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Rheological and Microcirculation System Disorders in Experimental Hyperthyroidism

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Parameters of activity of peripheral blood supply system of the liver and kidneys in interrelation with rheological functions of blood during an experimental hyperthyroidism have been studied. Disorders of rheological functions of blood and deeper violations of blood circulation in microhemocirculatory system of liver and kidneys have been established. Results of research testify more expressed violation of parameters of microcirculation of liver where hydrodynamic pressure is slightly lower than in the system of peripheral blood circulation of a cortical layer of kidneys.

Keywords: Hyperthyroidism; rheology; microcirculation; liver; kidney.

1. INTRODUCTION

Widespread introduction into clinical practice research methods microcirculation revealed that microcirculatory disorders are a major cause of metabolic disorders defining seriousness of illness and outcomes of different pathological conditions. Disorders of blood stream in system of microcirculation is an inevitable component of almost each pathological process [1,2]. Rheological parameters of blood also play an important role in ensuring exchange functions at

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the level of a peripheral link of the blood circulatory system. They are responsible for not only behaviour of blood, but also responsible for interaction of blood with structural components of the microcirculatory course. The system of microcirculation has specific features in different organs and tissues of an organism. Moreover, in separate sites of the same body the system of peripheral blood circulation can differ at any given moment: periodically one or the other parts of body function with different degree of activity. Therefore, the researches of rheological properties of blood in close interrelation with the microcirculatory course of internals will allow receiving more detailed and significant information about violations in organs, such as liver and kidney during thyrotoxicosis [3,4].

The structure and functions of almost all organs and systems of an organism are under influence of the thyroid hormones [5]. The maintenance of an adequate hepatic blood flow has crucial importance for ensuring parameters of homeostasis. Deterioration of microcirculation is characterized by narrowing of vessels, adhesion of leukocytes and platelets to endothelium of vessels, violation of sinusoidal blood circulation and hypoxia of parenchyma of the tissue [6]. Kidneys also respond to surplus of the thyroid hormones, increase of a glomerular filtration and mild polyuria [7,8,9].

These aspects define a purpose of the real research – comprehensive study of performance parameters of the peripheral blood circulation system of the liver and kidneys in interrelation to the rheological properties of blood in experimental hyperthyroidism.

2. MATERIALS AND METHODS OF RESEARCH

All experimental animals were bought by researcher account. Experiments have been held on 100 white outbred rats - males with the initial body weight of 130 - 180 g. Animals were kept in vivarium conditions on a usual diet. Researches were conducted on 7, 14, 21, 28 days after the beginning of oral insertion of L-thyroxin (Berlin – Chemie Germany) in a dose of 100 mg/kg [10]. Blood of experimental animals for researches was taken from a tail vein. The general condition, behaviour and dynamics of body weight of experimental animals were daily registered. This study was approved by an internal ethics committee animal experimentation of the Tashkent Medical Academy, Uzbekistan (ICP-TMAUZB 2016-017A).

Bio microscopic research of the microcirculatory course of a liver and kidneys was carried out by a luminescent microscope 'Ljumam - I3' (LOMO, Russia) with the use of a contact lens 10x0,40. Results of bio microscopy were recorded by the digital camera, which was connected to the television digital analyser of parameters of microstructures. Research was conducted under common thiopental anaesthesia in a dose of 70 mg/kg of body weight of animal. The diameter of micro vessels and linear speed of a blood flow in them were determined.

