DE GRUYTER OPEN

ПРИЛОЗИ. Одд. за мед. науки, XXXVII 2–3, 2016 **МАНУ**
CONTRIBUTIONS. Sec. of Med. Sci., XXXVII 2–3, 2016 **MASA**

10.1515/prilozi-2016-0020

ISSN 1857-9345
UDC: 616.25-003.2:612.115.1
616.24-002:612.115.1

THE ROLE OF SERUM COAGULATION FACTORS IN THE DIFFERENTIAL DIAGNOSIS OF PATIENTS WITH PNEUMONIA AND PARAPNEUMONIC EFFUSION

Sanja Petrusevska Marinkovic[1], Irena Kondova Topuzovska[1], Zvonko Milenkovic[1], Biserka Kaeva[2]

[1] University Infectious Diseases Clinic, Medical Faculty, Skopje, R. Macedonia
[2] University Pulmonology and Allergy Clinic, Medical Faculty, Skopje, R. Macedonia

Corresponding Author: Petrusevska Marinkovic S., University Infectious Diseases Clinic, Medical Faculty, Skopje, R. Macedonia; tel: +389 (0)2 3228 224; e-mail: sanjapm@yahoo.com

Abstract

The aim of this study was to identify the participations of the serum coagulations and fibrinolysis factors that contribute to the differential diagnosis of the patients with community-acquired pneumonia (CAP) without effusion, uncomplicated parapneumonic effusion (UCPPE) and complicated parapneumonic effusion (CPPE).

The coagulations system is fundamental for the maintenance of homeostasis, and contributes to the inflammatory process responsible for CAP and the parapneumonic effusion. The factors of coagulations and fibrinolysis participate in the cellular proliferation and migration as in the synthesis of the inflammatory mediators.

We evaluated the laboratory profile of coagulations and fibrinolysis in the serum of 148 patients with CAP without effusion, 50 with UCPPE and 44 with CPPE. We determined the test of the coagulation cascade which measures the time elapsed from the activation of the coagulation cascade at different points to the fibrin generation. As a consequence, there is an activation of the fibrinolytic system with the increased D- dimer levels measured in the plasma in the three groups.

The patients were with mean age ± SD (53,82 ± 17,5) min – max 18–93 years. A significantly higher number of thrombocytes was in the group with CPPE with median 412 × 10^9/L (rank 323–513 × 10^9/L). The extended activation of the prothrombin time (aPTT) was significantly higher in the same group of patients with median of 32 sec. (rank 30–35 sec). The mean D-dimer plasma level was 3266,5 ± 1292,3 ng/ml in patients with CPPE, in CAP without effusion 1646,6 ± 1204 ng/ml and in UCPPE 1422,9 ± 970 ng/ml.

The coagulations system and the fibrinolysis play important role in the development and pathophysiology of CAP and the parapneumonic effusions.

Keywords: coagulation factors, fibrinolysis, community-acquired pneumonia (CAP), parapneumonic effusion, uncomplicated parapnemonic effusion, complicated parapneumonic effusion, D-dimer

Introduction

Community-acquired pneumonia (CAP) is one of the leading cause of sepsis and death from infectious disease [1, 2]. In the recent years, attention has tuned to other events in the host response to bacterial challenge, notably the coagulation activation [2]. The acute lung injury is associated with both vascular and extravascular coagulation [3, 4]. The relevance of the interaction between the coagulation and inflammation as a response to the severe infection, in its most extreme form manifests as disseminated intravascular coagulation (DIC) and multiple organ failure, and is becoming increasingly clear [5]. It is assumed that there is an explanation about the epidemiologic link between

infection and the higher risk of death, particularly due to acute cardiovascular events [6]. The activation of the host response to infection may persist at hospital discharge when patients appear to have recovered clinically from the infection, and it increases the risk of acute deteriorations of the cardiovascular disease and subsequent death [1, 6]. During an acute infection, the activation of the hemostatic system leads to a prothrombotic state [6]. Abnormalities are common even during less severe infection [1, 6]. The factors of coagulations and fibrinolysis participate in the cellular proliferation and migration as in the synthesis of the inflammatory mediators.

