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PRESEPSIN AND PROCALCITONIN – MARKERS OF SEPSIS AND SEVERE PNEUMONIA

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Markers of inflammation procalcitonin (PCT), presepsin (PSP) are used against pneumonia, sepsis. The research objective was to study PCT, PSP to improve the diagnosis of severe pneumonia, sepsis. There was totally evaluated 172 patients at the age from 17 to 87. Out of them 118 patients had community-acquired pneumonia (CAP), sepsis, other purulent diseases. These patients were investigated for the level of PCT. PCT was determined quantitatively in ng/ml by the immunofluorescence analyzer miniVIDAS (Biomerye, France). 54 patients with pneumonia, sepsis and other inflammatory diseases have been investigated for the level of the presepsin. Presepsin level was determined quantitatively in pg/ml by means of chemiluminescent immunoassay analyzer Pathfast (Mitsubishi Chemical Medience Corporation, Japan). All patients had received antibacterial therapy in other health care organizations before entering the hospital. Results: 1. PCT research. PCT level of patients with community-acquired pneumonia (CAP) (2,1 ± 0,98, n = 10; ±m) and pneumogenic sepsis (3,7 ± 2,01,n = 12) upon admission did not differ (p>0.05). PCT of patients with severe CAP (3,4 ± 1,82, n = 5) did not differ from the PCT by pneumogenic sepsis without renal dysfunction (2,6 ± 1,52, n = 5, p> 0.05). 2. PSP research. There were revealed differences between PSP level by severe pneumonia (642,0 ± 140,59, n = 10) and sepsis of patients without renal dysfunction (1412,5 ± 180,27, n = 8, p <0.05).

***Key words**: procalcitonin, presepsin, pneumonia, sepsis.*

Biological markers, as indicators of biological and pathobiological processes, have been used since early 1990s of the past century [1]. The biological markers by pneumonia and sepsis are procalcitonin (PCT), presepsin (PSP), IL-6, C-reactive protein, leucocytes [2,3].

PCT is used to determine the bacterial nature of a respiratory disease for sepsis diagnostics [1]. PCT presents a prohormone – predecessor of calcitonin [4]. PCT is primarily generated in C-cells of thyroid gland and neuroendocrine lung cells. The stimulatory effect on PCT production is caused by lipopolysaccharide of the bacterial wall. By severe infection the level of PCT increases quite rapidly and preserves for a long time, which makes it a specific sepsis marker. PCT is used in clinical practice for diagnostics and control of the antibacterial therapy (ABT) effectiveness by the treatment of community-acquired pneumonia (CAP) and sepsis.

The American Medical Association had suggested the algorithms of ABT conduction in patients with infections of lower respiratory tracts considering the concentration of PCT and its interpolation by septicemic conditions [5]. The influence of vasoactive drugs, pain killers, anticoagulants or diuretic agents on the change of PCT was not revealed. The reduction of PCT concentration during several days indicated the efficiency of the therapy (surgical, antibacterial).

PSP – is a new biomarker of bacterial and fungal systemic infections [2]. A key role in PSP production is played by activation of macrophages/monocytes, on the surface of which there is situated membrane receptor proteinmCD14. This protein-receptor identifies the signal of presence of infectious bacteria and switches the system of nonspecific immunity and the inflammatory process connected with it. After the activation of macrophages, mCD14 detaches from the membrane, enters the circulation and becomes soluble sCD14. Further, there occurs the activation of phagocytosis by means of lysosomal proteinases. Proteinases split sCD14 forming sCD14-ST (PSP).

PSP possesses a number of advantages in comparison with the other anti-inflammatory markers: 1) early rise; 2) precise reflection of severity and dynamics of sepsis; 3) prognosis of outcomes; 4) prognosis of sepsis recurrence.

Objective: to study the markers of inflammation to improve the effectiveness of diagnosis of severe pneumonia and sepsis. For this purpose there was: 1) determined the level of PCT in patients with community-acquired pneumonia, sepsis with prior ABT; 2) determined the level of PSP in patients with pneumonia, sepsis with prior ABT.

Materials and methods

There were totally examined 172 patients at the age from 17 to 87 years. Out of them 118 patients were investigated for the level of PCT. These patients were under medical treatment in the pulmonary department, surgery infection department, resuscitation and intensive care department of FSBHI "Regional Clinical Hospital" for the period from 2010 to 2014.

