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# Lympho- and Hemodynamics in Dogs with Acute Experimental Pancreatitis

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Dogs with experimental pancreatitis showed increased lymph flow, impaired rheological properties of the lymph and blood plasma, and increased plasma and blood levels of glucose, ALT, and AST.

**Key Words:** *lymph; lymph flow; lipase; acute pancreatitis; α-amylase*

Acute pancreatitis (AP) is a polyetiological, but monopathogenetic disease. Approximately 20% patients with AP develop pancreatic necrosis with a mortality rate of 10-50% [4,6,7].

In AP, pathological changes occur in the whole body, so it is interesting to examine the state of the lymphatic system in this disease. The lymphatic system is involved in the pathology of a number of internal organs and other systems and is essential for the maintenance of homeostasis [1,9].

Here we studied lymphodynamics and biochemical composition of the lymph in dogs with experimental AP.

## MATERIALS AND METHODS

The work was carried out on adult mongrel male dogs ($n$=8) weighing 10-15 kg in compliance with the rules of bioethics approved by the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Purposes (Strasbourg, 1986). The animals were anesthetized with sodium thiopental (35-40 mg/kg intravenous). AP was simulated by intraparenchymal administration of a mixture of its own bile and trypsin (by 0.6 to 0.8 ml) into 7 to 8 sites of the pancreas [3].

Using the standard techniques, we evaluated glucose levels in blood and lymph (Accu-Chek Active glucometer), blood and lymph levels of α-amylase (amyloclastic method), lipase (enzyme method), total protein (biuret method), alkaline phosphatase (kinetic method), ALT and AST (by Reitman–Frankel using Bio-LA-Test reagents) [8]. Clotting time of the lymph and blood was determined by Sukharev [5], viscosity was measured using a viscometer VK-4. Lymph flow from the thoracic duct was recorded at the site of its confluence into the jugular vein in the neck using graded microcannula. All measurements were carried out before and 3 and 6 h after AP modeling.

The results were treated by the methods of variation statistics using Student's $t$ test. The values were considered significant at $p<0.05$.

## RESULTS

Significant increase in plasma and lymph α-amylase and lipase was observed in the dogs 3 to 6 h after AP modeling. Plasma level of α-amylase increased by 52%, lymph level, by 46.8% compared to baseline (Table 1). Maximum increase in lipase level in the lymph (by 5 times) and plasma (by 6.6 times) was observed 3 h after AP induction. According to published data [12,15], the manifold increase in the level of α-amylase after AP modeling associated with excessive activation of this enzyme and massive release into the blood indicates AP development.

Lymph flow rate in AP increased almost 1.7 times relative to baseline. Lymph flow rate increased by 70% during the first 1.5 h of the pathological process ($p<0.01$), but by the 4th hour it decreased by 20%, and

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by the 6th h of the experiment a sharp slowdown was observed (to 73% of baseline; Table 1).

Undulating variation of lymph flow was recorded in AP: lymph flow intensified during the early hours the amount of interstitial fluid increased, and hemorrhagic exudate accumulated in the abdominal cavity; the lymph from the thoracic duct turned blood-red instead of light yellow. Large numbers of red blood