Parapneumonic effusion occurs in 20 to 40% of patients who are hospitalized with pneumonia like most common complication [7]. The mortality rate in patients with parapneumonic effusion is higher than that in patients with pneumonia without a parapneumonic effusion [7, 8]. The evolution of the parapneumonic effusion can be divided into three stages that represent a continuous spectrum [7, 9]. There is: the uncomplicated parapneumonic effusion (UPPE) depending on how sterile the exudative pleural effusion is, followed by a treatment with antibiotic alone [7, 8]. Less become secondarily infected (complicated parapneumonic effusion) (CPPE), and sometimes it requires a drainage in order to be resolved [8]. Bacterial metabolism and neutrophil phagocytosis in the pleural space lead to lactic acid production and increased glucose utilization. [8, 9]. The ongoing infection eventually leads to the accumulation of pus in the pleural space (empyema). After a variable time interval, the pleural infection enters an "organizing" stage characterized by fibroblast proliferation and the development of solid fibrous peel. This inhibit lung re-expansion usually necessitates surgical thoracotomy and décorticatión [8, 10]. The development of infection is associated with activation of the coagulation cascade and inhibition of fibrinolysis within the pleural space [10]. The coagulation system, when chronically activated and in the presence of an inflammatory state, can generate adverse effects such as chronic relies of procoagulant factors (e.g., tissue factor), cellular activation (adhesion molecules), protein modulation (transformation of fibrinogen into fibrin), and even histological changes promoted by cytokines [11].

D-dimer is a metabolic substance produced during the catabolization of fibrin by plasmin and they are fibrin degradation products [1, 2, 11, 12]. D-dimer levels have shown disorders that trigger fibrin production and catabolization; these disorders include pulmonary emboli (PE), deep vein thrombosis (DVT), solid tumors, leukemia, severe infection, trauma or post-operative state, pregnancy, congestive heart failure etc. [1, 12].

In order to recognize the contribution of the coagulation system to the differential diagnosis of patients with CAP without parapneumonic effusion and with parapneumonic effusion, we evaluated the laboratory profiles of the coagulations and the D- dimmer.

Materials and methods

We analyzed the laboratory profile of coagulations and fibrinolysis in the serum of 148 patients with CAP without effusion, 50 with UCPPE and 44 with CPPE. The patients were diagnosed and treated at the University Infectious Diseases Clinic, Faculty of Medicine, Skopje, at the Department of Respiratory Diseases in the period from September 2011 to June 2015. Individuals were excluded from the study because of the cancer and malignant effusion, transudate effusion, vasculitis or sickle-cell anemia, pregnancy, pulmonary emboli (PE), younger than 18 years of age and thromboembolic diseases.

The demographic characteristics, the physical examination findings and the laboratory findings (sedimentation, thrombocytes (platelets), leucocytes, hemoglobin, hematocrit, glucose, sodium, potassium, urea, C-reactive protein (CRP), lactate- dehydrogenases (LHD), albumin and total protein) and the microbiological findings of all study participants were monitored regularly. Initial lung X-rays were taken for all patients at the Institute of Radiology, Medical Faculty in Skopje. After the admission all the patients underwent an ultrasound of the pleura and lung with a three-dimensional echo at the University Infectious Diseases Clinic for diagnosis of the pleural effusions and implementation of the diagnostic thoracentesis if the size of effusion was more than 10 mm. After the verification of pneumonia and pleural effusion, the distinction between the transudate and exudate was done

according to Light's criteria. Exudative pleural effusion is one that meets at least one of the criteria of Light. It is a transudate if the effusion meets all three criteria at the same time (1. To have intercourse protein p/s below 0.5, 2. Intercourse LDH p/s below 0.6 and 3. LDH in pleural fluid under 282 U/L which is the lowest limit in our laboratory. The exudative pleural effusion according to the evolution and on the basis of the pH, glucose and LDH value in the pleural fluid is divided into: – Uncomplicated parapneumonic effusions: pH > 7.2, glucose > 60 mg/dl, LDH < 1000UI/ml; – Complicated parapneumonic effusions: pH < 7.2, glucose < 60 mg/dl, LDH >/= 1000 UI/ml.

