Optimization of Parameters of Physiological Systems in Animals under Conditions of Experimental Stress Exposure

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Physiological and biomedical experiments were performed. We estimated the parameters of tree main levels of physiological systems as a response of an organism to stress. Mechanisms of physiological defense of an organism against stress should be considered systemically. The response of physiological systems of animal organism was modeled by the activation of latent functional reserves by various exposures to stress (abdominal surgery, cranial electrotherapy stimulation, cranial electrotherapy stimulation with simultaneous administration of droperidol, aminazine, vetranquil, and carbacholine).

Key Words: stress; functional systems; criterion optimization; physiological defense

Problem of stress has not lost its biomedical significance [1,10]. Stress is a mechanism helping an organism to survive under negative conditions, but it is not long-term mechanism. Summing of responses of organs and systems do not indicate the reaction of a whole organism. Effector organs and their functions should not be considered without transport and integrative physiological systems, *e.g.* circulatory, lymphatic, endocrine, and nervous systems [6]. The complex of physiological responses to various external stimuli is associated with adaptation and involvement of all possible (or necessary) defense systems, exhaustion of these systems leads to the development of a pathological process [9]. Physiological defense against stress unfolds at three levels: central or peripheral interruption of suprathreshold stimulus causing stress reaction; functional (metabolic changes); and compensation of functional changes and metabolic disorders [4].

It became now clear that each experiment should use systemogenetic approach and a complex of physiological, biochemical, and physicochemical parameters taking into account three levels of physiological defense. This approach allows adequate estimation of the possibilities of physiological defense, its intensity and disorders during stress.

Our aim was optimization of the parameters of physiological systems in animals during stress exposure.

MATERIALS AND METHODS

Acute and chronic experiments were performed in accordance to the principles of EC Directives (86/609/EC).

Acute experiment was conducted on 22 male Wistar rats weighting 180-240 g. The animals were randomized into 2 groups: group 1 rats (control) were not exposed to immobilization stress (IS), but received carbacholine (a stimulator of gastric secretion); group 2 rats were exposed to immobilization stress (IS), but received carbacholine (a stimulator of gastric secretion); group 2 rats received this substance after IS. IS was modeled by the fixation of rats by the limbs in supine position on an operating table for 18 h. During surgery, the ligature was placed on the pyloric part of the stomach of all rats, and after 90 min, carbacholine was injected intramuscularly in a dose of 25 μg/kg [2]. At the end of secretion (45 min), the rats were
decapitated, the stomach was isolated, and the gastric content was analyzed.

Chronic experiments were performed on 10 outbred male dogs weighting 15-22 kg with gastric fistula according to Basov, and 1.5-2-months Large White pigs \( (n=42) \) weighting 15-25 kg. Carbacholine in a dose of 6 μg/kg [3] was injected intramuscularly to dogs exposed or not exposed (control) to IS. Single IS was modeled by placing of dogs into small cages limiting their movements for 18 h. The duration of secretion in dogs was 2.5 h.

Pigs were randomized and operated: group 1 animals were exposed to cranial electrotherapy stimulation (CES; current frequency, 500 Hz; duration, 2 msec; current, 80 mA; S-shaped current-voltage; electrodes were placed in palatocervical area); group 2 animals were exposed to CES and simultaneous injection of droperidol (5 mg/kg, intramuscularly, inject) group 3 animals were exposed to CES and simultaneous injection of aminazine (2.5 mg/kg, intramuscularly); group 4 animals were exposed to CES and simultaneous injection of vetranquil (1 mg/kg, intramuscularly). The data before surgery served as a control. The dynamics of parameters after surgery were registered on days 1, 2, 5, 7, 12, and 21.

Autonomic and visceral reactions were estimated using visual analogous scale (adequacy of antinociceptive system in pigs [7]) and radiographic assay (emptying and motor activity of the stomach in pigs). Secretory function of the stomach in rats and dogs was evaluated by the level of gastric juice, acid activity, and fucose content reflecting mucus production [3]. Neurohumoral activity was estimated by the concentration of the following hormones in blood plasma: cortisol, corticosterone, ACTH, and somatotropic hormone (STH). The blood for assays was collected after decapitation (rats), from the saphenous vein (dogs), and from auricular and cranial veins (pigs) before surgery and on days 1, 2, 5, 7, 12, and 21 after surgery. Biochemical assays were performed using SF-2000 spectrophotometer, Konelab biochemical analyzer, Vctor multiscan, and photoelectric colorimeter. Thermo Fisher Scientific, Ølveks Diagnosticum, DRG Diagnostics Serotonin ELISA, DRG Diagnostics ACTH ELISA, Steroid IFA-cortisol 01, T-3 T-4 (Alkor-Bio), and Vital-FIE reagent kits were used. The significance of differences was estimated by Mann–Whitney criterion and Student’s \( t \) test.

**RESULTS**

The response of antinociceptive system to experimental surgical stress was scored using a visual analog scale as follows: no pain (0), mild pain (1), moderate pain (2), severe pain (3), very severe pain (4), and unbearable pain (5, active fight, cyanosis of mucoae, fast breathing, up to cardiac arrest; Table 1). Pain stimuli were modeled in all pigs from treatment groups before surgery by pinches of the skin on the ventral abdominal wall and ears with Kocher’s forceps.

Pain induced activation of the sympathetic nervous system, which resulted in decelerated evacuation of stomach content [5]. These changes were observed by radiography (slow passage of contrast mass from the stomach to the intestine). Normally, contrast mass passes the stomach within 1 h, in case of accelerated passage within 30 min. Our experiments demonstrated decelerated emptying of the stomach in groups 3 and 4 pigs [7]. Radiograms showed unequal spreading of contrast in the stomach without filling the duodenum; the stomach content, costal margin, and sternum were clearly visualized. In groups 1 and 2, contrast mass completely filled the stomach and had clear-cut outlines and signs of passage into the duodenum in some animals.

Carbacholine administration to rats after IS resulted in severe inhibition of secretory activity of the stomach: the volume of gastric juice decreased by 1.8 times, acidity decreased by 26 times, and intensity of \( H^+ \) secretion decreased by 20 times \( (p<0.05) \). Secretory activity of the stomach in dogs significantly varied in control experiments and the animals with various secretory activities were divided into 2 groups: group 1 with high secretory activity of the stomach (great volume of gastric juice with high intensity of \( H^+ \) secretion, hydrolytic potential, and fucose content) and group 2 with low secretory activity in comparison with group 1 animals [8]. The differences in the secretory potential of the stomach in dogs can be related to various initial tone of the autonomic nervous system. The parameters of gastric secretion significantly differed in these groups after stress exposure and carbacholine administration. The volume of gastric juice, \( H^+ \) concentration, and proteolytic activity decreased in group

<p>| Table 1. Adequacy of the Response of Antinociceptive System to Surgical Stress in Pigs (Score) |
| --- | --- | --- | --- | --- |</p>
<table>
<thead>
<tr>
<th>Observation period</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before surgery</td>
<td>3</td>
<td>3</td>
<td>2.8</td>
<td>3.4</td>
</tr>
<tr>
<td>During surgery</td>
<td>0</td>
<td>0</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>During cutting of the abdominal wall</td>
<td>0.2</td>
<td>0.6</td>
<td>2.6</td>
<td>2.4</td>
</tr>
<tr>
<td>After surgery</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
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