

ANNOTATION
of the dissertation work of

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on the topic
**ROLE OF DISTURBANCE OF PHYSICAL AND CHEMICAL PARAMETERS OF
ERYTHROCYTES IN PROGRESSION OF CHRONIC KIDNEY DISEASE**
for the Doctor of Philosophy (PhD) degree in specialty «6D110100- Medicine»

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The relevance of the topic

Currently, chronic kidney disease (CKD) is increasingly recognized as a key factor determining the poor state of public health. Analysis of the literature showed that globally, there were 2.6 million people on dialysis in 2010. In contrast to this, the number of people in need of renal replacement therapy was estimated at 4.9 - 9 million people. In Kazakhstan in 2010 also was noted the low provision of renal replacement therapy - 39 per 1 million population. By 2030, the number of people receiving renal replacement therapy around the world is projected to increase to 5.4 million people.

Still remain outstanding issues to create the conditions for slowing the progression of chronic kidney disease. This is due to insufficient knowledge of the mechanisms of CKD development and progression.

Current direction of research of chronic kidney disease formation and progradiently development mechanisms is to study the physical and chemical properties of erythrocyte membranes. The most promising is the study of membrane proteins and their role in the change of erythrocytes in patients with chronic renal pathologies.

The purpose of the research

Evaluate the role of changes in physical and chemical properties of erythrocytes membranes in progression of chronic kidney disease

The objectives of the research

1. To study the resistance of erythrocytes in hypo-osmotic and ammonia medium in patients with chronic kidney disease at different stages of its development.
2. To study the sorption properties of erythrocytes in patients with chronic kidney disease at different stages of its development.
3. To study the indices of oxidative stress in erythrocytes in patients with chronic kidney disease at different stages of its development.
4. To study the charge balance of erythrocytes in patients with chronic kidney disease at different stages of its development.
5. To develop the concept of the role of disturbance of physical and chemical parameters of erythrocytes in the progression of chronic kidney disease

Scientific novelty

For the first time the phenomenon of increasing the survival time of erythrocytes in ammonium medium in patients with chronic kidney disease was recorded.

For the first time the increase of the adsorption of extracellular nucleic acid fragments on erythrocytes of patients with chronic kidney disease was observed. On the erythrocytes of

patients with chronic glomerulonephritis prevailed the adsorption of RNA hydrolysates, on the erythrocytes of patients with chronic pyelonephritis RNA and DNA hydrolysates were adsorbed to an equal degree.

For the first time the increase of the content of membrane-bound hemoglobin in patients with chronic kidney disease was found and it had an inverse relationship with the stage of CKD.

For the first time the original device "The registrar of the electrical conductivity of biological fluids" in a single package with the software versatile meter-regulator TRM151 was designed.

For the first time the individual types of the thermograms of pH changes of erythrocytes in patients with chronic kidney disease were obtained.

For the first time the changes of structural and functional properties of erythrocytes in patients with chronic kidney disease patients were explained from the standpoint of changes in the activity of the membrane transport proteins.

For the first time the hypothesis about the role of changes in the physical and chemical properties of erythrocytes in the progression of chronic kidney disease was introduced.

The theoretical novelty and practical significance

The obtained data allow to expand and enhance the fundamental concepts of molecular and pathogenic mechanisms of the development and progression of chronic kidney disease. It enables to use in further the determination of physical and chemical properties of erythrocyte membranes as a prognostic criterion of CKD progression.

Implementation of results in practice

On thesis materials received: 1 innovative patent, 4 certificates of state registration of the copyright's object and 1 certificate of state registration of intellectual property.

The results of the thesis are used in the educational process on the elective disciplines of bachelor and master programs.

The main provisions of the thesis to be defended

In patients with chronic kidney disease increase the survival time of erythrocytes in ammonium medium was registered, along with this the decrease of the osmotic resistance of erythrocytes and the appearance of pool of low resistant erythrocytes according to the hypotonic environment was observed.

In patients with chronic kidney disease low and medium weight substances and nucleic acid fragments were adsorbed on the erythrocytes membrane. The adsorption of RNA fragments on the erythrocytes of patients with chronic glomerulonephritis prevailed on the adsorption of DNA fragments.

In patients with chronic kidney disease the amount of membrane-bound hemoglobin raised sharply in the early stages of the disease. With the progression of CKD number of membrane-bound hemoglobin in erythrocytes is reduced, but did not reach the control.

