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საქართველოს სამედიცინო სიახლენი

რეზიუმე

სითბური ტკივილის ზღურბლის ხარისხის და რეცეპტორული ცილა *TRPV1*-ის კონცენტრაციის კორელაცია ოვარიულ-მენსტრუალური ციკლის სხვადასხვა ფაზაში

მ. აფხაზავა, ი. კვაჭაძე, მ. ცაგარელი

თბილისის სახელმწიფო სამედიცინო უნივერსიტეტი, ფიზიოლოგიის დეპარტამენტი, საქართველო

ჯანმრთელი ქალის ორგანიზმში ოვარიულ-მენსტრუალური ციკლის (ომც) სხვადასხვა ფაზაში ტკივილის ზღურბლის ცვლილების ხარისხის დინამიკის შესახებ ბოლო ათწლეულის განმავლობაში გამოქვეყნებული ბევრი კვლევის შედეგების მიუხედავად, ამ ცვლილებების განმსაზღვრელი მექანიზმები დღემდე არაა ბოლომდე ახსნილი.

წარმოდგენილი კვლევის მიზანს შეადგენდა სითბური ტკივილის ზღურბლის ხარისხის და რეცეპტორული ცილა *TRPV1*-ის *(Transient receptor potential cation channel subfamily V member1)* კონცენტრაციის დინამიკის კორელაციის,ასევე,ქალების აგრესიულობის ხარისხის შეფასება ომც-ის ფოლიკულურ და ლუთეინურ ფაზებში.

დადგენილია რეცეპტორული ცილა *TRPV1*-ის მაჩვენებლის ზრდა და სითბური ტკივილის ზღურბლის ხარისხის შემცირება ლუთეინურ ფაზაში. დადგენილია ამავე ფაზაში პროგესტერონის დონის კორელაცია ცილა *TRPV1*-ის მაჩვენებლის ზრდასთან და სითბური ტკივილის ზღურბლის ხარისხის შემცირებასთან. დამოკიდებულება ტკივილის ზღურბლის ხარისხს,*TRPV1*-ის კონცენტრაციას, ფოლიკულმასტიმულირებელი, მალუთეინიზებელი ჰორმონების და პროლაქტინის კონცენტრაციას შორის არ გამოვლინდა; ასევე, არ დადგინდა *TRPV1*-ის დონისა და სითბური ტკივილის ზღურბლის ხარისხის კორელაცია აგრესიულობის ხარისხის მაჩვენებელთან.

THE MORPHOLOGICAL PICTURE OF LOCAL IMMUNE RESPONSES IN THE KIDNEYS, URETERS AND BLADDER OF THE FOETUSES AND NEWBORNS, WHO DEVELOPED IN CONDITIONS OF MATERNAL PREECLAMPSIA

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The immune system, together with the nervous and endocфrine ones, ensures the internal homeostasis of human. Besides identification and neutralization of genetically foreign substances the immune system also maintains control over proliferation and differentiation of cells in human tissues and organs as well as ensures processes of regeneration and detoxification [2]. The formation of the human immune system takes place mostly during the period of prenatal ontogenesis; in this connection, peculiarities in the course and complications of pregnancy in the mother produce a tremendous effect on the condition of the foetus and newborn [4].

Preeclampsia is one of the most severe complications of pregnancy. According to data of the World Health Organization, preeclampsia is observed in 2-5 % of pregnant women of Europe, but in developing countries the number of this complication increases up to 10-18 % [22]. Preeclampsia is one of the key factors of maternal and perinatal morbidity and mortality [17].

Scientific literature has information about the effect of maternal preeclampsia on the central and some peripheral organs of the immune system of foetuses and newborns [19], but there are no data about morphological characteristics of local immune responses in the urinary system organs of foetuses and newborns from the mothers, whose pregnancy was complicated with preeclampsia.

The purpose of the study was to reveal the morphological peculiarities of local immune responses in the kidneys, ureters and bladder of the foetuses and newborns, who developed in conditions of maternal preeclampsia with different degrees of its severity.

Material and methods. The material of the study was the tissue of the kidneys, ureters and bladder of mature foetuses and newborns from mothers with physiological pregnancy and those ones, whose pregnancy was complicated by preeclampsia of different degrees of severity. The above tissues were taken in the course of autopsies on the basis of the Public Health Protection Institution «Kharkiv City Perinatal Centre». Four groups were formed in this study: group I – foetuses (n=13) and newborns (n=15) from mothers with physiological pregnancy; group II – foetuses (n=12) and newborns (n=13) from mothers, whose pregnancy was complicated with a mild degree of preeclampsia; group III – foetuses (n=13) and newborns (n=14) from mothers, whose pregnancy was complicated with a moderately severe degree of preeclampsia; group IV – foetuses (n=13) and newborns (n=13) from mothers, whose pregnancy was complicated with severe preeclampsia.

During each case of autopsy, one tissue fragment was dissected out from each kidney and ureter as well as one tissue fragment from the bladder. The taken material was fixed in 10% formalin solution. Consolidation of the tissues, fixed in formalin, was achieved by processing through alcohols with an increasing concentration, celloidin and chloroform followed by embedding with paraffin. Serial sections, $4\text{-}5\times10^{-6}$ m thick, were made from the prepared blocks for subsequent staining. The resultant microspecimens, stained with haematoxylin and eosin, were studied using microscope«Olympus BX-41».

The peroxidase reaction with monoclonal antibodies to CD4 (the marker of helper T lymphocytes), CD8 (the marker of suppressor T lymphocytes), CD20 (the marker of B lymphocytes) and CD68 (the marker of macrophages) was carried out in the urinary system organs of foetuses and newborns for phenotyping immune cells. In order to identify the general population of T lymphocytes, we conducted immunohistochemical studies with the indirect Coombs test according to M. Brosman's technique (1979) using monoclonal antibodies to CD3 [3]. The absolute count of the cells, which expressed the above receptors, was revealed in each microspecimen in 5 randomly chosen microscope fields of view with magnification ×1000.

The immunoregulatory index was calculated as the ratio of the absolute count of CD4 cells to the absolute count of CD8 cells.

The nonparametric Mann-Whitney U test was used for statistical assessment of the obtained values. The significance of differences between the indices was accepted under the significance level of $p<0.05$. Statistical calculations were made using Statistic Soft 6.0 program.

Results and their discussion. Our examination of haematoxylin and eosin-stained microspecimens of renal tissue from foetuses and newborns of group I revealed few immune cells in capillary loops of glomeruli as well as a scanty and irregularly located infiltration with immune cells in the stroma of the renal cortex and medulla in the periglomerular, intertubular, peritubular and perivascular regions. The above immune cells, which we observed in the kidneys of foetuses and newborns from mothers with physiological pregnancy, participated in provision of local immune homeostasis and corresponded to the age norm [20].