The age of patients – from 19 to 87 years, the average age - 52,6±15,9 ($\overline{X}$ ±m). Among them 71 (60,2%) men, 47 (39,8%) women. The patients were divided into 4 groups. The 1st group consisted of patients with CAP (n=19, 16,1%), 2nd group – patients with pneumogenic sepsis (n=12, 10,2%), 3rd group – patients with abdominal sepsis (n=57, 47,3%), 4th group – other purulent diseases (pancreonecrosis, phlegmonous cholecystitis, phlegmon of anterior abdominal wall, acute suppurative mastitis) (n=30, 25,4%).

In 54 patients there was stated the level of PSP. The patients were under medical treatment in the pulmonary department, surgery infection department, resuscitation and intensive care department of FSBHI "Regional Clinical Hospital" for the period from 2010 to 2014. The age of patients – from 17 to 77 years, the average age - 54,4 ± 2,44 (X± m). Among them 34 (63,2 %), men, 20 (36,8%) women. The 1st group consisted of patients with pneumonia (n =16, 29,6 %), 2nd group – patients with pneumogenic sepsis (n = 14, 25,9 %), 3rd group – patients with abdominal sepsis (n = 16, 29,6 %), 4th group – other purulent diseases (purulent pyelonephritis, phlegmonous appendicitis, cholecystitis, etc.) (n = 8, 14,9 %).

The PCT level was was determined quantitatively by the immunofluorescence analyzer mini-VIDAS (Biomerye, France). The results are presented in nanograms per milliliter (ng/ml). PCT was determined upon admission, in 5 and more days.

The PSP level was determined quantitatively by means of chemiluminescent immunoassay analyzer Pathfast (Mitsubishi Chemical Medience Corporation, Japan). The results are presented in pictograms per milliliter (pg/ml). PSP was determined upon admission.

The management of patients was performed in accordance with current clinical recommendations and standards. The antibiotic treatment included: penicillins (ampicillin, ampicillin/ sulbactam, amoxycillin/clavulanate), cephalosporins (cefazoline, ceftriaxone, cefotaxime, ceftazidime, cefoperazone, cefoperazone/ sulbactam, cefepime, ceftaroline), carbapenems (meropenem, ertapenem, imipenem/cilastatin); aminoglycosides (amikacin, gentamycine); macrolides (azithromycin); glycopeptides (vancomycin); oxazolidinones (linezolid); other antibiotics (tigecycline); nitroimidazole (metronidazole); sulfanilamides and trimethoprim (co-trimoxazole); quinolones (levofloxacin, moxifloxacin, ciprofloxacin); antimycotics (f luconazole); antiviral agents (oseltamivir, acyclovir). All patients had been exposed to ABT in other healthcare organizations before admission to FSBHI "Regional Clinical Hospital".

The statistical data processing was conducted by means of Microsoft Exel program package. Statistically significant differences were determined by means of Student t-test.

Results and discussion

1. Results of PCT examination

The level of PCT in patients with CAP, pneumogenic sepsis and abdominal sepsis is presented in Table 1.

Table 1

PCT in patients with CAP, pneumogenic and abdominal sepsis

Index	Patients with CAP (1)	Patients with pneumogenic sepsis (2)	Patients with abdominal sepsis (3)	p		
	$\overline{X}$ ±m	$\overline{X}$ ±m	$\overline{X}$ ±m	1-2	1-3	2-3
PCT upon admission	2, 1±0,98 n=10	3,7±2,01 n=12	18,4±6,31 n=27	>0,05	<0,05	<0,05
PCT in 5 days and later	0,2±0,04 n=9	-	13,1±6,65 n=30	-	<0,05	-
PCT in all patients	1,2±0,55 n=19	3,7±2,01 n=12	15,6±4,57 n=57	>0,05	<0,05	<0,05

PCT level in patients with CAP and pneumogenic sepsis upon admission did not differ significantly. PCT in patients with CAP upon admission constituted 2,1±0,98, n=10, which was lower than the level of PCT in patients with abdominal sepsis - 18,4±6,31, n=27 (p<0,05). PCT in patients with pneumogenic sepsis upon admission - 3,7±2,01, n=12, which was lower than in patients with abdominal sepsis 18,4±6,31, n=27 (p<0,05).

PCT in patients with CAP in 5 days and later constituted 0,2±0,04, n=9, which was lower than in patients with abdominal sepsis - 13,1±6,65, n=30 (p<0,05).

