Characterization of vasoactive proteolytic systems in young children with chronic secondary pyelonephritis

Egorova I.R.[1], Kondratyeva E.I.[2], Terentyeva A.A.[2]

[1] Yakut Scientific Center of the CMP SD RAMS

[2] Siberian State Medical University

INTRODUCTION

In the pathogenesis of many diseases, including in nephropathies of various origins, vasoactive proteolytic systems of blood plasma play an important role. A special place among them belongs to the kallikrein-kinin (KKS) and renin-angiotensin (RAS) systems. KKS components among the first react to the damage and participate in the development of an inflammatory response [1-10]. Angiotensin-converting enzyme (ACE) is the main enzyme of RAS, which is a key link between the RAS and KKS. ACE is well known as an enzyme that regulates blood pressure and takes part in a number of processes in the body [1-10].

An important role in the regulation of proteolytic systems play a specific protein-inhibitors, have the property to bind proteolytic enzymes. Of particular interest are α_2-macroglobulin (α_2-MG) and α_1-proteinase inhibitor (α_1-PI), which are the main natural inhibitors of serine proteases of blood plasma. They have a high affinity for kallikrein and inhibit its, also, they are indicators of acute phase of inflammation [2, 3, 5-7, 9, 10].

PURPOSE OF THE STUDY

To study the activity of vasoactive proteolytic systems in infants with chronic secondary pyelonephritis.

MATERIALS AND METHODS

We examined 49 infants with chronic secondary pyelonephritis (33 children were examined in acute of the disease and 16 children - in remission of the disease). Control group consisted of 40 healthy children of similar age.

A survey of children performed in nephrology branch at Children's Hospital №1 (Tomsk) according to medico-economic standards (MES) study of children with nephropathies. We investigated the status of kallikrein-kinin and renin-angiotensin systems: kallikrein (KK) and kallikreinogen (KKG) activities determined by the method T.S. Pashina (1974), angiotensin-converting enzyme activity – by the method P.P. Golikov (1998), α_1-proteinase inhibitor and α_2-macroglobulin activities – by the method of V.F. Nartikova (1979).

The diagnosis of pyelonephritis was verified based on medical history and survey data in accordance with the classification proposed by M.Ya. Studenikin (1982).

Analysis of statistical data performed using the program «Statistica 6,0 for Windows». To determine the significance of differences of qualitative characteristics used analysis of contingency tables with calculation of the χ^2 Pearson's exact criterion and Fisher's exact criterion. Differences between the groups being compared were considered significant at $p<0,05$.

RESULTS AND DISCUSSION

Investigation of kallikrein-kinin system in young children with chronic secondary pyelonephritis has shown that in acute disease KK activity significantly increased in 2,2 times (p_{1-3} <0,001) and KKG activity reduced at 24% (p_{1-3} <0,001) compared with controls (table 1). In remission of chronic secondary pyelonephritis KK activity reduced and KKG activity increased, at the same time these parameters were significantly different from the parameters of the control group (p_{2-4} = 0,013 and p_{2-4} <0,001, adequately).

The study of renin-angiotensin system state showed that in children with exacerbation of chronic secondary pyelonephritis ACE activity statistically increase in 1,3 and 1,2 times compared with the control group (p_{1-3} <0,001). In achieving remission of chronic pyelonephritis ACE activity is reduced by 1,1 times, but remains higher than the parameter of healthy children (p_{2-3} <0,016) (table 1).

Investigation of parameters of kallikrein-kinin system in chronic secondary pyelonephritis depending on the type of congenital renal disease showed that during exacerbation of the disease on a background of hydronephrosis and pyeloectasia KK activity significantly increased by 1,7 times (p_{1-5} <0,001, p_{3-5} <0,001), while the activity of KKG is reduced by 23 and 25% (p_{1-5} <0,043, p_{3-5} <0,001) compared with controls (table 2). No statistically significant differences in the activities of KK and KKG in remission of the disease, depending on the type of congenital renal disease, compared with the control group was not revealed.

Received data reflect the participation of KKS in the inflammatory process pyelonephritis, in which the KKG level is reduced by the contact activation system (CAS), the latter is the trigger mechanism, which promotes the transformation of KKG in KK. KK is a plasma inflammatory mediator that participates in the regulation of intercellular interactions and increases vascular permeability. In addition, the KK induces activation of kinins (bradykinin), which have a powerful vasodilating effect on renal blood vessels leading to polyuria, that can contribute to the mechanical elimination of the pathogen from the urinary tract [9, 10].