The blood sample for coagulations and fibrinolysis factors were taken from the antecubital vein with an injector and placed into citrated tube (with sodium citrate anticoagulant, 3.2%) and transported immediately to the Institute of Transfusion Medicine, Faculty of Medicine in Skopje, where it was evaluated with the quantitative latex coagulation method. We determined the number of Tr (normal value 150–250 × 10^9), activation prothrombin time (aPTT), prothrombin time (PT) and thrombin time (TT). Also, the value of the D-dimmer in the three patients groups was measured. The plasma D-dimer level over 500 ng/ml were considered to be high. Maximum value of D- dimer is 4,500 ng/ml.

Statistical analysis

The statistical analysis was conducted using SPSS 17 for Windows. The testing of the normality in the distribution of the data was done using the Kolmogorov-Smirnov and Shapiro-Wilk's W test. The categorical traits were displayed by the absolute and relative representation with quantitative traits mean, SD, median, minimum, maximum, 25–75 percentiles. For the comparison of the three groups of subjects in relation to the analyzed variables were used the Kruskal-Wallis ANOVA and Mann-Whitney U test (Z). As level of significance or importance was taken the value of $p < 0.05$, a significantly higher value than $p < 0.01$.

Results

In the three group of patients the majority were the male patients (58.11%, 58%, 61.36%) consequently. The difference in the distribution of patients with CAP without effusion, UCPPE and CPPE in terms of their sex was insignificant ($p = 0.9$). The mean age of patients only with CAP was 54.58 ± 17.5 years, in UCPPE 55.5 ± 16.6 and in the group with CPPE was 51.91 ± 18.4 and there was no statistical difference ($p = 0.58$).

In addition, the distribution of participants according to the smoking status was insignificant ($p = 0.25$).

Table 1

Demographic characteristics of three group of patients

variable	CAP N=148	UCPPE N=50	CPPE N=44	p value
sex n (%)				
male	86(58.11)	29(58)	27(61.36)	[a]p = 0.9
female	62(41.89)	21(42)	17(38.64)	
Age (years) mean ± SD, min-max				
	54.58 ± 17.5 18–89	55.5 ± 16.6 21–83	51.91 ± 18.4 18–93	[b]p = 0.58
Smoking status n (%)				
smoker	92(62.16)	37(74)	31(70.45)	[a]p = 0.25
non smoker	56(37.84)	13(26)	13(29.55)	

[a]p(Chi-square test) [b]p (Analisys of variance)

Patients with complicated effusion had significantly higher values of thrombocytes compared to the patients with CAP without effusion ($p < 0.0001$), and compared to the patients with UCPPE ($p < 0.0001$). The median value of the thrombocytes in patients without effusion group with complicated and uncomplicated discharge was 216 × 10^9 (rang 158.5–298 × 10^9), 226 (rang 167–276 × 10^9), 412 × 10^9 (rang 323–513 × 10^9) consequently.

Platelets higher than 400 × 10^9 had 11.8% of the patients with CAP without effusion, 8 % of the patients with UCPPE, and 52.27% of the patients with CPPE.