The individual types of the thermograms of pH changes of erythrocytes in the conditions of thermoinduction have been registered in patients with chronic kidney disease.

Link of thesis with other research projects

Thesis was performed at the Department of Biological chemistry in the framework of a research project funded by MES RK "Molecular and cellular mechanisms of the development of chronic renal failure" (2013-2015), SRN0113PK00410.

Approbation of the work

The main provisions and the results of the work were presented at: International conference of young scientists "The world of science and youth: tradition and innovation", Karaganda, 19 February, 2014; 22nd International Congress of Clinical Chemistry and

Laboratory Medicine, Istanbul, 22 – 26 June, 2014; International Congress of The Federation of European Biochemical Societies “FEBS EMBO 2014”, Paris, 30 August – 4 September, 2014; International Conference of The Society for Free Radical Research Europe «Free Radicals: Insights in signaling and adaptive homeostasis», Paris, 5 - 7 September, 2014; International conference of young scientists “The world of science and youth: achievements and perspectives”, Karaganda, 26 February, 2015; Students and Young Scientists’ III International Scientific Conference, Tbilisi, 22 May, 2015, International Congress of The Federation of European Biochemical Societies FEBS 2015 «The Biochemical Basis of Life», Berlin, 4 - 9 July, 2015; VI All-Russian with international participation school-conference of the circulatory physiology, Moscow, 2 - 5 February, 2016.

Approval was held at the enlarged meeting of the Department of Biological chemistry of KSMU, report № 12 dated 17 June 2016.

Publication

On the thesis materials were published 27 publications, including 1 monograph, approved by the Department of Science and Human Resources of Department of Health and Social Development of the Republic of Kazakhstan. In editions recommended by the Committee for Control of Education and Science, published 9 papers, in journals, which have Thomson Reuters Impact Factor and included in the Scopus database, published 7 publications, including 1 article and 6 theses.

Materials and methods

During the study 195 people were surveyed. The control group consisted of 33 healthy individuals. 162 patients with CKD were divided into 11 groups based on the etiological nosology (chronic pyelonephritis and chronic glomerulonephritis) and the stage of CKD.

Research methods: the study of the ammonium and osmotic resistance of erythrocytes; estimating the number of adsorbed on the erythrocyte’s membrane medium weight molecular and DNA and RNA fragments; determining the ability of erythrocyte’s membrane binding methylene blue; determining the concentration of malondialdehyde, carbonyl derivatives of proteins and membrane-associated hemoglobin in erythrocytes; the study of the charge balance of erythrocytes in the conditions of thermoinduction.

Conclusions

1. In patients with chronic kidney disease the osmotic resistance of erythrocytes was reduced, the pool of low resistant and middle resistant erythrocytes was increased. In the group of patients with chronic pyelonephritis the smallest osmotic resistance of erythrocytes was observed in the later stages of CKD development. In patients with chronic glomerulonephritis the smallest osmotic resistance of erythrocytes was observed in the early stages of CKD development.

2. In patients with chronic kidney disease erythrocytes were more stability in ammonium medium compared with the control. In patients with chronic pyelonephritis and in patients with chronic glomerulonephritis the longest time of the survival of erythrocytes in ammonium medium was observed in the groups of patients with the stage 4 of CKD.

3. On the erythrocyte’s membranes in patients with chronic kidney disease compared with control greater number of medium weight substances and the fragment of extracellular and nucleic acids were sorbed. With the progression of CKD increases the amount of the sorbed metabolites. The adsorption of RNA fragments on erythrocytes in patients with chronic glomerulonephritis prevails over the adsorption of DNA fragments.

4. In patients with chronic kidney disease in erythrocytes increased level of membrane-bound hemoglobin - the main indicator of remote oxidative stress products. The maximum of the membrane-bound hemoglobin in patients with chronic pyelonephritis and in

patients with chronic glomerulonephritis observed in the groups of patients with the stage 2 of CKD.

5. In patients with chronic kidney disease in comparison with healthy persons the change in the charge balance of erythrocytes was observed. In patients with chronic kidney disease have been reported individual types of erythrocyte thermograms.

6. On the one hand the change of structural and functional properties of the erythrocyte's membrane increases with the progression of chronic kidney disease and on the other hand its self leads to a worsening of the course of chronic kidney disease.