During the period of exacerbation of chronic secondary pyelonephritis on the hydronephrosis and pyeloectasia background activity of ACE significantly increased in 1,3 times that is equivalent to the control group (p_{1-5} <0,001, p_{3-5} <0,001) (table 2). In remission of chronic secondary pyelonephritis on the pyeloectasia background activity of ACE remains significantly

high (p_{4-5} = 0,003), but on the background of hydronephrosis the activity of ACE does not differ from the control group.

The obtained data indicate that in chronic secondary pyelonephritis RAS is activated, it leads to an increase of intraglomerular pressure and transient disruption of renal glomerular filtration due to vasoconstrictor effect of ACE. Due to the activity of ACE breakdown of bradykinin catalyzed, that prevents its vasodilatory action through the activation of AT II.

Preservation of the high activity of KK and ACE during remission of chronic pyelonephritis can be regarded as an unfavorable indicator. Answer the question of how quickly and how completely indicators of KKS and RAS normalized is only possible when monitoring patients over time.

The study of activities of specific proteinase inhibitors in chronic secondary pyelonephritis showed that during exacerbation of disease α_2-macroglobulin (α_2-MG) activity was significantly reduced by 28% (p_{1-4} = 0,001), while in remission α_2-MG activity was increased and was not statistically different from the parameter of the control group (table 3).

During the period of exacerbation of chronic pyelonephritis with the hydronephrosis and pyeloectasia background α_2-macroglobulin activity significantly reduced by 44 and 28% (p_{1-5} = 0,036, p_{3-5} = 0,037). In remission of the disease activity of α_2-MG does not differ from the control group (table 4).

Activity of the α_1-proteinase inhibitor (α_1-PI) in chronic secondary pyelonephritis had no significant differences when compared with the control group, so the data not shown.

It is known that protein-inhibitors are markers of the acute phase of inflammation and their function is aimed at reducing excessive proteolysis in pathological states. So, decrease in activity α_2-MG, which is the main regulator of the kallikrein activity, causes high levels of kallikrein in blood plasma, contributes to the manifestation of its pathogenic functions in pyelonephritis in children.

CONCLUSION

Thus, in chronic secondary pyelonephritis in young children, regardless of the type of congenital anomalies of the kidney, there is activation of the KKS: KK activity increases, KKG and α_2-MG levels reduce. This reflects an imbalance between vasoactive proteolytic enzymes and their inhibitors in response to inflammation in the kidney and is the adaptive-protective. Decrease in activity α_2-MG, which is the main regulator of the kallikrein activity, causes high levels of kallikrein in blood plasma, contributes to the manifestation of its pathogenic functions in pyelonephritis.

Also, in chronic secondary pyelonephritis RAS is activated, particularly angiotensin-converting enzyme, which catalyses the breakdown of bradykinin and prevents its vasodilator action, provides vasoconstriction through activation of angiotensin II (ATII). By stimulating macrophage activation and phagocytosis, angiotensin II increases inflammation in the damaged tissue.

BIBLIOGRAPHY:

1. Altshuler B.Yu. Clinical and diagnostic significance of determination of serum angiotensin converting enzyme activity / B.Yu. Altshuler, A.P. Roitman, V.V. Dolgov / / Clin. lab. diagnosis. - 2001. - № 7. - P. 23-27.

2. Vaganova T.V. Clinical and diagnostic significance of vasoactive systems in nephropathies in children: Author. Dis. ... Candidate. med. Science / T.V. Vaganova - Tomsk, 2007. - 22 p.

3. Gorev V.V. Status of proteolytic systems of the vascular endothelium and cerebral hemodynamics in infants with hypoxic damage of CNS: Author. Dis. ... Candidate. med. Science / V.V. Gorev - Tomsk, 2008. - 24 p.

4. Eliseeva Yu.E. Angiotensin-converting enzyme, its physiological role / Yu.E. Eliseeva / / Quest. med. chemistry. - 2001. - Vol. 47, № 1. - P. 43-54.

5. Zhabin S.G. Macroglobulins of the blood plasma: structure, biological activity, the clinical use / S.G. Zhabin, A.A. Terentyev, V.S. Gorin. - Novosibirsk, 1999. – 252 p.

6. Clinical, genealogical and biochemical mechanisms of diabetic nephropathy formation in children / Kondratyeva E.I., Puzyrev V.P., Sukhanova G.A. etc. / / Problems of Endocrinology. - 2005. - Vol. 51, № 1. - P. 30-34.