Rheological functions of blood were determined by the speed of its shift and the dynamic viscosity determined in a capillary tube by Copley method in V. M. Udovichenko's modification [8]. Indicators of viscosity of blood were determined by applying various sizes of hydrostatic pressure (2, 4, 8, 12, 16 mmHg) to a stream of blood as they correspond to pressure in vessels of various calibre. The speed of blood stream shift was counted based on a formula:

$$U = 4R2 \cdot L/r3 \cdot tp \ (sec^{-1})$$

The dynamic viscosity of whole blood was counted based of the obtained data of shift speed with a formula:

$$\eta = 100g \cdot r4 \cdot l/8R2 \cdot L \cdot U \ (sP),$$

where

η – dynamic viscosity; U-blood shift speed; R-radius of capillaries in wide part; L-length of wide part of a capillary; r-the radius of capillaries in narrow part; l - length of narrow part of a capillary; t - movement time; p - pressure size enclosed to blood flow; g – acceleration of gravity.

Digital material is processed by method of variation statistics with definition of criteria of Student – Fischer.

3. RESULTS AND DISCUSSION

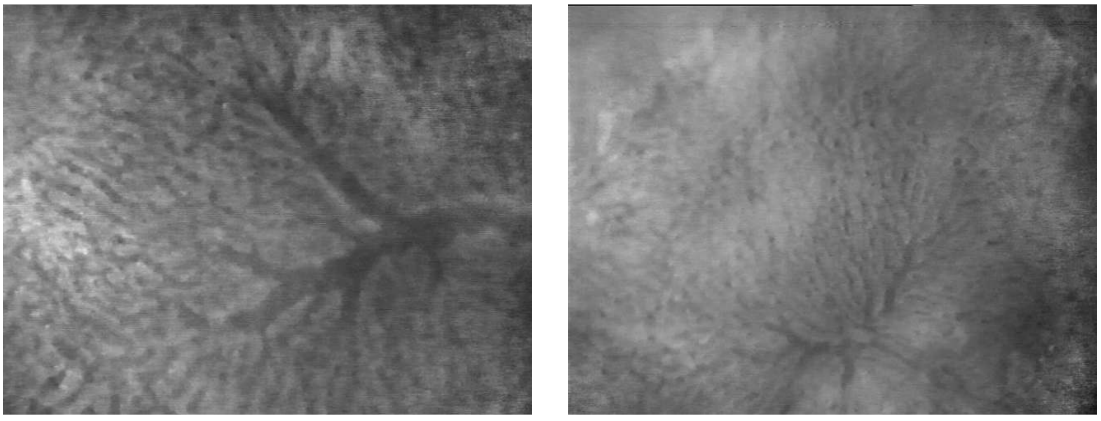
Angioarchitectonics of the microvascular course of the liver of intact animals is characterized by accurate contours of vessels, equal and thin walls of sinusoid. The intersinusoidal space is filled with almost homogeneous transparent contents. Sinusoids come to light in the form of branched anastomosing capillary blood system. Some branches, which approach a segment, wash all parenchyma. Diameter of these vessels

among animals of intact group makes 34.27+2.03 microns, and blood flow speed is equal on average to 0.331+0.026 mm/sec. The blood flow in sinusoids is characterized by uniformity, homogeneity and a continuity of a stream. Liver sinusoids from a portal venula to the central collective go in the form of beams of light. Diameter of sinusoid is equal 9.04+0.41 microns, and blood flow speed is equal in them on average to 0.266+0.023 mm/sec. The blood-groove in all components of microcirculator unit of a liver is characterized by uniformity, homogeneity and a continuity of a stream. In sinusoids of the segments located in the centre, blood-groove is quicker in comparison with blood-groove in sinusoids on the periphery of segments. Along with the functioning sinusoids in a parenchyma of a liver, the insignificant quantity of the nonfunctioning sinusoid, which are usually settling down on the periphery of segments, are detected. Before a confluence of sinusoid with terminal hepatic venules, which usually occurs at right angle or close to that, narrowing of a sinusoid gleam on average for 19.7+2.5% is noted.

Terminal hepatic venules where sinusoids fall into have a form close to cylindrical or a treelike form when 2 – 3 collective venules fall into them. Diameter of central – collective venules is 27.85±1.93 mkm, and blood-groove speed - 0.227±0.018 mm/sec. Diameter of the portal venules is equal to 34.27±2.03 mkm, and blood-groove speed in them – 0.331±0.026 mm/sec.