The kidneys of foetuses and newborns from groups II-IV also revealed an infiltration with immune cells, it being more marked versus group I and having the similar localization. It should be noted that in the kidneys (Fig. 1) of foetuses and newborns from groups II-IV the above infiltration with immune cells was more marked in foci of sclerosis in the interstitium, around glomerular and tubular cysts, immature glomeruli and tubules as well as glomeruli with fibroplastic changes.

The infiltration with immune cells in the ureters and bladder of foetuses and newborns from groups II-IV was more marked versus group I too. In groups I-IV in the epithelial layer between epitheliocytes of the foetuses and newborns ureters and bladder immune cells were found; in the lamina propria and submucosa it was revealed some places of a focal infiltration with immune cells and some places of the diffuse one, but the latter infiltration prevailed.

If in foetuses and newborns from group I the focal character of an infiltration with immune cells in the lamina propria and submucosa was more marked in the bladder versus the ureter, no such feature was found in groups II-IV. All the groups also revealed an infiltration with immune cells in the muscular and adventitial layers of the ureters and bladder, which localized mostly around vessels.

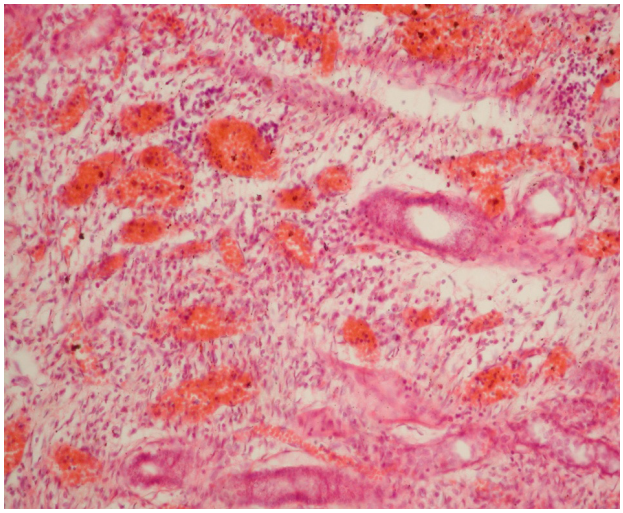

Fig. 1. Group IV. Infiltration with immune cells in the foetus kidney. Haematoxylin and eosin, ×200

Our analysis of the expression of an infiltration with immune cells in the ureter and bladder of foetuses and newborns revealed that in group I the above infiltration was more marked in the mucous and submucous layers, while in groups II-IV this infiltration with immune cells was marked in all layers.

Immunohistochemistry of the renal, ureteri and bladder tissues of foetuses and newborns of all groups found out that the infiltration with immune cells, which we revealed, included Tlymphocytes (Fig.2), containing T helpers and T suppressors (Fig.3), B lymphocytes and macrophages (Fig.4).

The immune system of the foetus and newborn is known to be the most vulnerable to the effect of various unfavorable factors of the environment that is more manifested in peculiarities of development and course of diseases including those of the urinary system organs [8]. Previous clinical examinations demonstrated disturbances in immunological blood values of newborns from the mothers, whose pregnancy was complicated with preeclampsia [7].

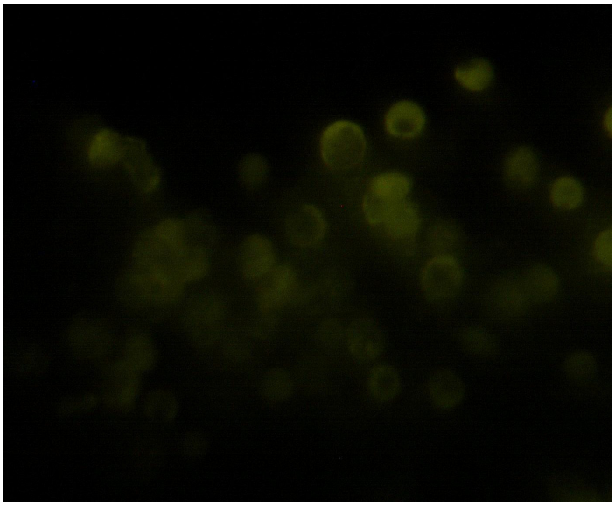

Fig. 2. Group III. A group of CD3 positive cells in the bladder of a newborn. The indirect Coombs reaction with monoclonal antibodies to CD3, ×600

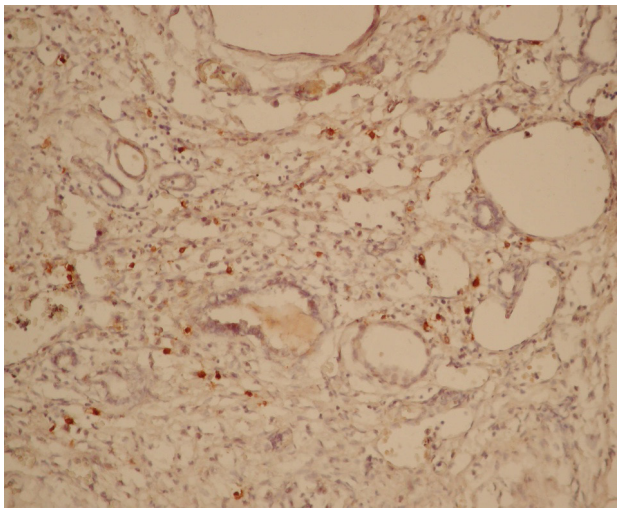

Fig. 3. Group IV. CD8 positive cells in a newborn's kidney. The peroxidase reaction with monoclonal antibodies to CD8, ×200

Mild maternal preeclampsia in the kidneys, ureters and bladder of foetuses and newborns activates the macrophage system, T cell and B cell immunity, as it was shown by a significant ($p<0.05$) increase in the mean count of macrophages, T lymphocytes and B lymphocytes versus group I (Tables 1-3). Our analysis of the subpopulation of T lymphocytes in group II revealed prevalence of the fraction of suppressor-induced lymphocytes over T helpers, while group I demonstrated prevalence of the helper potential over the suppressor one. Besides we revealed a significant ($p<0.05$) decrease of the count of T helpers and an increase of the count of Tsuppressors in group II versus group I with a resultant significant ($p<0.05$) decrease of the immunoregulatory index.