7. Tkachuka V.A. Clinical Biochemistry. - Moscow: GEOTAR - MED, 2002. – 688 p.

8. Chumakova O.V., Kuznetsova A.V., Rudenskaya G.N. Activity of endogenous proteases in glomerulonephritis in children / O.V. Chumakova, A.V. Kuznetsova, G.N. Rudenskaya / / Quest. med. chemistry. - 1999. - № 5. - P. 11-18.

9. Yarovaya G.A. Kallikrein-kinin system and blood plasma proteolysis inhibitors in various nephropathies in children / G.A. Yarovaya, N.A. Korovina, M.P. Magomedova / / Quest. med. chemistry. - 1994. - № 3. - P.16-18.

10. Yarovaya G.A. Kallikrein-kinin system: new facts and concepts (review) / G.A. Yarovaya / / Quest. med. chemistry. - 2001. - № 1. - P. 5-10.

Information about the authors:

Egorova Iraida Rufovna, Candidate of Medical Science, Senior Scientist YSC CMP SD RAMS, mob. tel: 8-924-591-29-19, e-mail.ru: douce23@yandex.ru

Kondratyeva Elena Ivanovna, Doctor of Medical Sciences, Professor of pediatrics Faculty of Advanced Studies of postgraduate training of specialists SSMU

Terentyeva Alla Alexandrovna, Candidate of Medical Science, Assistant professor of pediatrics Faculty of Advanced Studies of postgraduate training of specialists SSMU

e-mail.ru: eukon@inbox.ru

Table 1

The activity of kallikrein-kinin system's indicators in children with chronic secondary pyelonephritis

Indicator		Chronic secondary PN		Control group n=40 (3)
		Period of exacerbation n=33 (1)	Period of remission n=16 (2)	
KKG (IU / ml)	M±m	224,99±9,92	250,58±16,77	298,21±7,79
	Me	235,8	258	297,04
	Q3	173,16	204	274,19
	Q1	268,37	318	340,36
	$p_{intergroup}$	0,44		
	p_{pairs}	-		
	p_{norm}	$p_{1-3}<0,001$ $p_{2-3}=0,013$		
KK (IU / ml)	M±m	126,20±7,33	97,84±5,44	75,69±4,34
	Me	127,52	93,6	66,375
	Q3	93,18	82,1	62,105
	Q1	147,05	116	78,16
	$p_{intergroup}$	0,048		
	p_{pairs}	$p_{1-2}=0,02$		
	p_{norm}	$p_{1-3}<0,001$ $p_{2-3}<0,001$		
ACE (mol / min • L)	M±m	60,20±2,16	53,13±3,04	47,04±1,51
	Me	61,68	54,2	46,17
	Q3	54,31	47,6	41,315
	Q1	69,9	59,2	51,18
	$p_{intergroup}$	0,12		
	p_{pairs}	–		
	p_{norm}	$p_{1-3}<0,001$ $p_{2-3}=0,016$		

Note: PN - pyelonephritis, p_{1-3} - reliability of differences between children with chronic secondary PN during the exacerbation and healthy, p_{2-3} - reliability of differences between children with chronic secondary PN in remission and healthy.

Table 2

Kallikreinogen (KKG) and kallikrein (KK) activities in infants with chronic secondary pyelonephritis depending on the type of congenital renal pathology

Indicator		Chronic PN on the background of hydronephrosis		Chronic PN on the background of pyeloectasia		Control group n=40 (5)
		Period of exacerbation n= 7 (1)	Period of remission n=4 (2)	Period of exacerbation n=22 (3)	Period of remission n=12 (4)	
KKG (IU / ml)	M±m	229,58±28,41	260,06±35,77	221,90±11,82	247,42±19,79	298,21±7,79
	Me	235,8	227,77	217,625	224,175	297,04
	Q3	159,99	218,18	173,16	202,355	274,19
	Q1	292,665	301,95	266,36	319,175	340,36
	p intergroup	0,001				
	p pairs	p_{1-5}=0,043 p_{3-5}<0,001				
KK (IU / ml)	M±m	131,98±14,50	101,74±14,17	128,47±8,92	96,54±5,92	75,69±4,34
	Me	127,52	92,215	131,72	93,6	66,375
	Q3	122,145	81,67	95,34	79,1	62,105
	Q1	139,085	121,81	147,05	117,8	78,16
	p intergroup	0,001				
	p pairs	p_{1-5}<0,001 p_{3-5}<0,001				
ACE (mol / min • L)	M±m	60,13±5,95	47,34±10,26	60,54±2,38	55,06±2,4	47,04±1,5
	Me	61,68	47,925	59,98	54,155	46,17
	Q3	55,21	30,005	54,31	48,33	41,315
	Q1	67,825	64,68	69,38	58,22	51,18
	p intergroup	0,001				
	p pairs	p_{1-5}<0,001, p_{3-5}<0,001, p_{4-5}=0,003				