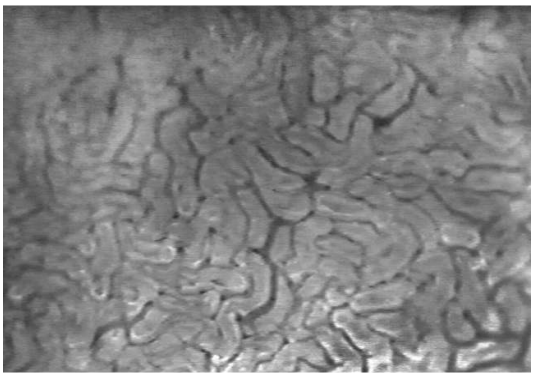
Peritubular capillaries of an external cortical layer of kidneys are available to the biomicroscopy. Tissue of kidneys of intact animals, available to research, at bio microscopy is presented by loops of the proximal convoluted tubules between which vessels of capillary type with a dark shade, accurate contours are visible. The type of a branching of capillaries and appearance of capillary networks isn't casual and chaotic, but reflect a configuration of the tubular structures. Now it is established that distal sites of separate nephrons are supplied with efferent capillary networks from many glomeruli. The only site in which the efferent vessel of the glomerulus perfuses a tubule of the same glomerulus is the area of a proximal crimped tubule, the surface cortical layer.

In rare instances, it was managed to observe small part of an efferent arteriole, which is situated horizontally in relation to bark and gives branches on an extent. Diameter of arteriole fluctuates ranging from 18.7 to 25.8 microns. A blood-groove in them is rapid and continuous with flow. Linear speed of a blood-groove in the arteriole is equal to 0.557±0.073 mm/sec. The peritubular capillaries, departing from an efferent arteriole, form a network with the polygonal cells extended along tubules widely anastomosing among themselves. The border between tubules and capillaries differed accurately because of the hazy convoluted strips appearing at light refraction by an epithelium of tubules. Deserves attention that practically all the fact that almost all visible capillaries function deserves attention. Diameter of capillaries is equal to 8.58+0.45 microns on average, a blood-groove in them is rapid and continuous, and the speed of a blood-groove is equal to 0.436±0.028 mm/sec.



(a) 7th day **(b) 28th day**

Picture 1. Liver microcirculation



Picture 2. Renal microcirculation, under the microscope, 28th day of the experiment

In the group of experimented animals, in comparison with intact group, the speed of shift of stream of blood at the size of the enclosed pressure 2 mmHg was equal to 9.07±0.74 c^{-1}, and at 16 mmHg this indicator was equal to 102.47±6.28 c^{-1} that are respectively lower for 46.9% and 13.4% than in intact group of animals. According to shift speed, dynamic viscosity of blood changed. Therefore, when applying pressure was 2-mmHg dynamic viscosity increased by 32.8% and made 11.27±1.28 sP, and at 16 mmHg dynamic viscosity increased by 12.3% and made 2.48±0.15 sP (Table 1). Indicators of diameter of a liver sinusoid was 10.21±0.79 microns, blood-groove speed in them made 0,169±0,017 mm/sec. that is 36.6% lower than the corresponding values of intact group of animals. Diameter of venules made 35.04±1.80 microns and blood-groove speed in them - 0.140±0.012 mm/sec. that is 38.4% lower than in intact group (Table 2).