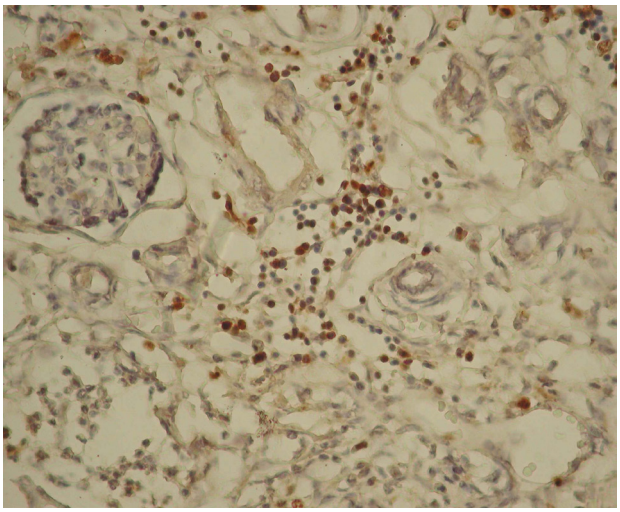

Fig. 4. Group III. CD68 positive cells in a newborn's kidney. The peroxidase reaction with monoclonal antibodies to CD68, ×400

The immunological theory is one of the basic theories of the development of preeclampsia [22]. The activation of the macrophage system, T cell and B cell immunity, revealed by us in the kidnes, ureters and bladder of foetuses and newborns, is likely to be a response to the antigenic stimulation, caused by maternal preeclampsia. Subpopulation changes among T lymphocytes characterized by an increased count of T suppressors, which inhibit an activation of T helpers, B lymphocytes and plasmocytes [1], and a decreased count of T helpers, whose main function consists in identification of foreign antigens represented by macrophages, as well as secretion of interleukins, which stimulate differentiation of B lymphocytes and formation of plasmocytes on them followed by production of immunoglobulins [1], are, from our point of view, the compensatory response.

In cases of moderately severe and severe maternal preeclampsia in the kidneys, ureters and bladder of foetuses and newborns it was revealed a significant ($p<0.05$) increase of the absolute count of CD3, CD20 and CD68 positive cells versus group I (Tables 1-3). Our analysis of the absolute number of subpopulations of T lymphocytes in groups III and IV demonstrated prevalence of the helper potential over the suppressor one, we considering this fact as evidence of the stage of decompensation, as well as a significant ($p<0.05$) increase of the absolute count of CD4 and CD8 positive cells versus group I. In foetuses and newborns from group III versus group I, the immunoregulatory index in the kidneys significantly ($p<0.05$) increased, but in the ureters and bladder had a tendency ($p>0.05$) to increase. In the kidneys, ureters and bladder of foetuses and newborns from group IV the immunoregulatory index significantly ($p<0.05$) increased versus group I.

Table 1. The mean values of the absolute count of immune cells and immunoregulatory index in the kidneys of foetuses and newborns

Group No.	Foetus/Newborn	The mean values of the absolute count of immune cells					Immunoregulatory index
		CD3	CD4	CD8	CD20	CD68	
I	Foetus	10.52±0.27	5.06±0.15	2.68±0.09	3.15±0.15	5.20±0.19	1.99±0.08
	Newborn	13.88±0.26 p_1<0.05	7.56±0.16 p_1<0.05	3.41±0.10 p_1<0.05	4.99±0.16 p_1<0.05	6.77±0.20 p_1<0.05	2.30±0.08 p_1<0.05
II	Foetus	12.63±0.31 p_2<0.05	3.82±0.13 p_2<0.05	6.12±0.15 p_2<0.05	5.63±0.19 p_2<0.05	7.85±0.21 p_2<0.05	0.63±0.02 p_2<0.05
	Newborn	15.65±0.20 p_1<0.05 p_2<0.05	5.14±0.20 p_1<0.05 p_2<0.05	7.46±0.18 p_1<0.05 p_2<0.05	8.32±0.24 p_1<0.05 p_2<0.05	10.63±0.25 p_1<0.05 p_2<0.05	0.74±0.05 p_1>0.05 p_2<0.05
III	Foetus	15.93±0.28 p_2<0.05 p_3<0.05	7.46±0.14 p_2<0.05 p_3<0.05	3.35±0.13 p_2<0.05 p_3<0.05	7.58±0.18 p_2<0.05 p_3<0.05	8.89±0.24 p_2<0.05 p_3<0.05	2.47±0.12 p_2<0.05 p_3<0.05
	Newborn	17.91±0.20 p_1<0.05 p_2<0.05 p_3<0.05	10.83±0.20 p_1<0.05 p_2<0.05 p_3<0.05	4.36±0.13 p_1<0.05 p_2<0.05 p_3<0.05	10.07±0.18 p_1<0.05 p_2<0.05 p_3<0.05	11.67±0.23 p_1<0.05 p_2<0.05 p_3<0.05	2.68±0.12 p_1>0.05 p_2<0.05 p_3<0.05
IV	Foetus	18.12±0.35 p_2<0.05 p_4<0.05	11.05±0.22 p_2<0.05 p_4<0.05	4.71±0.18 p_2<0.05 p_4<0.05	10.51±0.22 p_2<0.05 p_4<0.05	13.03±0.31 p_2<0.05 p_4<0.05	2.69±0.16 p_2<0.05 p_4>0.05
	Newborn	20.25±0.22 p_1<0.05 p_2<0.05 p_4<0.05	13.92±0.21 p_1<0.05 p_2<0.05 p_4<0.05	5.25±0.25 p_1>0.05 p_2<0.05 p_4<0.05	13.36±0.28 p_1<0.05 p_2<0.05 p_4<0.05	15.46±0.27 p_1<0.05 p_2<0.05 p_4<0.05	3.40±0.29 p_1>0.05 p_2<0.05 p_4>0.05

p_1 – versus the foetal value; p_2 – versus the value from group I; p_3 – versus the value from group II; p_4 – versus the value from group III

Table 2. The mean values of the absolute count of immune cells and immunoregulatory index in the ureters of foetuses and newborns