Note: PN - pyelonephritis, p_{1-5} - reliability of differences between children with chronic secondary PN on the background of hydronephrosis during the exacerbation and healthy, p_{3-5} -

reliability of differences between children with chronic secondary PN on the background of pyeloectasia during the exacerbation and healthy.

Table 3

Activity of α_2-macroglobulin (α_2-MG) in infants with chronic secondary pyelonephritis

Indicator		Chronic secondary pyelonephritis		Control group n=40 (3)
		Period of exacerbation n=33 (1)	Period of remission n=16 (2)	
α_2-MG IU / ml	M±m	2,36±0,25	2,77±0,30	3,28±0,16
	Me	1,9	2,73	3,1
	Q3	1,4	2,26	2,48
	Q1	3,05	3,29	4,1
	$p_{intergroup}$	0,29		
	p_{pairs}	–		
	p_{norm}	p_{1-3}=0,001		

Note: p_{1-3} - reliability of differences between children with chronic secondary pyelonephritis during the exacerbation and control group.

Table 4

Activity of specific proteinase inhibitors in infants with chronic secondary pyelonephritis depending on the type of congenital anomalies of the kidney

Indicator		Chronic pyelonephritis on the background of hydronephrosis		Chronic pyelonephritis on the background of pyeloectasia		Control group n=40 (5)
		Period of exacerbation n= 7 (1)	Period of remission n=4 (2)	Period of exacerbation n=22 (3)	Period of remission n=12 (4)	
α_2-MG IU / ml	M±m	1.84±0,33	1,82±0,53	2,34±0,31	3,55±0,35	3,28±0,16
	Me	1,82	1,92	1,81	3,06	3,1
	Q3	1,27	0,91	1,4	2,46	2,48
	Q1	2,45	2,73	3,07	3,59	4,1
	$p_{intergroup}$	0,002				
	p_{pairs}	p_{1-5}=0,036 p_{3-5}=0,037				

Note: p_{1-5} - reliability of differences between children with chronic secondary pyelonephritis on the background of hydronephrosis during the exacerbation and control group, p_{3-5} - reliability of differences between children with chronic secondary pyelonephritis on the background of pyeloectasia during the exacerbation and control group.

ABSTRACT

Vasoactive proteolytic system involved in the regulation of various physiological systems and the development of many pathological states. In this work we investigated the activity of kallikrein, kallikreinogen, angiotensin-converting enzyme, α_1-proteinase inhibitor, α_2-macroglobulin in infants with chronic secondary pyelonephritis.
In chronic secondary pyelonephritis, no matter what type of congenital renal disease, there is activation of vasoactive proteolytic systems that may have diagnostic and prognostic significance.

Key words: kallikrein, kallikreinogen, angiotensin-converting enzyme α_2-macroglobulin, young children.

UDC 616-007.7:616-053.7 (571.1 / 5)

Constitutional features of sexual dimorphism and PHYSICAL DEVELOPMENT OF YOUNG MEN (YOUTHS) IN CENTRAL SIBERIA

A.S. Pulikov, O.L. Moskalenko, O. I. Zaitseva
Medical Research Institute for Northern Problems of Medical Sciences (Krasnoyarsk)
A.S. Pulikov, O.L. Moscalenko, O.I. Zaitseva

Scientific research institute of medical problems of the North, Krasnoyarsk
Summary of Anthropometric survey of young men in Central Siberia has revealed uneven distribution of somatotype on sexual differentiation dominated mainly gynecomorphous somatotype and asthenia, with a gradual leveling age indicators. Found that, in adolescence the process of physical and sexual maturation is not completed.

Key words: physical constitution, sexual dimorphism, male, Siberia.

Introduction

It is well known that the formation of the same part of the Constitution shall take the external environment and heredity. Hereditarily is determined by the main features of the constitution - the longitudinal dimensions of the body and the dominant type of metabolism, the latter is inherited only if in