Research of speed of blood stream shift and its dynamic viscosity during an experimental thyrotoxicosis showed the existence of essential changes almost at all sizes enclosed to pressure blood stream. For the 7th days of experiment in the group of experimented animals, in comparison with intact group, the speed of shift of a blood stream went down, and dynamic viscosity of blood raised. According to change of rheology, the angioarchitectonics of the microcirculatory course of liver and cortical layer of kidneys changed. Contours of sinusoid were a little vague. At the level of separate sinusoid there are centres of aggregation of elements with a blood-groove stop, obviously coincides with increase of dynamic viscosity of blood. Borders of the central collective I faded are accurately outlined, without visible changes. Continuous character of a blood-groove in these vessels is kept. Perivascular changes weren't revealed. Blood-groove in vessels of a cortical layer of kidneys is fast, equal, in a continuous stream; walls of capillaries of the proximal convoluted tubules are accurate, equal. Blood-groove speed in them also doesn't undergo essential changes. There is a place lack of a characteristic luminescence of an epithelium of separate tubules. Non-functioning capillaries are not observed.

Table 1a. The dynamics of blood viscosity changes

Terms	The amount of pressure enclosed to a blood stream				
	2 mmHg.	4 mmHg.	8 mmHg.	12 mmHg.	16 mmHg.
Intact group	8,49±0,57	6,12±0,42	4,73±0,25	3,62±0,21	2,21±0,11
7 days	11,27±1,28*	7,86±0,58*	5,81±0,46*	4,20±0,29*	2,48±0,15*
14 days	12,25±1,07*	8,42±0,59*	6,13±0,41*	4,53±0,32*	2,69±0,15*
21 days	13,08±1,43*	8,91±0,73*	6,44±0,53*	5,01±0,35*	2,80±0,23*
28 days	13,69±1,25*	9,76±0,62*	7,32±0,41*	5,47±0,28*	3,29±0,27*

Table 1b. The dynamics of movement speed during hyperthyroidism

Terms	The amount of pressure enclosed to a blood stream				
	2 mmHg.	4 mmHg.	8 mmHg.	12 mmHg.	16 mmHg.
Intact group	17,09±0,88	34,43±1,51	59,12±2,79	80,04±5,58	118,31±6,94
7 days	9,07±0,74*	23,95±1,39*	40,02±2,71*	64,19±3,38*	102,47±6,28*
14 days	7,31±0,42*	19,26±1,55*	35,57±3,12*	61,30±3,53*	98,67±4,71*
21 days	5,96±0,38*	14,85±1,14*	32,61±2,37*	50,34±3,72*	93,29±5,25*
28 days	4,32±0,21*	12,33±1,24*	26,45±2,59*	47,81±4,07*	86,75±5,83*

Notes: The numerator indicates a viscosity of blood [sP];
The denominator indicated the speed shift of blood stream (sec.-1);
** - distinctions concerning the data of intact group are reliable (p<0,05)*

Table 2. The changes in parameters of liver microcirculation during experimental hyperthyroidism

Terms	Portal venula		Sinusoids		The central collective venula	
	Diameter, micron	Speed of blood stream mm/sec	Diameter, micron	Speed of blood stream mm/sec	Diameter, micron	Speed of blood stream mm/sec
Intact group	34,27±2,03	0,331±0,026	9,04±0,41	0,266±0,023	27,85±1,93	0,227±0,018
7 days	35,44±1,77	0,226±0,018	10,21±0,79	0,169±0,017	35,04±1,80	0,140±0,012
14 days	38,67±2,93	0,204±0,013	12,36±0,62	0,146±0,013	47,04±2,01	0,119±0,008
21 days	41,82±2,19	0,183±0,014	12,61±0,56	0,118±0,011	47,65±2,28	0,095±0,010
28 days	44,36±3,01	0,149±0,006	12,87±0,88	0,099±0,010	48,63±3,19	0,079±0,005

*Note: * - The numbers are reliable (P <0,05)*

Table 3. The changes in parameters of kidney microcirculation during experimental hyperthyroidism

