Simultaneous Stress-Induced Metabolic Changes in the Stomach and Periodontium

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Stress-induced changes in the stomach and periodontium were studied in animals with various types of nervous regulation pretreated with the regulatory peptide thymopentin. The interrelation between metabolic and structural changes in these highly sensitive to stress organs was revealed. Behaviorally active rats were most sensitive to stress. Pretreatment with thymopentin produced a stress-protective effect and attenuated stress-induced degradation of glycoproteins in digestive organs.

Key Words: *stress; type of nervous regulation; stomach; periodontium; thymopentin*

Oral cavity diseases are often accompanied by pathological processes in other organs and systems. It is believed that gastrointestinal diseases are primary pathology, while pathological changes in the oral cavity result from systemic diseases [1].

Here we studied acute stress-induced metabolic changes in the stomach and periodontium in animals with different types of nervous regulation and against the background of pretreatment with the regulatory peptide thymopentin.

MATERIALS AND METHODS

Experiments were performed on 60 male Wistar rats weighing 170-200 g and receiving food and water *ad libitum*. The animals were deprived of food for 24 h before euthanasia. The open field test was used to reveal the rats with active, passive, and intermediate patterns of behavioral reactions to stress [6]. Intact rats served as the control.

In series I, the animals were divided into 4 groups. Group 1 rats served as the control. Group 2 rats were subjected to acute stress (electrical shock) [13]. Group 3 rats were injected with thymopentin. Group 4 rats were stressed 30 min after thymopentin administration. Thymopentin (Arg32-Lys-Asp-Val-Tyr36, Institute of Organic Synthesis, Latvian Academy of Sciences) was injected intraperitoneally in a dose of 100 mg/kg. Two hours after stress, the animals were anesthetized with hexenal (50 mg/kg intraperitoneally) and euthanized by bloodletting.

The gastric mucosa (GM) was examined, the content of fucose in the periodontium, GM, and blood serum was measured [14], and histological studies of tissues were performed. Ulcerogenic effects of stress were evaluated by the incidence and number of gastric ulcers [2]. For morphological studies, gastric and periodontal tissues were fixed in 12% neutral formalin. Paraffin slices were stained with hematoxylin and eosin.

In series II, the role of reflex stimuli from the duodenal zone to gastric and periodontal tissues was analyzed. The animals were divided into 3 groups. Group 1 rats served as the control. Group 2 rats were sham-operated (laparotomy without stimulation of the duodenal zone). In group 3 rats, the duodenal zone was stimulated as described elsewhere [3]. The animals were decapitated under hexenal narcosis 10 days after surgery, and gastric ulceration [2] and resorption of periodontal bone tissue (the coefficient of exposed root portions of molar teeth) were evaluated [8].

The results were analyzed by Student's t test and pairwise linear correlation analysis (Pearson coefficient, r).

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RESULTS

Stress is a systemic body reaction realized via 2 major regulatory systems of homeostasis, the sympathoadrenal and hypothalamic-pituitary-adrenal systems [11]. Neuroendocrine factors regulate vascular reactions, metabolic processes, and functional activity of digestive organs. Sympathetic stimuli change the tone and blood circulation in periodontal vessels [5]. Acute stress is accompanied by marked hemodynamic changes in the periodontium [12]. It was shown that ischemia of GM is the major mechanism of gastric ulceration [13].

The similarity of pathogenetic mechanisms of damages to the periodontium and stomach can be confirmed by parallel analysis of their metabolism during acute stress. Studies of the connective tissue playing a role in the metabolic exchange between the blood and specialized tissue cells showed that glycoproteins and proteoglycans, components of the connective tissue matrix, are highly sensitive to catabolic effects of stress factors [9,10]. It was shown that acute stress decreases the resistance of the gastric mucosa by stimulating degradation of glycoproteins and reducing the thickness of GM. Similar changes were observed in GM of humans with ulcer disease [10].

We measured fucose content (fucoprotein monomer) in periodontal and gastric tissues of rats with the same behavioral reactions (Table 1). The content of fucose increases in both tissues, which attests to decreased synthesis of fucoproteins during stress. These changes are typical of ulcer disease [9].