PCT level in patients with CAP and pneumogenic sepsis in the general group did not differ. PCT in the general group by CAP was 1,2±0,55, n=19, which was lower than in patients with abdominal sepsis - 15,6±4,57, n=57 (p<0,05). PCT in patients with pneumogenic sepsis in the general group equaled 3,7± 2,01, n=12, in patients with abdominal sepsis - 15,6±4,57, n=57 (p<0,05).

The concentration of PCT upon admission in patients with severe pneumonia constituted 3,4±1,82, n=5, which did not differ from PCT by pneumogenic sepsis without renal dysfunction - 2,6±1,52, n=8, (p>0,05).

The level of PCT in patients with CAP, pneumogenic sepsis and abdominal sepsis in comparison with the patients with other inflammatory diseases is presented in Table 2.

Table 2

PCT in patients with CAP, pneumogenic and abdominal sepsis in comparison with the patients with other inflammatory diseases

Index	Patients with CAP (1)	Patients with pneumogenic sepsis (2)	Patients with abdominal sepsis (3)	Patients with other inflammatory diseases (4)	p		
	$\overline{X}$ ±m	$\overline{X}$ ±m	$\overline{X}$ ±m	$\overline{X}$ ±m	1-4	2-4	3-4
PCT upon admission	2, 1±0,98 n=10	3,7±2,01 n=12	18,4±6,31 n=27	24,7±11,63 n=21	>0,05	>0,05	>0,05
PCT in 5 days and later	0,2±0,04 n=9	-	13,1±6,65 n=30	3,4±1,43 n=9	<0,05	-	>0,05
PCT in all patients	1,2±0,55 n=19	3,7±2,01 n=12	15,6±4,57 n=57	17,7±8,04 n=30	<0,05	>0,05	>0,05

The level of PCT in patients with CAP, pneumogenic sepsis and abdominal sepsis in comparison with the patients with other inflammatory diseases did not differ significantly.

PCT in patients with CAP in 5 days and later constituted 0,2±0,04, n=9, which was lower than in patients with abdominal sepsis - 3,4±1,43, n=9, (p<0,05). The level of PCT in 5 days since admission and later in patients with abdominal sepsis and other inflammatory diseases did not differ significantly.

PCT in patients with CAP in the general group equaled 1,2±0,55, n=19, which was lower than in patients with other inflammatory diseases - 17,7±8,04, n=30, (p<0,05).

2. Results of PSP examination

The level of PSP in patients with sepsis and other inflammatory diseases is presented in Table 3.

Table 3

PSP in patients with pneumogenic, abdominal sepsis and other inflammatory diseases

Index	Patients with pneumogenic sepsis (1)	Patients with abdominal sepsis (2)	Patients with other inflammatory diseases (3)	p		
	$\overline{X}$ ±m	$\overline{X}$ ±m	$\overline{X}$ ±m	1-2	1-3	2-3
PSP upon admission	3083,8±598,10 n=14	2867,4±503,64 n=16	873±132,92 n=8	>0,05	<0,05	<0,05

The level of PSP upon admission by pneumogenic sepsis in the general group constituted 3083,8±598,10 pg/ml, n=14, by abdominal sepsis in the general group - – 2867,4±503,64 pg/ml, n=16 (p>0,05). In patient with other inflammatory diseases PSP was 873±132,92 pg/ml, n=8, which differed from PSP by pneumogenic and abdominal sepsis (p<0,05).

The level of PSP by pneumonia and pneumogenic sepsis is presented in Table 4.

Table 4

PSP in patients with pneumonia and pneumogenic sepsis

Index	Patients with severe pneumonia (1)	Patients with pneumogenic sepsis without renal dysfunction (2)	Patients with severe pneumogenic sepsis with renal dysfunction (3)	p	
	$\overline{X}$ ±m	$\overline{X}$ ±m	$\overline{X}$ ±m	1-2	2-3
PSP	642,0±140,59 n=10	1412,5±180,27 n=8	5434,5±881,41 n=4	<0,05	<0,05

The level of PSP by pneumogenic sepsis by exclusion of patients with severe sepsis, chronic kidney disease and acute renal dysfunction, exposed to hemodialysis, constituted 1412,5±180,27 pg/ml, n=8, in comparison with PSP of patients with with pneumogenic sepsis and renal dysfunction, exposed to hemodialysis - 5434,5±881,41 pg/ml, n=4, (p<0,05).

