 + ½ M = 0.8 h). A large dose of the hormone (3 mg) had a similar action and increased the duration of the presynthetic period to 12.9 h and of the postsynthetic to 2.3 h.

KEY WORDS: pyloric glands of stomach; mitotic cyle; hydrocortisone.

The inhibitory action of glucorticoids (when their level in the body is raised) on cell renewal processes in the epithelium of the stomach and duodenum weakens the resistance of the mucosal-epithelial protective barrier of these organs to the ulcerative action of the gastric juice and of various types of mechanical trauma [1-8, 10, 12, 13, 16]. However, the development of this pathological process has been inadequately studied. In particular, there is no information in the literature on the effect of a raised glucocorticoid level on the duration of the mitotic cycle of the pyloric epithelial cells.

The duration of the mitotic cycle and its periods in this part of the alimentary tract has not yet been studied. The only available data, of Lipkin et al. [11] and Wegener et al. [15], were obtained under pathological conditions and cannot be taken as normal.

The object of the present investigation was to determine the duration of periods of the mitotic cycle of the pyloric epithelial cells in the stomach of intact mice and to study its changes under the influence of various doses of hydrocortisone, injected into the animals' peritoneal cavity.

EXPERIMENTAL METHOD

Experiments were carried out on 153 male hybrid C57BL x CBA mice weighing 20-23 g. The animals were divided into 3 groups. The mice of group 1 (control) received an intraperitoneal injection of 0.2 ml distilled water at 5:00 a.m., whereas mice of groups 2 and 3 received 0.1 mg (a low, physiological dose) and 3 mg (a high, definitely nonphysiological dose) of hydrocortisone respectively. At 6:00 a.m. all the animals received an intraperitoneal injection of the labeled DNA precursor, thymidine-H^3 (USSR) with specific activity 1.4 Ci/nmole (0.7 μCi/g body weight).

The mice were sacrificed, three from each group, 1, 2, 3, 4, 6, 9, 10, 12, 15, 16, 18, 21, 25, 28, 31, 34, and 37 h after injection of thymidine-H^3.

The stomachs were fixed in Carnoy's fluid by Timashkevich's method [9].

Dewaxed sections, 5 μ thick, were coated with Lipkin type R liquid radiosensitive emulsion. After exposure for 9 days the sections were developed and stained with Carazzi's hematoxylin and eosin.

During examination of autoradiographs of 80-100 longitudinally divided gastric pyloric glands the fol-

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TABLE 1. Duration of Mitotic Cycle and Its Periods (in h) in Pyloric Epithelium of Mouse Stomach after Administration of Various Doses of Hydrocortisone

Dose of hydrocortisone (in mg)	Mucus-forming cells of gland				All cells of gland taken together			
	$G_1+\frac{1}{2}M$	S	$G_2+\frac{1}{2}M$	T	$G_1+\frac{1}{2}M$	S	$G_2+\frac{1}{2}M$	T
Control	7,6	5,3	0,6	13,5	8,5	6,0	0,5	15,0
0,1	11,6	7,8	0,8	20,2	10,0	6,0	1,0	17,0
3	12,9	7,5	2,3	22,7	11,0	7,5	1,5	20,0

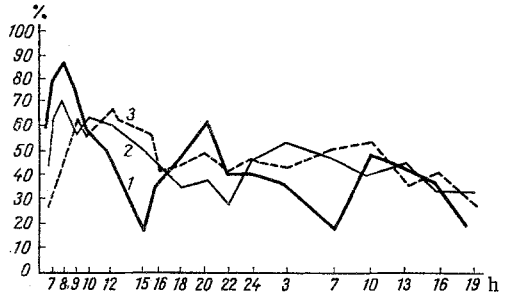

Fig. 1. Change in percentage of labeled mitoses in mucus-forming cells of gastric pylorus in control (1) and after administration of hydrocortisone in doses of 0.1 mg (2) and 3 mg (3). Abscissa, time of sacrifice (24-hour clock); ordinate, index of labeled mitoses (in %).

lowing were counted: 1) percentage of labeled mitoses per 100 mitoses, 2) the mean index of labeled nuclei for mice killed at 8, 9, and 10 A. M. The counts were carried out for all cells of the glands together and for the mucus-forming (surface-epithelium and mucosal cells of the neck) cells of the gland separately. Curves showing changes in the percentage of labeled mitoses with time were drawn and the duration of the mitotic cycle and its periods determined by the method of Quastler and Sherman [14] and Dondua and Dondua [3].

EXPERIMENTAL RESULTS

Each mouse pyloric gland consisted on the average of 65 cells, including 23 surface-epithelial cells, 27 mucosal cells of the neck, and 14 basal cells.

The results of these tests are given in Table 1. In the control mice the duration of the mitotic cycle calculated for all cells of the gland as a whole was 15 h. In the experimental animals receiving a small dose of hydrocortisone the duration of the mitotic cycle was increased by 2 h, of the presynthetic period by 1.5 h, and of the postsynthetic period by 0.5 h; the duration of the period of DNA synthesis was unchanged relative to the control. The mean percentage of cells synthesizing DNA was 16.7 in the control mice, but in the experimental mice it was down to 12.6. In the mice of group 3 receiving the large dose of hormone the duration of the mitotic cycle was 20 h, on account of an increase in the duration of all periods compared with the mice of groups 1 and 2.

Under the same experimental conditions the duration of the mitotic cycle of the mucus-forming cells of the pyloric glands alone was 13.5 h (Fig. 1). After administration of the small dose of hydrocortisone the duration of the mitotic cycle of these cells was increased by 6.7 h: the presynthetic period by 4 h, the period of DNA synthesis by 2.5 h, and the postsynthetic period by 0.2 h. The mean index of labeled nuclei fell to 5%, i.e., by 2.5 times compared with the control (12.9%). The effect of the large dose of the hormone on the duration of DNA synthesis did not differ significantly from the effect of the small dose, but the duration of the presynthetic and postsynthetic periods increased by 1.3 and 1.5 h respectively.

Changes in the periods of the mitotic cycle after administration of the physiological dose of the hormone were thus more marked if the percentage of labeled mitoses was determined separately for the mucus-forming cells of the gastric pyloric glands. This may indicate that the glandular cells of the fundus of the mouse pyloric gland have a longer mitotic cycle and are less sensitive to administration of a physiological dose of hydrocortisone than cells of the surface epithelium and neck of the gland. When the cells as a whole are counted, smaller changes are thus obtained in the duration of the periods of the mitotic cycle than when the periods are determined in the mucus-forming cells of the gland separately.

The observed slowing of the cell renewal process in the mucus-forming cells of the gastric pyloric glands is analogous to the effect produced by the same doses of hydrocortisone in the mucus-forming cells of glands of the gastric fundus and the epithelium of the duodenum in the writer's earlier investigations [1, 6].

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