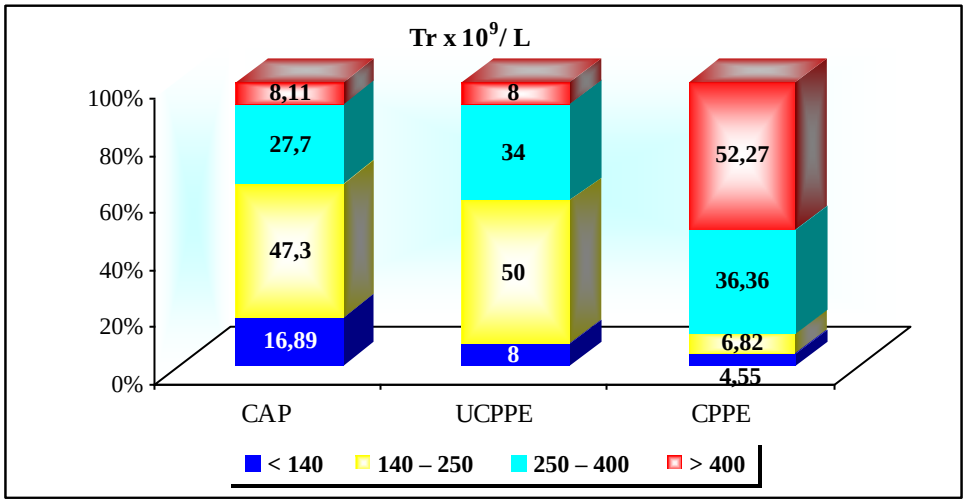

Figure 1 - Distribution of thrombocytes in the three clinical different patient groups

Statistically significant differences were confirmed between the three groups analyzed and compared to the values of the activated partial time (aPTT) (p = 0.0032). This significance is due to significantly higher values of this parameter in the group of patients with CPPE as compared with the group with CAP without effusion – median of 32 sec. (range 30–35 sec.) vs. median 29 (rang 27–33), and as compared with the group with uncomplicated effusion – median 32 (range 30–35) vs 29 (range 26–32).

The measured values of prothrombin (PT) and thrombin time (TT) are not statistically proved different among the respondents from the three analyzed groups (p = 0.092, p = 0.33 accordingly T). These results are shown in Table 2.

Table 2

Test of coagulation cascade in three clinical different group of patients

variable	CAP N = 148	UCPPE N = 50	CPPE N = 44	p value
Trx10^9/ L				
< 140	25(16.89)	4(8)	2(4.55)	
140–250	70(47.3)	25(50)	3(6.82)	
250–400	41(27.7)	17(34)	16(36.36)	
> 400	12(8.11)	4(8)	23(52.27)	
Trx10^9 mean ± SD median (25–75thquartiles)				
	237.67 ± 124	241.86 ± 93.2	452.75 ± 202.2	^{c}p < 0.0001
	216(158.5–298)	226(167–276)	412(323–513)	1vs3 p < 0.0001
				2vs3 p < 0.0001
PT sek mean ± SD median (25–75thquartiles)				
	17.89 ± 45.8	12.52 ± 2.3	13.36 ± 4.0	^{c}p = 0.092
	13(12–14.5)	12(12–13)	12(12–14)	
aPTT sek mean ± SD median (25–75thquartiles)				
	31.09 ± 7.7	30.48 ± 6.5	33.02 ± 5.5	^{c}p = 0.0032*
	29(27–33)	29(26–32)	32(30-35)	1вс2 p = 0.0018**
				1вс3 p = 0.003**
TT sek mean ± SD median (25–75thquartiles)				
	17.12 ± 1.8	17.12 ± 1.7	18.2 ± 4.4	^{c}p = 0.33
	17(16–18)	17(16–18)	17.5(16–19)	

^{c}p (Kruskal-Wallis test) ^{d}p (Mann-Whitney test) *p < 0.05 **p < 0.01

The D-dimer level was with statistically important differences between both group with parapneumonic effusion ($p < 0.0001$), and between the group with CPPE and CAP without effusion ($p < 0.0001$). The median of D-dimer level was higher in CPPE, 3792 ng/ml, (rang 14–4500ng/ml), lower in patients with CAP, 1136 ng/ml (rang 794–2366 ng/ml) and lowest in the group with UPPE 1112 ng/ml (rang 689–1712 ng/ml). The average D-dimer plasma level was 3266.5 ± 1292.3 ng/ml in patients with CPPE, in CAP without effusion 1646,6 ± 1204 ng/ml and in UCPPE 1422,9 ± 970 ng/ml. This statistically significant difference in favor of CPPE is shown in Table 3 and figure 2.