Group No.	Foetus/Newborn	The mean values of the absolute count of immune cells					Immunoregulatory index
		CD3	CD4	CD8	CD20	CD68	
I	Foetus	9.08±0.15 p_2<0.05	4.77±0.11 p_2>0.05	2.42±0.07 p_2>0.05	2.60±0.13 p_2<0.05	4.28±0.18 p_2<0.05	2.08±0.08 p_2>0.05
	Newborn	12.88±0.20 p_1<0.05 p_2<0.05	6.40±0.12 p_1<0.05 p_2<0.05	2.88±0.08 p_1<0.05 p_2<0.05	3.89±0.18 p_1<0.05 p_2<0.05	5.33±0.20 p_1<0.05 p_2<0.05	2.37±0.09 p_1>0.05 p_2>0.05
II	Foetus	11.20±0.20 p_2<0.05 p_3<0.05	2,35±0,12 p_2<0,05 p_3<0,05	5.02±0.13 p_2<0.05 p_3<0.05	4.73±0.16 p_2<0.05 p_3<0.05	6.33±0.18 p_2<0.05 p_3<0.05	0.48±0.03 p_2<0.05 p_3<0.05
	Newborn	14.17±0.24 p_1<0.05 p_2<0.05 p_3<0.05	3.83±0.14 p_1<0.05 p_2<0.05 p_3<0.05	6.58±0.13 p_1<0.05 p_2<0.05 p_3<0.05	7.25±0.17 p_1<0.05 p_2<0.05 p_3<0.05	9.06±0.18 p_1<0.05 p_2<0.05 p_3<0.05	0.59±0.02 p_1<0.05 p_2<0.05 p_3<0.05

III	Foetus	14.12±0.18 p_2<0.05 p_3<0.05 p_4<0.05	6.02±0.15 p_2<0.05 p_3<0.05 p_4<0.05	2.88±0.10 p_2<0.05 p_3<0.05 p_4<0.05	5.91±0.18 p_2<0.05 p_3<0.05 p_4<0.05	7.68±0.16 p_2<0.05 p_3<0.05 p_4<0.05	2.26±0.10 p_2>0.05 p_3>0.05 p_4<0.05
	Newborn	16.21±0.19 p_1<0.05 p_2<0.05 p_3<0.05 p_4<0.05	9.19±0.21 p_1<0.05 p_2<0.05 p_3<0.05 p_4<0.05	3,86±0.14 p_1<0.05 p_2<0.05 p_3<0.05 p_4<0.05	8.96±0.21 p_1<0.05 p_2<0.05 p_3<0.05 p_4<0.05	10.10±0.25 p_1<0.05 p_2<0.05 p_3<0.05 p_4<0.05	2.57±0.10 p_1<0.05 p_2>0.05 p_3>0.05 p_4<0.05
IV	Foetus	16.66±0.22 p_2<0.05 p_3<0.05 p_5<0.05	9.11±0.16 p_2<0.05 p_3<0.05 p_5<0.05	3.85±0.10 p_2<0.05 p_3<0.05 p_5<0.05	8.69±0.20 p_2<0.05 p_3<0.05 p_5<0.05	11.35±0.25 p_2<0.05 p_3<0.05 p_5<0.05	2.44±0.06 p_2>0.05 p_3<0.05 p_5<0.05
	Newborn	18.95±0.22 p_1<0.05 p_2<0.05 p_3<0.05 p_5<0.05	11.66±0.17 p_1<0.05 p_2<0.05 p_3<0.05 p_5<0.05	4.28±0.12 p_1<0.05 p_2<0.05 p_3<0.05 p_5<0.05	11.26±0.21 p_1<0.05 p_2<0.05 p_3<0.05 p_5<0.05	13.95±0.24 p_1<0.05 p_2<0.05 p_3<0.05 p_5<0.05	2.89±0.11 p_1<0.05 p_2>0.05 p_3<0.05 p_5<0.05

p_1 – versus the foetal value; p_2 – versus the corresponding value of the kidney;
p_3 – versus the value from group I; p_4 – versus the value from group II; p_5 – versus the value from group III

Table 3. The mean values of the absolute count of immune cells and immunoregulatory index in the bladder of foetuses and newborns

Group No.	Foetus/Newborn	The mean values of the absolute count of immune cells					Immunoregulatory index
		CD3	CD4	CD8	CD20	CD68	
I	Foetus	9.40±0.16 p_2<0.05 p_3>0.05	4.82±0.15 p_2>0.05 p_3>0.05	2.54±0.08 p_2>0.05 p_3>0.05	2.42±0.14 p_2<0.05 p_3>0.05	4.18±0.16 p_2<0.05 p_3>0.05	1.99±0.07 p_2>0.05 p_3>0.05
	Newborn	12.63±0.25 p_1<0.05 p_2<0.05 p_3>0.05	6.49±0.15 p_1<0.05 p_2<0.05 p_3>0.05	2.93±0.10 p_1<0.05 p_2<0.05 p_3>0.05	3.96±0.13 p_1<0.05 p_2<0.05 p_3>0.05	5.48±0.16 p_1<0.05 p_2<0.05 p_3>0.05	2.36±0.10 p_1<0.05 p_2>0.05 p_3>0.05
II	Foetus	11.38±0.20 p_2<0.05 p_3>0.05 p_4<0.05	2.65±0.20 p_2<0.05 p_3>0.05 p_4<0.05	5.32±0.17 p_2<0.05 p_3>0.05 p_4<0.05	4.95±0.16 p_2<0.05 p_3>0.05 p_4<0.05	6.07±0.17 p_2<0.05 p_3>0.05 p_4<0.05	0.54±0.03 p_2>0.05 p_3>0.05 p_4<0.05
	Newborn	14.03±0.26 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05	3.82±0.11 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05	6.29±0.14 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05	7.45±0.15 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05	9.55±0.20 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05	0.66±0.02 p_1<0.05 p_2>0.05 p_3>0.05 p_4<0.05
III	Foetus	13.97±0.25 p_2<0.05 p_3>0.05 p_4<0.05 p_5<0.05	6.20±0.19 p_2<0.05 p_3>0.05 p_4<0.05 p_5<0.05	2.98±0.10 p_2>0.05 p_3>0.05 p_4<0.05 p_5<0.05	6.03±0.19 p_2<0.05 p_3>0.05 p_4<0.05 p_5<0.05	7.26±0.22 p_2<0.05 p_3>0.05 p_4<0.05 p_5<0.05	2.23±0.10 p_2>0.05 p_3>0.05 p_4>0.05 p_5<0.05
	Newborn	16.69±0.21 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_5<0.05	9.04±0.19 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_5<0.05	3.89±0.12 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_5<0.05	8.70±0.19 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_5<0.05	10.24±0.29 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_5>0.05	2.53±0.12 p_1>0.05 p_2>0.05 p_3>0.05 p_4>0.05 p_5<0.05