Terms	Capillaries of the proximal convoluted tubule		Venula	
	Diameter, micron	Speed of blood stream mm/sec	Diameter, micron	Speed of blood stream mm/sec
Intact group	8,58±0,26	0,436±0,028	44,23±2,19	0,267±0,021
7 days	8,62±0,22	0,399±0,031	48,77±3,15	0,230±0,014
14 days	8,79±0,36	0,382±0,040	50,32±4,24	0,216±0,027
21 days	9,32±0,45	0,362±0,027	54,89±4,31	0,207±0,022
28 days	11,33±0,56	0,341±0,025	61,14±5,60	0,203±0,016

*Note: * - numbers are reliable (P<0,05)*

Parameters of the proximal convoluted tubules capillaries diameter of kidneys is equal to 8.62+0.22 mkm that practically does not differ from results of intact animals. Blood-groove speed in them also doesn't undergo essential changes and is equal to 0,399+0,031 mm/sec. The diameter of venules is 48.77+3.15 microns, and the speed of a blood-groove decreased by 13.7%, below control values and became equal to 0,230+0,014 mm/sec. (Table 3).

For the 14th days of experiment, violation of the studied parameters of rheological properties and violation of dynamic viscosity of blood continued to be aggravated. Dynamics of shift speed when applying the minimum quantity of pressure was equal to 7.31+0.42 C-1, and at the maximum – 98.67+4.71 C-1 that are lower than the corresponding results of intact group for 57.2% and 16.6%, respectively. Reflecting deterioration of rheological properties of blood on microcirculation of a liver, it slows down a blood-groove. Delay is more expressed at the level of the central collective venules (47.5% lower than an indicator of intact group). Diameter of venules makes 47.04+2.01 microns, the speed of a blood-groove – 0.119+0.008 mm/sec. Diameter of the portal venules is 38.67+2.93 microns, the speed of a blood-groove is equal to 0.204+0.013 mm/sec. that is 38.3% lower than the corresponding indicator of intact animals. In a liver the alternation of expanded sinusoid with sites which are stopped from a blood-groove are noticed. In the majority of vessels the blood-groove is significantly slowed down. The blood-groove in the functioning vessels gains granular content. The single centres of a perivascular diapedesis of erythrocytes are revealed. Different from a liver, an angioarchitectonics of a cortical layer of kidneys are saved. The single centres of washing out of borders between a wall of a capillary and a convoluted tubule are noted maybe because of plasmatic soaking of a capillary wall. In kidneys, the diameter of capillaries of the proximal convoluted tubule is equal to 8.79+0.36 mkm. Character and speed of a blood-groove didn't undergo essential changes. Blood-groove speed in capillaries of the proximal convoluted tubule is 0.382+0.040 mm/sec. that is 12.4% lower than results of other group. Diameter of venule is 50.32+4.24 microns, blood-groove speed is equal in them to 0.216+0.027 mm/sec. that is 19.2% lower than results of intact group of animals.

Within 21 days of experiment the progress of disorders of rheological properties in blood. The speed of a blood stream shift - when it was under pressure - 2 mmHg - was 5.96+0.38 c-1 that is 65.1% lower than indicators of intact group of animals. Indicators of dynamic viscosity increased by 54.1% made 13.08+1.43 sP in a zone of the minimum values enclosed to pressure of blood stream. When applying pressure 16 mmHg, dynamic viscosity increased by 26.5% and made 2.80+0.23 sP.

Disorders in the microcirculatory course of a liver gained more expressed character in comparison with the previous terms. A venous hyperaemia and stasis are sharply expressed. The specified changes didn't have such expressed character in the system of the portal venules. In the functioning sinusoids extent of violations of blood circulation had more expressed character in comparison with the previous terms of researches. Perivascular diapedesis of erythrocytes gained generalized character that led to disorder in angioarchitectonics with disappearances of characteristic vascular drawing of a hepatic segment. Diameter of the central collective venules increased to 47.65+2.28 mkm, and the speed of a blood-groove decreased to 0.095+0.010 mm/sec. that is less than the results of the intact animals by 58.2%. Diameter of these micro vessels was equal to 41.82+2.19 mkm, and the speed of a blood-groove decreased to 0.183+0.014 mm/sec. that is 44.8% lower than control results. Diameter of sinusoid was equal to 12.61+0.56 mkm, and the speed of a blood-groove decreased in comparison with values of intact animals by 56.1% and made 12.61+0.56 mm/sec.