Table 3

Value of D-dimer in three clinical different group of patients

variable	CAP N = 148	UCPPE N = 50	CPPE N = 44	p value
D dimeri ng/ml	**mean ± SD median (25–75thquartiles)**			
	1646.6 ± 1204	1422.9 ± 970.7	3266.5 ± 1292.3	$^{c}p < 0.00001$
	1136(794–2366)	1112(689–1712)	3792(1814–4500)	1вс3 $^{d}p < 0.0001$
				2вс3 $^{d}p < 0.0001$

^{a}p(Chi-square test ^{c}p (Kruskal-Wallis test) ^{d}p (Mann-Whitney test) *p < 0.05 **p < 0.01

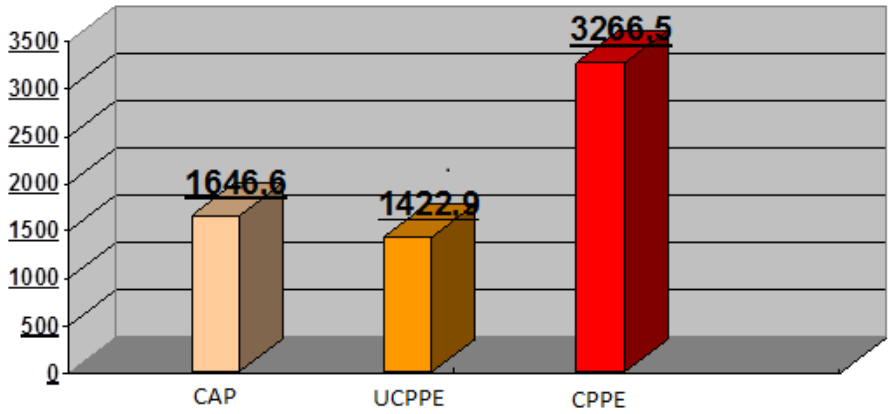

Figure 2 – Mean values of D-dimers in serum in ng/ml

Discussion

Acute lung injury is associated with both vascular and extravascular coagulation [3, 4]. Our study shows that coagulation factors and fibrinolysis in the serum distinguishing patients with CPPE on one side, and patients with CAP without effusion and UCPPE on the other.

CAP without effusion and UCPPE usually treated with antibiotic therapy have a good resolution without the need for additional interventions. UCPPE are sterile exudate and in the coagulation and fibrinolysis tests in the serum there are no significant differences. Differences are found between these two group and CPPE concerning the fibropurulent advanced stage in the development of parapneumonic effusions. The patients with CPPE have more severe clinical picture and they are with higher biomarker of inflammation and higher mortality rate, unlike the patients with CAP without effusion and the patients with UCPPE [10, 11, 13, 14].

The classic coagulation tests had significant difference in the activated partial time (aPTT) that was prolonged in patients with CPPE, unlike the two mentioned groups previously ($p = 0.0032$). The coagulation pathway that occurs in the aPTT test represents the intrinsic coagulation pathway. The extended aPTT shows incising abnormality and deficiency and severe infection associated with the prolonged aPTT without clinical signs of bleeding [14, 15]. Such findings also published Satoshi in a multicenter, prospective study in critically ill patients [15]. Because the prolonged aPTT is

good screening test for factor IX deficiency, in the Kale study the factor IX, thrombin- antithrombin complex, antithrombin and plasminogen activator inhibitor- 1 are with significantly higher value in patients with severe CAP and of older age (after the age of 65). A prolonged aPTT cannot be completely normalized with the addition of normal plasma it can be explained only with the presence of a circulating inhibitor of coagulation. The presence of these inhibitors is almost always acquired, and their exact nature is not always apparent. [12, 13, 15]. From a clinical point of view, the most common inhibitors should be considered the antithrombins. These compounds inhibit the activity of thrombin on the conversion of fibrinogen to fibrin. One of the two most common inhibitors of prolonged aPTT is heparin [15–17]. The measured value of prothrombin (PT) and thrombin time (TT) is not statistically proven to be different among the respondents from the three analyzed groups ($p = 0.092$, $p = 0.33$ accordingly). They are not specific test for coagulation disorders caused by infection [15–17].