The PSP concentration in one patient with abdominal sepsis constituted 3150 pg/ml. The level of PSP in patients with severe abdominal sepsis - 2601,2±650,85 pg/ml, n=12. Patients with abdominal sepsis did not receive hemodialysis.

The level of PSP in patients with severe pneumonia was 642,0±140,59 pg/ml, n=10, while in patients with light form of pneumonia it constituted 231,3±54,26 pg/ml, n=6, (p<0,05).

PSP in patients with severe pneumonia constituted 642,0±140,59 pg/ml, n=10, which was lower than in patients with pneumogenic sepsis without renal dysfunction - 1412,5±180,27 pg/ml, n=8, p<0,05.

In current research the level of PCT upon admission in patients with CAP with prior ABT constituted 2,1±0,98 ng/ml. In the work of M. Bafadhel et al., it is shown, that by CAP in primary health care, the level of PCT was 1,27 ng/ml [6].

In this study, we determined the PCT values in patients with pneumogenic, abdominal sepsis and other inflammatory diseases with prior ABT. The literature sources concerning this issue are limited.

The differences between PCT by CAP and pneumogenic sepsis in patients with prior ABT were not found in our study. The level of PCT by CAP was lower, than by abdominal sepsis and other inflammatory diseases. The difference between PCT by abdominal sepsis and other inflammatory diseases in patients with prior ABT was not revealed.

The determination of PCT level is used to improve ABT prescription. According to literature, the implementation of "biomarker-oriented" therapy reduces the terms of ABT and the number of antibiotic associated adverse events compared to the standard therapy by CAP [4]. The use of procalcitonin-oriented therapy did not effect mortality and hospital admission to the resuscitation and intensive care department by infections of lower respiratory tracts.

In terms of the study, the level of PSP in patients with pneumogenic sepsis constituted 1412,5±180,27 pg/ml (n=8). In patients with severe abdominal sepsis - 2601,2±650,85 pg/ml, n=12. Our data differ slightly from the literature sources. The recommendations on patient management by suspected sepsis include the following values of PSP (pg/ml): <200 – very low risk of sepsis development; 200-300 – low risk of sepsis; 500-1000 – sepsis; ≥1000 – severe sepsis, sepric shock [2]. In the study by M. Behnes et al., the diagnostic levels of PSP were the following: ≥530 pg/ml by sepsis; ≥600 pg/ml by severe sepsis. In the research, presepsin is considered significant by determination of the severity of sepsis. Consequently, by diagnostics and determination of the severity of sepsis, it is reasonable to consider the recommended values of PSP.

The results of our study showed, that PSP in patients with pneumogenic sepsis exposed to hemodialysis constituted 5434,5±881,41 pg/ml (n=4), which does not contradict the literature data. PSP is filtrated in renal glomerules, reabsorbed and metabolized in proximal convoluted tubules. There exist data on the increase of PSP concentration in patients with renal dysfunction even by lack of infection [7]. The PSP concentration in patients with terminal renal insufficiency before kidney transplantation was 1252±451 pg/ml. After the surgery the level of PSP reduced. These data indicate, that kidneys play an important role in presepsin clearance.

The level of PSP by mild and severe forms of pneumonia in our research corresponds to the literature data [2].

We revealed the difference between PSP by severe pneumonia and sepsis in patients without renal dysfunction, while the concentration of PCT by severe pneumonia and sepsis did not differ. Thus, PSP reflects the severity of infectious disorder more precisely, than PCT, which does not contradict literature [2].

Conclusion

1. PCT level in patients with prior CAP (2,1 ± 0,98 ng/ml) and pneumogenic sepsis (3,7±2,01ng/ml) did not differ significantly. These data indicate an extremely severe course of CAP in examined patients.

2. It is reasonable to consider the level of PCT by managements of patients with CAP, sepsis and other inflammatory diseases with prior ABT.

3. There was revealed the difference of PSP level by severe pneumonia (642,0±140,59 pg/ml) and sepsis in patients without renal dysfunction (1412,5±180,27 pg/ml), the level of PCT by severe pneumonia and sepsis did not differ significantly. Thus, PSP reflects the severity of infection more precisely, than PCT. The implementation of the new PSP marker is reasonable by diagnostics and determination of the severity of sepsis.

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