**TABLE 1.** Parameter of Lymphodynamics and Rheological Properties of Blood in Experimental AP

| Parameter | Baseline | Time after AP modeling | |
|---|---|---|---|
| | | 3 h | 6 h |
| Lymph flow, ml/min | 0.41±0.05 | 0.70±0.06** | 0.30±0.04* |
| ***Lymph*** | | | |
| Viscosity, units | 3.09±0.30 | 5.43±0.20** | 5.48±0.30** |
| Clotting, min | 4.70±0.01 | 3.77±0.02* | 2.86±0.01** |
| α-Amylase, μcat/liter | 14.10±0.10 | 22.00±0.30** | 19.40±0.10* |
| Lipase, μcat/liter | 5.60±0.30 | 22.90±0.60** | 27.20±0.40** |
| Glucose, mmol/liter | 5.81±0.70 | 9.74±0.90* | 12.30±0.10* |
| Total protein, g/liter | 51.20±2.30 | 62.40±0.20* | 64.10±2.10** |
| Alkaline phosphatase, μmol/liter | 446.00±2.40 | 685.00±4.10* | 805.00±5.30** |
| AST, μcat/liter | 0.40±0.01 | 0.48±0.02** | 0.55±0.03* |
| ALT, μcat/liter | 0.41±0.03 | 0.66±0.06* | 0.67±0.04* |
| de Ritis coefficient | 0.97±0.02 | 0.72±0.30* | 0.82±0.30* |
| Leucocytes, $\times 10^3$/μl | 5.45±0.30 | 7.90±0.20* | 5.85±0.20 |
| Erythrocytes, $\times 10^3$/μl | – | 0.030±0.001** | 0.040±0.001** |
| Thrombocytes, $\times 10^3$/μl | – | 8.10±0.03** | 10.30±0.05** |
| Hemoglobin, g/dl | – | 0.600±0.001** | 0.700±0.001** |
| Lymphocytes, % | 85.90±1.60 | 92.70±2.40* | 87.20±1.80* |
| Lymphocytes, $\times 10^3$/μl | 5.00±0.30 | 7.25±0.10** | 5.35±0.30* |
| ***Blood plasma*** | | | |
| Viscosity, units | 3.48±0.30 | 5.03±0.10** | 6.20±0.20** |
| Clotting, min | 3.68±0.02 | 2.56±0.01* | 2.41±0.01* |
| α-Amylase, μcat/liter | 11.60±0.40 | 19,20±0,30** | 16.10±0.50* |
| Lipase, μcat/liter | 2.80±0.40 | 20.20±0.20** | 16.8±0,5** |
| Glucose, mmol/liter | 5.49±0.50 | 9.25±1.20* | 14.60±2.30** |
| Total protein, g/liter | 67.20±1.40 | 69.10±1.20 | 72.30±3.50* |
| Alkaline phosphatase, μmol/liter | 481.00±2.30 | 857.00±4.30** | 951.00±5.20** |
| AST, μcat/liter | 0.38±0.02 | 0.79±0.03** | 0.49±0.01 |
| ALT, μcat/liter | 0.41±0.01 | 1.05±0.02** | 0.69±0.02* |
| de Ritis coefficient | 0.92±0.02 | 0.75±0.04** | 0.71±0.03* |
| Leucocytes, $\times 10^3$/μl | 6.80±0.30 | 5.20±0.30* | 5.00±0.80* |
| Erythrocytes, $\times 10^3$/μl | 11.80±0.50 | 11.30±0.40 | 10.70±0.60* |
| Thrombocytes, $\times 10^3$/μl | 181.50±2.60 | 360.00±3.30** | 569.50±6.50** |
| Hemoglobin, g/dl | 112.00±2.30 | 92.00±1.40* | 87.00±1.60** |
| Lymphocytes, % | 97.00±2.50 | 88.90±1.90* | 94.70±2.10* |
| Lymphocytes, $\times 10^3$/μl | 8.50±1.30 | 11.70±1.80** | 9.30±1.70* |

**Note.** *$p<0.05$, **$p<0.01$ in comparison with the baseline.

cells were found in the lymph, clotting of the lymph decreased and viscosity, increased.

The volume of blood plasma in AP (according to hematocrit indicators) decreased by 6% from the baseline, lymph and blood viscosity increased by 1.8 times.

Measuring viscosity of the lymph provides insight into severity of the disorders of vascular permeability and the state of the transport function of the lymphatic system under pathological conditions [2,10,14]. Thus, lymph viscosity depends on tissue metabolism and is closely associated with impaired vascular permeability.

Rheological properties of the lymph changed simultaneously with disorders of the coagulation system. Clotting was accelerated, which deteriorated fluidity of blood and lymph. The clotting time of the lymph 3 and 6 h after AP modeling decreased by 20 and 39%, and blood clotting time, by 30 and 34.5%, respectively from baseline (Table 1). These findings attest to impaired rheological properties of the blood and lymph.

AP deteriorated endocrine function of the pancreas: the lymph and blood glucose were elevated in comparison with the initial level (Table 1). Total protein content in the lymph and blood increased by 23 and 5.2%, respectively, alkaline phosphatase, by 53.5 and 80% and 78 and 97% 3 h and 6 h after AP modeling (Table 1). Lymph levels of AST and ALT were elevated 3 h after AP compared to baseline (34 and 67.5%), and plasma levels, by 28 and 68% (Table 1). De Ritis coefficient during AP was significantly below normal ($p<0.05$) indicating the changes in the pancreas.

Analysis of the results suggests that decreased lymph flow corresponds to changes in not only biochemical, but also rheological properties of the lymph. Shortening of the clotting time and increasing viscosity of the blood and lymph was observed in dogs with AP. Enhanced lymph viscosity in AP and the presence of erythrocytes increases the risk of thrombosis. Acceleration of blood clotting and development of hypocoagulation phase of the thrombohemorrhagic syndrome are known to occur in AP that is an essential element of AP pathogenesis [13].

The results of our experiments show that decreased lymph flow rate corresponds to not only biochemical, but also rheological changes in the blood and lymph. Thus, we observed the same type of disorders in functional tests of liver and pancreas, in the lymph and blood in experimental AP in dogs. Our data confirm the findings of other authors that functional disorders occur in the liver during AP [11]. However, along with them, we observed dramatic changes in the lymph flow from the thoracic duct, reduction of drainage and transport function of lymph vessels, and change in the enzyme level in the lymph that suggests the involvement of the lymphatic system in the of development of experimental AP in the dogs.

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