IV	Foetus	16.80±0.23 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	9,03±0.16 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	3.86±0.12 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	8.54±0.18 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	11.66±0.28 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	2.49±0.09 p_2>0.05 p_3>0.05 p_4<0.05 p_6<0.05
	Newborn	18.72±0.20 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	11.75±0.16 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	4.20±0.11 p_1>0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_6>0.05	11.69±0.26 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	14.06±0.23 p_1<0.05 p_2<0.05 p_3>0.05 p_4<0.05 p_6<0.05	2.94±0.10 p_1<0.05 p_2>0.05 p_3>0.05 p_4<0.05 p_6<0.05

p_1 – versus the foetal value; p_2 – versus the value of the kidney; p_3 – versus the value in the ureter; p_4 – versus the value from group I; p_5 – versus the value from group II; p_6 – versus the value from group III

Our comparative analysis of the absolute count of basic clones of immune cells and the immunoregulatory index in groups II-IV (Tables 1-3) revealed an increase of the immune cell infiltration in the kidneys, ureters and bladder of foetuses and newborns depending upon an aggravation of maternal preeclampsia. Thus, in group III versus group II the absolute count of CD3, CD8, CD20 and CD68 cells and the immunoregulatory index in foetuses and newborns in the majority of cases significantly ($p<0.05$) increased (except for the absolute count of CD68 cells in the bladder of newborns that tended ($p>0.05$) to increase), the absolute count of CD4 cells significantly ($p<0.05$) decreased. In group IV versus group III: in the kidneys of foetuses and newborns it was revealed a significant ($p<0.05$) increase of the absolute count of CD3, CD4, CD8, CD20 and CD68 cells, the immunoregulatory index having a tendency ($p>0.05$) to increase; in the ureters of foetuses and newborns it was demonstrated a significant ($p<0.05$) increase of the absolute count of CD3, CD4, CD8, CD20 and CD68 cells and the immunoregulatory index; in the bladder of foetuses and newborns it was revealed a significant ($p<0.05$) increase of the absolute count of CD3, CD4, CD20 and CD68 cells and the immunoregulatory index, the absolute count of CD8 cells significantly ($p<0.05$) increasing in foetuses and tending ($p>0.05$) to increase in newborns.

In newborns versus foetuses from groups I-IV, the absolute count of CD3, CD4, CD8, CD20 and CD68 cells in the kidneys was in the majority of cases significantly ($p<0.05$) larger (except for the absolute count of CD8 cells in group IV, which tended ($p>0.05$) to increase), while the immunoregulatory index was significantly ($p<0.05$) larger in group I and had a tendency ($p>0.05$) to increase in groups II-IV; the absolute count of CD3, CD4, CD8, CD20 and CD68 cells in the ureters was significantly ($p<0.05$) larger, while the immunoregulatory index in group I tended ($p>0.05$) to increase and was significantly ($p<0.05$) larger in groups II-IV; the absolute count of CD3, CD4, CD8, CD20 and CD68 cells in the bladder was in the majority of cases significantly ($p<0.05$) larger (except for the absolute count of CD8 cells in group IV, which tended ($p>0.05$) to increase), while the immunoregulatory index in group III tended ($p>0.05$) to increase and was significantly ($p<0.05$) larger in groups I, II and IV. The age-dependent, i.e. from the foetus to the newborn, quantitative increment of immune cells in the urinary system organs that we revealed in group I demonstrates the functional activity growth of the immune system [21]. But in groups II-IV the above quantitative increment of immune cells in the urinary system organs is caused, from our viewpoint, by the effect of maternal preeclampsia rather than by age-specific peculiarities only, as it is known that the earlier the foetus is affected by a pathogenic factor the more marked are disorders in the morphofunctional state of different organs and systems in the newborn [5].

When we analysed the count of basic clones of immune cells and the immunoregulatory index in the urinary system organs of foetuses and newborns from groups I-IV, in the majority of cases in their kidneys it was revealed significantly ($p<0.05$) larger values of the absolute count of CD3, CD4, CD8, CD20 and CD68 cells (except for the absolute count of CD4 and CD8 cells in the ureters and bladder of foetuses from group I and the absolute count of CD8 cells in the bladder of foetuses from group III, which had a tendency ($p>0.05$) to lowering) versus the ureters and bladder. The immunoregulatory index in the kidneys of foetuses and newborns from groups I-IV in the majority of cases did not significantly ($p>0.05$)differ versus the corresponding index in the ureters and bladder, but in group II the above value in the ureters of foetuses and newborns was significantly ($p<0.05$) less. The absolute count of basic clones of immune cells and the immunoregulatory index in the ureters versus the bladder in foetuses and newborns from groups I-IV did not differ significantly ($p>0.05$). A more marked infiltration with immune cells in the kidneys versus the ureters and bladder in both foetuses and newborns from groups I-IV shows that this organ is more functionally active versus other organs of the urinary system [10].

Our study has demonstrated that local immune responses in the kidneys, ureters and bladder of foetuses and newborns from the mothers, whose pregnancy was complicated with preeclampsia, pass with some abnormal deviations and are characterized by an extreme activation of the macrophage system, T cell and B cell immunity. Notably, the failures of local immune responses in the kidneys, ureters and bladder that we revealed increase from the foetus to the newborn and with an aggravation of maternal

preeclampsia, thereby affecting the morphofunctional state of the urinary system organs in such children.

The participation of immune cells in the development of pathology of the urinary system organs in children does not cause any doubts. For example, at present macrophages are attributed to not only functions of destruction of defected damaged cells, but also their participation in the development of a pathological process [6,16].

Studies on experimental animals have shown that a selective removal of cells of the macrophage line decreases the degree of damage of the renal parenchyma and intensity of the fibrotic process, whereas a transfusion of macrophages, on the contrary, potentiates phenomena of alteration in the kidneys [9].

Macrophages take an active part in the mechanisms of development of glomerulonephritis. The tubulointerstitial accumulation of macrophages has been proved to correlate with the degree of renal dysfunction and be the prognosis for progression of the disease[11].

Macrophages have such an important property as phenotypical plasticity, i.e. they are able to change their phenotype depending upon the character of their microenvironment. For example, at early stages of an inflammation macrophages acquire M 1 phenotype, which is characterized by production of such inflammation mediators as active forms of oxygen, tumour necrosis factor α, interferon γ, interleukin 1β, interleukin 6, interleukin12, interleukin 18, interleukin 23, nitrogen monoxide and matrix metalloproteinase 12 that facilitate secondary alteration of the renal tissue. With the progression of a pathological process and development of fibrosis a gradual transformation of M 1 phenotype into M 2 phenotype is observed. M 2 macrophages produce transforming growth factor β1, insulin-like growth factor 1, thrombocyte growth factor, fibroblast growth factor 2 and other profibrotic cytokines. It has been proved that an accumulation of a large number of macrophages in the interstitial space causes an intrarenal haemodynamic disorder and an increased formation of angiotensin II, which produces a marked profibrotic effect. It has been also observed that macrophages themselves can transform into collagen-producing myofibroblast-like cells after a change in their microenvironment [9, 15].

