Changes in Lymph Microcirculation during Pathological Stress

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Stress caused by immobilization and acoustic stimulation produces considerable changes in lymph microcirculation. These changes manifested in dilation of microvessels, enhanced phasic contractile activity and its abnormal pattern, accelerated lymph flow, and recruitment of new lymphangions in drainage functions.

Key Words: *lymphatic microvessels; lymph flow; stress*

Stress plays an important role in the pathogenesis of various diseases and serves as a nonspecific component of the general organism's response [1]. Previous studies of the mechanisms underlying the stress response focused on changes in the heart and blood vessels that contribute to the development of coronary heart disease, hypertension, atherosclerosis, and other stress-induced human disorders [3,5,8]. Changes in lymph microcirculation under stress conditions are poorly known. At the same time, these changes play a role in the development of disturbances in the vascular and tissue homeostasis [4,6,9].

Here we studied functional activity of mesenteric lymphatic microvessels in rats during stress caused by immobilization and acoustic stimulation.

MATERIALS AND METHODS

Experiments were performed on 68 male outbred albino rats weighing 180-220 g and narcotized with nembutal (40 mg/kg intramuscularly). Lymph microcirculation in mesenteric vessels of the small intestine was assayed by vital videomicroscopy. Video images were processed as described elsewhere [2]. We measured the diameter of microvessels in the central (extravalvular) part of the lymphangion and determined phasic contractile activity of lymphangions, rate of contractions, amplitude of phasic contractions, duration of contraction, relaxation, and stable constriction, total time of the contraction cycle, and average rate of wall movements. If the working valve was present in the field of view, its activity was evaluated. We recorded the rate of closing of valve cusps, time of closing and opening, duration of the closed-cusp period, and total time of the valve cycle. The average rate of lymphocyte flow in lymphangions was estimated. We performed 8-10 measurements in 1 region of the lymphangion.

The animals were divided into 2 groups. The control group included 35 intact rats. Experimental animals were immobilized on the back and placed in a special chamber. Intermittent acoustic signal (120 dB, 150-500 Hz) was delivered for 2 h. This treatment excluded the development of protective inhibition [7]. After stress the rats were narcotized with nembutal, the mesentery was dissected, and lymph microcirculation was studied for 30-40 min.

The results were analyzed by Student's t test and exact Fischer's test. The differences were significant at $p \leq 0.05$.

RESULTS

Two-hour ISS markedly increased the average diameter of lymphatic microvessels and the number of lymphangions with phasic contractile activity (Table 1). In intact rats large microvessels displayed spontaneous contractile activity. After stress no differences were revealed between the average lumen of contracting and non-contracting microvessels (Table 1). Therefore, after stress phasic contractions were observed in vessels with various diameters. Stress changed parameters and structure of phasic contractions

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(Table 2). After stress the amplitude of phasic contractions increased by 2 times ($p<0.001$), while the rate of contractions decreased by 41% ($p<0.001$). Sometimes, we observed asynchronous movements of the vascular walls resulting in the appearance of hour-glass figures. Stress increased the rate of movements of the lymphangion wall during phasic contractions by 64%. After stress the rate of relaxation increased by 53% compared to the control ($p<0.001$). The period of stable constriction in stressed rats decreased by 42% ($p<0.001$). The total time of the contraction cycle was the same in intact and stressed rats.

These results indicate that stress causes dilation of lymphatic vessels and produces phasic contractions differing from spontaneous contractile activity of intact lymphangions.

Apart from phasic contractions, functional activity of the valves plays an important role in lymph flow. Intact and stressed rats did not differ in the number of working valves and average rate of their activity (Table 3). The valve cycle consists of 3 phases: closing of cusps, period of closed cusps (plateau phase), and opening of cusps [2]. In intact lymphangions the plateau phase is characterized by maximum duration (70% of the total time). Closing and opening phases are equally short. Stress abolished the differences between opening, closing, and plateau phases (35.0±2.9, 30.2±2.9, and 35.0±5.6%, respectively).

Under physiological conditions lymph does not circulate in some lymphangions. In our experiments lymph flow was detected in 86% intact lymphangions, but was absent in 14% lymphangions. After stress lymph flow was observed in all lymphangions, which was probably related to the involvement of non-functioning microvessels. The average rate of lymph flow markedly increased (Table 1). As differentiated from intact rats, no relationship was found between phasic contractile activity and lymph flow in stressed animals. Under normal conditions the rate of lymph flow in contracting lymphangions surpasses that in non-contracting lymphangions.

Our results indicate that lymph microcirculation undergoes changes during pathological stress. Microvessels are involved in drainage functions, which is manifested in the increase in their diameter, induction of phasic activity, acceleration of lymph flow, and opening of non-functioning vessels. These changes maintain vascular and tissue homeostasis (at least, in the early stage of stress reactions). Changes in the neurohormonal regulation of lymph microcirculation under stress conditions determine the development of these disturbances. The mechanisms of these changes require further investigations.

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TABLE 1. Effect of ISS on Lymph Microcirculation in Rat Mesentery (*M*±*m*)

Parameter	Control	Stress
Diameter of lymphangion, μ	137±3	153±5**
Lymphangions with phasic activity, %	44	66**
Diameter of vessels with phasic contractions, μ	148±5	158±6
Lymphangions with lymph flow, %	86	100**
Diameter of resting lymphangions, μ	122±3+	142±9
Average rate of lymph flow, μ/sec	227±8	295±12*

Note. *$p<0.001$ and **$p<0.02$ compared to the control; +$p<0.001$ compared to lymphangions with phasic activity.

TABLE 2. Phasic Contractile Activity of Lymphatic Microvessels in Control and Stressed Rats (*M*±*m*)

Parameter	Control	Stress
Amplitude, μ	17.6±1.7	35.8±4.6*
Rate, per 1 min	12.7±0.8	7.5±0.9*
Period of stable constriction, sec	1.20±0.08	0.70±0.04*
Duration of contraction cycle, sec	2.7±0.1	2.60±0.14
Rate of contraction, μ/sec	24.2±1.7	40.0±2.4*
Rate of relaxation, μ/sec	23.2±2.1	35.4±1.9*

Note. Here and in Table 3: *$p<0.001$ compared to the control.

TABLE 3. Functioning of Valves in Lymphatic Micro-vessels in Control and Stressed Rats (*M*±*m*)

Parameter	Control	Stress
Rate of valve activity, per 1 min	11.5±1.6	14.4±1.6
Time of cusp opening, sec	0.20±0.02	0.65±0.1*
Time of cusp closing, sec	0.20±0.02	0.6±0.1*
Plateau, sec	1.33±0.50	0.7±0.2
Valve cycle, sec	1.5±0.2	1.9±0.3

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