EFFECT OF HYPOXIA ON GASTRIC SECRETION AND EXCRETION

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Oxygen insufficiency plays an important role in the development of pathology of the gastroduodenal system. It has been shown that the stomach is distinguished among organs of the alimentary tract by highest sensitivity to the hypoxic state [5]. The aim of the present investigation was to study functional changes in the gastric mucosa of dogs during the development of primary adaptive reactions to hypoxia.

EXPERIMENTAL METHOD

Experiments were carried out on mongrel male dogs with Pavlov gastric pouches. Gastric secretion was stimulated by meat (10 g/kg), and, since secretion is inhibited by hypoxia, samples of gastric juice were collected every hour for 4 h. The volume of gastric juice (expressed per kilogram body weight), its acidity [3], its content of pepsin [6], ammonia [4], and the exogenous dye neutral red [1], and also the volume of visible mucus and the quantity of mucin in it [7] were determined. After a control series of experiments the animals were exposed to hypoxia, by creating a reduced atmospheric pressure in a standard pressure chamber corresponding to an altitude of 7000 m; the velocity of "ascent" and "descent" was 10 m/sec, and the animals remained at the "high altitude" for 3 h.

EXPERIMENTAL RESULTS

Hypoxia has an inhibitory action on the secretion of juice: the volume of juice secreted during the whole period of the experiment was reduced from 1.17±0.08 ml/kg (in intact animals) to 0.66±0.04 ml/kg ($P < 0.05$). The time course of juice secretion remained unchanged, but the volume of the hourly portions of juice was considerably reduced (Table 1). The latent period of appearance of juice in response to meat feeding was significantly increased to 17.6±1.3 min (10.8±0.9 min before hypoxia). Inhibition of gastric secretion was expressed as a decrease in the volume of juice secreted in both the nervous and the humoral phase of gastric secretion. Acute hypoxia may act on gastric secretion through a change in the water and electrolyte exchange of the body as a whole. Inhibition of juice secretion may be due to changes in permeability of the cell membranes and disturbance of transport mechanisms in the membrane, which develop where there is an acute oxygen deficiency in the tissue [9].

Under the influence of hypoxia the production of pepsin in the gastric secretion was reduced. The quantity of pepsin in the juice of intact animals in the course of the experiment was 31.28±0.91 μmoles tyrosine/kg

TABLE 1. Parameters of Gastric Function in Intact Dogs and Dogs Exposed to Hypoxia (M±m)

Parameter	Experimental conditions	Test No.			
		1	2	3	4
Juice secretion, ml/kg	Intact animals (40)	0,49±0,05	0,26±0,05	0,24±0,03	0,17±0,03
	Hypoxia (40)	0,20±0,02*	0,19±0,04	0,13±0,02*	0,13±0,03
Pepsin production, μmoles tyrosine/kg body weight	Intact animals (40)	13,68±1,53	6,41±0,90	6,42±1,00	3,59±0,64
	Hypoxia (40)	3,04±0,47*	3,44±0,52*	2,24±0,46*	1,78±0,46*
Neutral red excretion, nmoles/kg body weight	Intact animals (40)	33,83±4,26	18,79±1,32	7,76±0,94	3,74±0,64
	Hypoxia (40)	15,83±2,74*	12,20±1,46	4,36±0,90*	2,98±0,66

Legend. *$P < 0.05$ compared with control. Number of experiments given in parentheses.

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body weight, whereas after hypoxia it was 10.41±0.97 μmoles tyrosine/kg body weight ($P < 0.05$). This decrease in pepsin production during the experiment was caused by inhibition of secretion of the enzyme throughout the experiment and by a change in the time course of its secretion (Table 1). Since pepsin secretion depends on both the formation of pepsinogen and its elution, it is possible that the decrease in enzyme secretion during hypoxia is due to inhibition of synthesis of secretory protein and to a decrease in the volume of juice excreted.

The rate of secretion of active H^+ ions also was observed to be reduced: secretion of H^+ in intact dogs was 40.98±6.91 μmoles/kg, falling after exposure to hypoxia to 23.58±1.65 μmoles/kg ($P < 0.05$). The considerable fall of the H^+ level in the gastric contents may have been due to an increase in rediffusion of

Besides the reduction in volume of gastric juice produced and the active H^+ and pepsin concentrations in the gastric juice, the quantity of visible mucus also was considerably and significantly increased after exposure to hypoxia to 0.190±0.004 ml/kg (0.122±0.005 ml/kg before hypoxia). At the same time, the mucin concentration in the visible mucus was increased. Mucin production after the action of hypoxia therefore increased: whereas in intact animals it was 87.7±8.6 μg/kg, after exposure to hypoxia it rose to 281.4±10.0 μg/kg ($P < 0.05$). This may be evidence of strengthening of the protective mucous barrier of the stomach, possibly associated with sustained activation of the sympathetic nervous system.

Excretion of exogenous dyes with the gastric juice depends on two main factors: binding and transport of the dye in the stomach wall and the volume of blood flowing to the stomach. The quantity of dye excreted also depends on the intraluminal pH [2]. Neutral red (2 mg/kg) was injected intravenously at the beginning of collection of the first sample of juice. It was shown that after the action of hypoxial, neutral red production during the period of the experiment decreased. Whereas before hypoxia the total quantity of neutral red excreted was 64.12±4.91 nmoles/kg, after exposure to hypoxia it fell to 35.38±3.57 nmoles/kg ($P < 0.05$). The latent period of appearance of the dye was increased: in intact animals it was 8.5±0.8 min, and after hypoxia 12.6±1.3 min ($P < 0.05$). Consequently, the character of the change in excretion of neutral red coincides closely with that of juice secretion, and it evidently reflects the changing conditions of the hemodynamics in the stomach. However, changes in the time course of neutral red excretion during the experiment show (Table 1) that hypoxia also affects the level of exchange processes in the stomach wall. Reduction of excretion of the dye, it will be noted, coincided with reduced acid secretion in the stomach.

Changes in the conditions of the hemodynamics and also, possibly, in urease activity during hypoxia also are reflected in ammonia excretion. The ammonia concentration, for instance, increased from 4.19±0.75 mM/l to 8.56±0.98 mM/l ($P < 0.05$); however, the rate of ammonia production was unchanged, since the volume of juice secreted was considerably reduced after hypoxia. Before hypoxia the ammonia production was 4.89±0.7 μmoles/kg, but after exposure it was 5.16±0.91 μmoles/kg ($P > 0.05$).

Hypoxia thus reduces the secretion of gastric juice, the pepsin concentration, the rate of secretion of active H^+ ions, and the rate of excretion of the dye neutral red. The time course of these changes was determined. Secretion of visible mucus and the level of mucin in the secretion were increased. Ammonia production was unchanged. The results supplement those of previous investigations of the adaptive changes in gastric functions in response to hypoxia.

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