Lymphoid infiltration is one of the principal mechanisms in the development of, for example, chronic glomerulonephritis, chronic renal disease and pyelonephritis. A considerable part in pathogenetic mechanisms of development of chronic glomerulonephritis is played by lymphocyte-produced interleukins, growth factors. In certain conditions interleukins take part in stimulation of proliferation of mesangial cells and development of crescents [12-14,18].

Thus, as a result of an excessive antigenic stimulation caused by maternal preeclampsia the local immune responses in the organs of the urinary system, which in physiological conditions fulfill exclusively protective functions, can become alterative and develop morphofunctional changes in the kidneys, ureters and bladder of foetuses and newborns.

Conclusions.

1. Local immune responses in the kidneys, ureters and bladder of the foetuses and newborns pass with some abnormal deviations characterized by quantitative changes of CD 3, CD 4, CD 8, CD 20 and CD 68 cells, whose degree of manifestation increases from the foetus to the newborn and with an aggravation of maternal preeclampsia.

2. The mild, moderately severe as well as severe degrees of preeclampsia result in an extreme activation of the macrophage system, T cell and B cell immunity in the kidneys, ureters and bladder of foetuses and newborns that manifests itself with an increase of the absolute count of CD3, CD20 and CD68 cells.

3. Mild preeclampsia causes an increase of the absolute count of CD8 cells and a decrease of the absolute count of CD4 cells in the kidneys, ureters and bladder of foetuses and newborns with a resultant lowering of the immunoregulatory index. The moderately severe and severe degrees of preeclampsia cause an increase of the absolute count of CD4 cells and a decrease of the absolute count of CD8 cells with a corresponding elevation of the immunoregulatory index.

4. In foetuses and newborns from mothers with physiological pregnancy as well as from mothers, whose pregnancy was complicated with preeclampsia having different degrees of severity, their kidneys are characterized by a more marked infiltration with immune cells versus their ureters and bladder.

REFERENCES

1. Гистология: Учебник /Ю.И. Афанасьев, Н.А. Юрина, Е.Ф. Котовский и др. Под ред. Ю.И. Афанасьева, Н.А. Юриной. - 5-е изд., перераб. и доп. - М.: Медицина; 2002: 744 с: ил. (Учеб. лит. для студ. мед. вузов).
2. Борисов А.Г. Клиническая характеристика нарушения функции иммунной системы // Медицинская иммунология 2013; 15(1): 45–50.
3. Brosman M. Immunofluorescence vysetrovanie formal-parafinovego material // Cs. Patol. 1979; 15(4): 215-220.
4. Chistiakova G.N. Immunological aspects in relationships between the maternal and foetal organisms in physiological and pathological pregnancy. The Herald of the Ural Medical Academic Science. – 2009. – No. 4. – P. 59-62.
5. Chistiakova G.N. Immunological peculiarities in the period of early postnatal adaptation of newborns from women with a pathological course of pregnancy. The Mother and Child in the Kuznetsk Basin. – 2005. – No. 3 (22). – P. 17-21.
6. Ivanova Ye.A. Individual peculiarities in the reaction of lymphoid formations of the jejunum of rats under a stress influence. Morphology. – 2011. – Vol. 139, No. 2. – P. 45-48.
7. Kolesnikova S.M., Levkova Ye.A. Clinical-immunological peculiarities in infants born by mothers with pathology of their gestational process. The Herald of Novosibirsk State University. Series: Biology, Clinical Medicine. – 2010. – Vol. 8, No. 2. – P. 72-77.
8. Kudin M.V., Skripkin A.V. An immunology research in children with renal diseases, who live in ecologically unfavourable regions. Medical Immunology. – 2009. – Vol. 11, No. 6. – P. 587-592.
9. Morozova O.L., Budnik I.A., Morozov D.A., Maltseva L.D., Melnikova Yu.A. Macrophages are a new target for antifibrotic

therapy in children with obstructive uropathies. Paediatrics. – 2015. – Vol. 94, No. 3. – P. 182-187.
10. Myroshnychenko M.S. Local immune responses in the kidneys, ureters and bladder of foetuses and newborns from mothers with physiological pregnancy. Problems of Continuous Medical Education and Science. – 2017. – No. 4. – P. 66-70.
11. Nikolic-Paterson D.J., Atkins R.C. The role of macrophages in glomerulonephritis. Nephrology Dialysis Transplantation 2001; 16(Suppl. 5): 3-7.
12. Nikolic-Paterson D.J. CD4 T cells: a potential player in renal fibrosis. Kidney International. 2010; 78: 333-335.
13. Pleshkova Ye.M. The role of the immune system in the development and course of infection of the urinary system in children. The Herald of Smolensk State Medical Academy 2014; 13(3): 35-40.
14. Riabova T.S., Aryev A.L. On the problem of proliferation of mesangial cells in ontogenesis // Successes of Gerontology 2010; 23(3): 349-356.
15. Sakharov V.N., Litvitsky P.F. The role of different macrophage phenotypes in the development of human diseases // The Herald of the Russian Academy of Medical Sciences 2015;– 1: 26-31.
16. Sarah C., Huen, Lloyd G. Cantley. Macrophages in renal injury and repair. Annual Review of Physiology. 2017; 79: 449-469.
17. Sidorova I.S., Unanian A.L. Comprehensive prevention of preeclampsia in a high-risk pregnancy using organic magnesium salts combined with pyridoxine // The Russian Herald of the Obstetrician-Gynaecologist. 2013; 13(4): 74-78.
18. Sokurenko S.I., Fedoseev A.N., Borisova T.V. Immunological disorders in patients with chronic renal diseases. Prospects of immunosupportive therapy. Clinical Practice. 2014; 3: 83-88.
19. Sorokina I.V., Galata D.I. Analysis of organometric data of the thymus and spleen in foetuses and newborns from mothers with preeclampsia depending upon their anthropometric features and severity of preeclampsia. Theoretical and Experimental Medicine. 2010; 2: 4-9.
20. Syrtsov V.K., Voloshin N.A., Alieva Ye.G. The peripheral organs of the immune system. Urgent Problems of the Pharmaceutical and Medical Science and Practice. – 2011. – Vol. XXIV, No. 1. – P. 8-11.
21. Titova N.D. The development of the immunity system of the foetus, newborn and infants. Immunopathology, Allergology, Infectology. – 2007. – No. 4. – P. 38-46.
22. Veropotvelian P.N., Veropotvelian N.P., Smorodskaya Ye.P. Modern approaches to the diagnosis of preeclampsia. Woman's Health. – 2013. – No. 8 (84). – P. 79-84.