Accumulation of fucose in tissues induced by EPS was most pronounced in rats with active behavior (Table 1). The incidence and the number of gastric ulcers in these rats (42.8% and 1.2±0.8, respectively) 2.5- and 6-fold surpassed those in passive animals (16.6% and 0.2±0.2, respectively). High contents of fucose in GM homogenate and periodontal tissues correlated with the number of gastric ulcers (r=0.71 and r=0.78, respectively), which attests to common pathogenetic mechanisms of stress-induced damages to these organs resulted from dysregulation of metabolic processes.

Severe destructive changes in the neck and ostium of fundal glands and hemodynamic disturbances in the submucosal layer (stasis and parietal thrombosis) constituted the morphological substrate of metabolic dysfunction in GM. Microcirculatory disturbances in the periodontium induced by stress appeared as dilatations of small vessels in the connective tissue layer and periodontal vessels. Hemodynamic changes were most pronounced in rats with active behavior.

Hence, simultaneous morphofunctional changes in the periodontium and stomach of rats with different behavioral patterns induced by stress confirm the similarity of their pathogenetic mechanisms.

Common pathogenetic processes in the periodontium and stomach of rats were also confirmed by enhanced resorption of the mandibular alveolar process in response to reflex stimuli from the duodenal zone. In 62.5% rats, gastric ulceration was accompanied by increased exposure of molar roots due to enhanced resorption of jaw bones and impaired osteogenesis (Table 2).

TABLE 1. Contents of Fucose in Blood Serum (mmol/liter), Gastric Mucosa Homogenate, and Periodontal Tissues (mmol/g) in Rats with Different Behavioral Reactions to Acute Stress Injected with Thymopentin ($M\pm m$, n=5-6)

Group	Tissue	Behavioral pattern		
		active	intermediate	passive
Intact	Blood	0.95±0.08	1.12±0.12	1.06±0.06
	Stomach	0.57±0.01	0.64±0.01	0.66±0.05
	Periodontium	1.64±0.16	1.47±0.11	1.47±0.23
Acute stress	Blood	1.37±0.10*	1.16±0.09	1.11±0.12
	Stomach	0.94±0.03*	0.80±0.04*	0.75±0.03
	Periodontium	2.50±0.18	1.63±0.21	1.67±0.38
Thymopentin	Blood	1.08±0.09	1.08±0.04	1.09±0.02
	Stomach	0.51±0.01	0.51±0.02	0.69±0.07
	Periodontium	1.53±0.17	1.78±0.09	1.45±0.15
Thymopentin+acute stress	Blood	1.06±0.11**	1.06±0.04	1.10±0.04
	Stomach	0.70±0.03**	0.73±0.05	0.72±0.07
	Periodontium	1.65±0.08**	1.56±0.07	1.52±0.04

Note. p<0.05: *compared to intact animals, **compared to acute stress.

TABLE 2. Effects of Stimulation of the Duodenal Zone on Resorption of Alveolar Process of the Lower Jaw ($M\pm m$, n=5-6)

Experiment	Exposure of molar roots, %			Loss of teeth, %
	1st molar	2nd molar	3rd molar	
Control	43.90±2.32	43.40±2.75	44.00±2.74	0
Sham-operation	49.10±1.76	48.50±2.06	50.40±2.38	0
Duodenal zone stimulation	54.70±2.96*	55.30±3.09*	51.40±2.45	7.4

Note. *p<0.05 compared to the control.

Activation of lipid peroxidation is a universal mechanism of stress-induced damages. It was shown that chronic antioxidant deficiency promotes resorption of jaw bones and induces pathomorphological changes typical of periodontitis, which are accompanied by severe gastric ulceration in 42% animals [12].

To confirm the major role of metabolic dysregulation in damages to the periodontium and stomach, we studied the effects of thymopentin possessing considerable stress-protective properties [15] in rats with different behavioral reactions. Thymopentin attenuated stress-induced degradation of tissue fucoglycoproteins: this protective effect was most pronounced in rats with active behavior compared to the control (Table 1). We assume that stress-protective effects of thymopentin in active rats are realized via the blockade of catecholaminergic neurons in the hypothalamus. Hence, simultaneous stress-induced changes digestive organs are mediated by the same pathogenetic mechanisms.

Our findings indicate that the periodontium and stomach are highly sensitive to stress factors, which initiate simultaneous damages to these organs. Reflex stimuli from the gastric and intestinal zones can promote the development of dystrophic changes in periodontal tissues [12].

The interrelation between metabolic and structural changes in gastric and periodontal tissues is related to the similarity of neurohormonal effects, behavioral reactions in animals, and high sensitivity of both portions of the digestive tract to pathogenic factors.

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