In a cortical layer of kidneys in comparison with a liver the changes did not have so obviously expressed character. Angioarchitectonics remained, contours of capillaries were equal, accurate, but, as well as in a liver, sites of vessels in which there were congestions of aggregate gained widespread character. Diameter of capillaries of the proximal convoluted tubule was 9.32+0.45 mkm, blood-groove speed in them decreased by 16.9% below control values and became equal to 0.362+0.027 mm/sec.

The last term of researches, (the 28th day) was characterized by aggravation of blood rheology and microcirculation of a liver and the kidneys described in the previous terms. On this term of experiment shift speed with a pressure of 2 mmHg decreased to 4.32+0.21 c-1 that is 74.7% lower than results of intact animals. When applying pressure 16 mmHg the speed of shift was equal to 86.75+5.83 c-1 that is 26.7% lower than the control corresponding indicators (Table 1).

Diameter of sinusoid was 12.87+0.88 mkm, and blood-groove speed in them - 0,099+0,010 mm/sec (Table 2). Diameter of the functioning capillaries was equal to 11.33+0.56 mkm, the speed of a blood-groove was reduced by 21.8% and was equal to 0,341+0,025 mm/sec. (Table 3).

Angioarchitectonics of a liver was completely broken, in the most part of sinusoid; stasis was noticed with expressed blood extravasation in perisinusoidal space. Changes in kidneys weren't so noticeable in comparison with disorders in the microcirculatory course of a liver. Angioarchitectonics of a cortical layer of kidneys remained the same, in general. There were places of the microvascular course with the blocked blood flow and washing out of a contour of micro vessels.

Thus, the received results testify more expressed disorders of parameters of microcirculation of a liver where hydrodynamic pressure is slightly lower than in the system of peripheral blood circulation of a cortical layer of kidneys. The explanation of this phenomenon can be found in the features of action of high concentration of the thyroid hormones. The change of thyroid function leads to endothelial dysfunction and disorder of a thin balance in the system of coagulation and fibrinolysis. These aspects of pathogenesis of the hyperthyroid states also define more expressed disorders of microcirculation in liver where the hydrodynamic pressure of blood and linear speed of blood-groove is significantly lower than in kidneys. The important role is also played by features of blood supply of a liver, receiving ¾ of blood on portal system and kidneys whose blood supply is carried out directly from belly department of an aorta.

We can see that difference between Tables 2 and 3. In Table 2 was given liver microcirculation changes in experimental hyperthyroidism. There are found that diameter of portal venules are increasing more than 10.09±2.52 from intact group to 28 days animals' results. Speed of blood stream (mm/sec) in portal venula is decreased from 0.331±0.026 to 0.149±0.006 because of enlargement of venula diameter. In sinusoids, there is determined that diameter of sinusoids is also risen from intact group to 28

days animals. However, you may see that differences of blood flow between sinusoids of the liver and venules of the kidney.

4. CONCLUSIONS

1. Hyperthyroidism is followed by disorders of dynamic and static parameters in system of peripheral blood circulation of a liver and kidneys.
2. Expressiveness of disorders is connected both with a limitation period of a hyperthyroidism, and regional features of blood circulation of organs. Low indicators of hydrodynamic pressure in microhaemocirculator system of a liver and kidneys lead to emergence of deeper disorders in blood circulation.
3. Experimental hyperthyroidism is followed by reduction in the blood stream shift rate and increase in dynamic viscosity.
4. Changes of rheological parameters of blood are more expressed in zones of low sizes enclosed to blood stream pressure, especially at the level of an exchange link of the vascular course.

CONSENT

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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