SUMMARY

THE MORPHOLOGICAL PICTURE OF LOCAL IMMUNE RESPONSES IN THE KIDNEYS, URETERS AND BLADDER OF THE FOETUSES AND NEWBORNS, WHO DEVELOPED IN CONDITIONS OF MATERNAL PREECLAMPSIA

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The purpose of the research consisted in revealing morphological peculiarities of local immune responses in the kidneys, ureters and bladder of the foetuses and newborns, who developed in conditions of maternal preeclampsia with different degrees of its severity.

The research was conducted on autopsy material: the kidneys, ureters and bladders of mature foetuses and newborns. Four groups were formed in the study: group I – foetuses and newborns from mothers with physiological pregnancy; group II – foetuses and newborns from mothers, whose pregnancy was complicated with a mild degree of preeclampsia; group III – foetuses and newborns from mothers, whose pregnancy was complicated with a moderately severe degree of preeclampsia; group IV – foetuses and newborns from mothers, whose pregnancy was complicated with severe preeclampsia. An immune infiltration in the organs of the urinary system of foetuses and newborns was studied with help of histological, immunohistochemical and morphometric methods of examination.

In the course of the study it was revealed that local immune responses in the kidneys, ureters and bladder of the foetuses and newborns passed with some abnormal deviations characterized by quantitative changes of CD3, CD4, CD8, CD20 and CD68 cells, whose degree of manifestation increased from the foetus to the newborn and with an aggravation of maternal preeclampsia. Mild, moderately severe as well as severe preeclampsia resulted in an extreme activation of the macrophage system, T cell and B cell immunity in the kidneys, ureters and bladder of foetuses and newborns that manifested itself with an increase of the absolute count of CD3, CD20 and CD68 cells. Mild preeclampsia caused an increase of the absolute count of CD8 cells and a decrease of the absolute count of CD4 cells with a resultant lowering of the immunoregulatory index. Moderately severe and severe preeclampsia caused an increase of the absolute count of CD4 cells and a decrease of the absolute count of CD8 cells with a corresponding elevation of the immunoregulatory index. In foetuses and newborns from mothers with physiological pregnancy as well as from mothers, whose pregnancy was complicated with preeclampsia having different degrees of severity, their kidneys were characterized by a more marked infiltration with immune cells versus their ureters and bladder.

Thus, as a result of an excessive antigenic stimulation caused by maternal preeclampsia the local immune responses in the organs of the urinary system, which in physiological conditions fulfill exclusively protective functions, can become alterative and develop morphofunctional changes in the kidneys, ureters and bladder of foetuses and newborns.

Keywords: local immune responses, kidney, ureter, bladder, foetus, newborn, preeclampsia.

РЕЗЮМЕ

МОРФОЛОГИЧЕСКАЯ КАРТИНА МЕСТНЫХ ИММУННЫХ РЕАКЦИЙ В ПОЧКАХ, МОЧЕТОЧНИКАХ И МОЧЕВОМ ПУЗЫРЕ ПЛОДОВ И НОВОРОЖДЕННЫХ, КОТОРЫЕ РАЗВИВАЛИСЬ В УСЛОВИЯХ МАТЕРИНСКОЙ ПРЕЭКЛАМПСИИ

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Целью исследования явилось выявление морфологических особенностей местных иммунных реакций в почках, мочеточниках и мочевом пузыре плодов и новорожденных, которые развивались в условиях материнской преэклампсии различной степени тяжести.

Исследование проведено на аутопсийном материале – почках, мочеточниках и мочевом пузыре, доношенных плодов и новорожденных. Сформировано четыре группы: группа I – плоды и новорожденные от матерей с физиологической беременностью; группа II – плоды и новорожденные от матерей, беременность которых осложнилась преэклампсией легкой степени тяжести; группа III – плоды и новорожденные от матерей, беременность которых осложнилась преэклампсией средней степени тяжести; группа IV – плоды и новорожденные от матерей, беременность которых осложнилась тяжелой преэклампсией. Иммунную инфильтрацию в органах мочевыделительной системы плодов и новорожденных изучали посредством гистологических, иммуногистохимических и морфометрических методов исследования.

В ходе исследования установлено, что местные иммунные реакции в почках, мочеточниках и мочевом пузыре плодов и новорожденных протекают с определенными отклонениями от нормы, которые характеризуются количественными изменениями CD3, CD4, CD8, CD20, CD68 клеток, степень выраженности которых нарастает от плода к новорожденному и с утяжелением материнской преэклампсии. Преэклампсия легкой степени тяжести, средней степени, а также тяжелая преэклампсия приводит к чрезмерной активации макрофагальной системы, Т-клеточного и В-клеточного иммунитета в почках, мочеточниках и мочевом пузыре плодов и новорожденных, что проявляется увеличением абсолютного количества CD3, CD20, CD68 клеток.

Таким образом, местные иммунные реакции в органах мочевыделительной системы, выполняя в физиологических условиях исключительно защитные функции, в результате чрезмерной антигенной стимуляции, обусловленной материнской преэклампсией, могут принимать альтеративный характер и приводить к морфофункциональным изменениям в почках, мочеточниках и мочевом пузыре плодов и новорожденных.

რეზიუმე

ადგილობრივი იმუნური რეაქციების მორფოლოგიური სურათი დედის პრეეკლამფსიის პირობებში განვითარებული ნაყოფისა და ახალშობილების თირკმლებში, შარდსაწვეთსა და შარდის ბუშტში

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[1]ხარკოვის ეროვნული სამედიცინო უნივერსიტეტი, პათოლოგიური ანატომიის კათედრა; [2]ხარკოვის ვ. კარაზინის სახელობის ეროვნული უნივერსიტეტი, ადამიანის ანატომიის კათედრა, უკრაინა

კვლევის მიზანს შეადგენდა ადგილობრივი იმუნური რეაქციების მორფოლოგიური თავისებურებების შეფასება დედის სხვადასხვა ხარისხის სიმძიმის პრეეკლამფსიის პირობებში განვითარებული ნაყოფისა და ახალშობილის თირკმლებში, შარდსაწვეთსა და შარდის ბუშტში.

