PHYSIOLOGY

Effect of Acute and Moderate Repeated Stress on Disturbances in Reactivity of Mesenteric Lymphatic Vessels during Inflammation in Rats


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We studied the effect of acute (single immobilization for 1 h) and repeated (daily immobilization for 1 min, 5 days) moderate stress on disturbances in contractility of mesenteric lymphatic vessels in rats with experimental peritonitis. Acute stress was shown to potentiate, while moderate repeated stress attenuate the effect of inflammatory stimulus. It can be hypothesized that moderate repeated stress improves adaptive capacities of the organism, which manifests in reduction or prevention of dysfunction in contractile activity of lymphatic vessels.

Key Words: inflammation; stress; lymphatic vessels

Chronic and severe stress can induce serious disturbances in various systems of the organism, which results in the development of diseases. The pathogenesis of these diseases is often associated with the inflammatory process. Strong evidence exists that stress exposure increases susceptibility of the organism to inflammatory agents. These changes are related to the exhaustion of stress-limiting systems and reduced release of anti-inflammatory mediators [4,5]. However, moderate and short-term stress can activate the endogenous protective mechanisms improving organism’s resistance to subsequent exposure to adverse factors [6]. For example, repeated restraint stress has a strong inhibitory effect on vascular endothelial permeability (major component of the inflammatory response) [9]. Pre-exposure to moderate stress prevents gastric ulceration in rats under conditions of severe stress [10].

Lymphatic vessels have close functional relations with the hematopoietic, nervous, and other systems in the organism and are involved in the adaptive response to stress and inflammation. Rhythmic activity of lymphatic vessels plays a crucial role in the negative and positive course of the diseases (e.g., inflammation) [8,11].

Our previous studies showed that the development of inflammation in rats (experimental peritonitis) is followed by paradoxical changes in the tone of mesenteric lymphatic vessels in response to standard contraction-inducing agent norepinephrine [3]. The majority of vessels responded by dilation without subsequent contraction (instead of expected constriction and phasic contractions). Changes in the tone of lymphatic vessels were accompanied by impairment of vascular contractility (increase in the latency, decrease in the frequency of contractions, and shortening of the response). Similar changes were observed in rats after single exposure to various stress factors [1]. However, the effect of moderate repeated stress on the function of lymphatic vessels remains unknown.
Stress is an etiological or risk factor for the development of inflammation. The effects of acute and moderate stress are mediated by various physiological mechanisms. Here we studied the influence of stress factors on reactivity of mesenteric lymphatic vessels in rats with experimental peritonitis.

**MATERIALS AND METHODS**

Experiments were performed on male outbred albino rats (n=70) weighing 150-180 g. The study was conducted in accordance with the recommendations of the European Science Foundation (ESF).

Inflammation (acute peritonitis) in rats was induced by an intraperitoneal injection of 40% sodium thioglycollate (1 ml per 100 g body weight; Fluka) [7].

The mesenteric microcirculatory bed was visually examined by intravital microscopy. Contractility of mesenteric lymphatic vessels was evaluated from the response to norepinephrine [2]. Under normal conditions, norepinephrine (10^-6 M) causes constriction of lymphatic vessels and increases the frequency of contractions. Abnormal response to norepinephrine attests to dysfunction of lymphatic vessel. We evaluated the latency of response (period between application of norepinephrine and start of contractions), frequency of contractions over the 1st minute, and duration of the response. Changes in the vascular tone and number of norepinephrine-responding vessels were recorded. The mesentery was examined visually.

The following two types of stress exposure were used: single acute stress (1-h immobilization in the supine position on a table) and moderate repeated stress (daily immobilization for 1 min, 5 days). After stress, the animals received an intraperitoneal injection of thioglycollate. Reactivity of lymphatic vessels was evaluated 2 h after the induction of inflammation. The animals exposed to moderate repeated stress were treated with thioglycollate immediately or 1 day after the last episode of immobilization.

The significance of differences was estimated by Student’s t test.

**RESULTS**

In series I, contractile activity of mesenteric lymphatic vessels in rats was studied after acute and moderate repeated stress (Fig. 1). Thioglycollate (inflammatory agent) caused dysfunction of lymphatic vessels, which manifested in an increase in the latency of contractions, decrease in the frequency of contractions (1st minute of the response), and shortening of contractions...