კვლევა ჩატარებულია აუტოფსიურ მასალაზე – ვადამდე მისული ნაყოფის და ახალშობილის თირკმლებზე, შარდსაწვეთებსა და შარდის ბუშტზე. გამოყოფილი იყო ოთხი ჯგუფი: I – ნაყოფები და ახალშობილები ფიზიოლოგიური ორსულობის მქონე დედებისგან,II ჯგუფი - ნაყოფები და ახალ-შობილები მსუბუქი ხარისხის პრეეკლამფსიით გართულებული ორსულობის შემდეგ, III ჯგუფი - ნაყოფები და ახალშობილები საშუალო ხარისხის პრეეკლამფსიით გართულებული ორსულობის შემდეგ, IV ჯგუფი - ნაყოფები და ახალშობილები მძიმე პრეეკლამფსიით გართულებული ორსულობის შემდეგ. საშარდე სისტემის ორგანოების იმუნური ინფილტრაცია შეისწავლებოდა კვლევის ჰისტოლოგიური,იმუნოჰისტოქიმიური და მორფომეტრიული მეთოდებით.

დადგენილია,რომ ნაყოფისა და ახალშობილის თირკმლებში, შარდსაწვეთსა და შარდის ბუშტში ადგილობრივი იმუნური რეაქციები მიმდინარეობს ნორმიდან გარკვეული გადახრით და ხასიათდება CD3, CD4, CD8, CD20, CD68 უჯრედების რაოდენობრივი ცვლილებებით, რომელთა გამოხატულობის ხარისხი მატულობს ნაყოფიდან ახალშობილამდე და დედის პრეეკლამფსიის სიმძიმის შესაბამისად. მსუბუქი,საშუალო ხარისხის და მძიმე პრეეკლამფსია ნაყოფისა და ახალშობილის თირკმლებში, შარდსაწვეთსა და შარდის ბუშტში იწვევს მაკროფაგური სისტემის, Т- და В-უჯრედოვანი იმუნიტეტის გადაჭარბებულ აქტივაციას, რაც ვლინდება CD3, CD20, CD68 უჯრედების აბსოლუტური რაოდენობის ზრდით.

ამრიგად, ფიზიოლოგიურ პირობებში საშარდე სისტემაში მხოლოდ დაცვითი ფუნქციის შემსრულებელმა ადგილობრივმა იმუნურმა რეაქციებმა დედის პრეეკლამფსიით გამოწვეული გადაჭარბებული ანტიგენური სტიმულაციის პირობებში შეიძლება მიიღოს ალტერნატიული ხასიათი და განაპირობოს მორფოფუნქციური ცვლილებები ნაყოფისა და ახალშობილის თირკმლებში, შარდსაწვეთსა და შარდის ბუშტში.

OCCUPATIONAL HAZARDS AS A RISK FACTOR OF ONSET AND UNFAVORABLE OUTCOME OF ISCHEMIC HEART DISEASE

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Worldwide annual mortality due to coronary artery disease (CAD) exceeds 7 million people, including almost 2 million Europeans. Developed countries utilizing new technologies in diagnosis and treatment are experiencing a trend towards decrease of CAD-related mortality. However, in Ukraine the mortality rate remains high. Intrahospital mortality in acute myocardial infarction (AMI) is within 4% to 6% in many countries, but as high as 11% to 14% in our country [9,14-16].

Acute myocardial infarction with ST segment elevation (STEMI) presents a particular problem. Complete coronary artery occlusion due to formation of thrombus on a destabilized atherosclerotic plaque necessitates immediate reperfusion in order to prevent irreversible damage to cardiomyocytes. If reperfusion is delayed or not performed, necrosis of a significant portion of the myocardium develops, and this is what happens to the majority of STEMI patients in Ukraine [1,9].

Loss of substantial myocardial mass impairs contractility of the left ventricle (LV), thus increasing the risk of intrahospital complications, including ventricular arrhythmias and acute heart failure (HF), which are more frequent in patients affected by occupational hazards (OH) [10,11].

It has been shown that myocardial infarction (MI) in this group is usually associated with a non-typical pattern of pain. This group is also characterized by higher incidence of early dysrhythmias, acute aneurysm, and higher mortality during the early period following the MI [11].

According to WHO, urbanized air causes 5% of deaths worldwide and is a major cause of mortality in developing countries [19].

Objective -to identify the role of occupational hazards as a risk factor of onset and unfavorable outcome of CAD.

Material and methods. Retrospective study included analysis of 307 archived case records of CAD patients. Prospective study included observation of 244 STEMI patients during their in-patient treatment. On days 1 and 19-20 the levels of pro-inflammatory molecules were measured (C-reactive protein [CRP], interleukins 6, 1β, 8 [IL-6, IL-1β, IL-8], tumor necrosis factor α [TNF-α], intercellular adhesion molecule [ICAM-1]) using RDG (USA) and Roche (Switzerland) assays and Cobas Integra 400 plus analyzer; echocardiography (EchoCG) was performed on Sonoline Versa Plus scanner, Siemens, Germany), 24 hour ECG recording with heart rate variability (HRV) analysis was performed using the Solveig HRV enabled Holter system (Kyiv), and ECG was recorded repeatedly (using the INNOMED Heart Screen device).

113 study subjects (group A, including 98 men (86.73%) and 15 women (13.27%) aged from 29 to 65, mean age 55.18±4.53) had been continuously exposed to technogenic xenobiotics as part of their OH history. 131 patients (group B, 112 men (85.50%) and 19 women (14.50%) aged from 27 to 65, mean age 54.24±6.34 years) had not been exposed to OH.

Patients were included into the main group (group A) based on the long term (at least 10 years) exposure to OH. Available data on long- and short term adverse effects of exposure to air polluted with technogenic toxins in regard to the cardiovascular risk have been considered [12, 19].

No patients in the main group had any occupational diseases as documented in the case records. OH experienced by these patients included long term exposure to petrol, diesel fuel, fuel incineration products (drivers), pesticides, mineral fertilizers (agricultural workers), paints, glues, lacquers (painters, carpenters, plasterers, shoe-makers), metals (locksmiths, turners), welding or lead-tin aerosols (welders, solderers, radio equipment assemblers), as well as xenobiotics (dioxins, polyaromatic hydrocarbons, chlorine-containing pesticides, nitrosamines, dibenzene-furanes, heavy metal compounds, etc.).

Due to the variability of professions the main group patients had been exposed to different xenobiotics. We included these patients into the same group (group A) based on the results of studies performed by the school of the Ukrainian pathologist D.D.Zerbino [2,4,5,8], which demonstrated the uniform response of the vascular wall to various xenobiotics, with inflammation as the first step, since inflammation is the universal response to injury caused by various agents.

According to this scientist, and according to his long term pathological histological studies, circulating xenobiot-