Patients with complicated effusion had significantly higher values of thrombocytes compared to the patients with CAP without effusion ($p < 0.0001$), and compared to the patients with UCPPE ($p < 0.0001$). The median of Tr was 412 $x10^9$/L (rank 323–513 $\times 10^9$/L). Thrombocytes contribute to hemostasis and consist of vascular platelet phase of hemostasis. With their adhesion, activation and aggregation they form platelet plug (primary hemostasis) which is associated with the activation of the coagulation cascade with resultant fibrin deposition and linking (secondary hemostasis) [16–18]. In 2008 Chalmers et al. in prospective observational study of patients with CAP, analyzed 92 patients about the development of CPPE. With multivariate logistic regression, the value of the thrombocytes of more than 400×10^9 was identified as the independent predictor of the subsequent development of CPPE and empyema and it is part of the scoring system with "good" performance for predicting the development of CPPE and empyema in patients with CAP(18).

As a consequence, there is activation of the fibrinolytic system with increased levels of fibrin degradation products, including the D-dimer, which was measured in the plasma in the three patients groups. The value of D-dimer in not measured in the pleural fluid because some authors suggest that there is no significant difference between the value of D-dimer in the exudative effusions of different etiologies [11, 17, 19, 20]. Apart from this fact they found significant differences between the value of the D-dimer between the exudative and the transudate pleural effusion with higher value in the exudative effusions [11, 19, 20]. The D-dimer like part of the fibrinolysis has higher value in the infection and the value correlated with the severity of the infection [1, 5, 6, 11, 12, 21, 22]. Our conducted study confirmed expectations of statistically higher values of D-dimer in patients with CPPE than those with CAP without effusion and UCPPE. But, we have statistically important differences also between both group with parapneumonic effusion ($p < 0.0001$). The average D-dimer plasma level was 3266.5 ± 1292.3 ng/ml in patients with CPPE, in CAP without effusion 1646.6 ± 1204 ng/ml and in UCPPE 1422.9 ± 970 ng/ml.

The level of the D-dimer was lower in the group with UCPPE, probably because of the less severe clinical condition of the patients with UCPPE, than of the patients with CAP without effusion. The D-dimmers in a growing number of studies has been proven a robust biomarker that indicates the severity of the clinical condition and disorders in fibrinolysis as part of a cascading process of coagulation which is important for maintaining the homeostatic mechanism. They are biomarker which indicated the severity of CAP [1, 6, 21, 22]. Lately there are studies that indicate it as a significant marker for the differentiation of malignant, parapneumonic and tuberculous effusion [11, 17, 19]. In this study patient are not divided according to the severity of the clinical picture, which is the lack of this study.

Yet the differences that exist among the aforementioned coagulation factors and D-dimer indicate significant disorders which may have contributed to the demarcation of patients with pneumonia with or without pleural effusion, especially when it comes to CPPE. Coagulation disorders can lead to death in a patient as a result of developing pulmonary embolism [12, 23]. Different disorders can lead to dysfunction of various organs as a result of the

interplay of inflammation, coagulation and organic dysfunction [13, 23].

The study of Yende and the associates from 2011 in a large cohort of patients hospitalized with CAP, show that hemostasis makers are elevated during recovery, as evident with the higher thrombin – antithrombin complex (TAT) and D-dimer levels at hospital discharge. The higher concentration of these hemostasis markers was associated with the higher risk of death over 1 year, particularly due to the acute deterioration of the cardiovascular disease [6, 25]. This suggests that a persistent prothrombotic state even after infection may explain the epidemiologic link between the infection and the higher risk of cardiovascular disease [6, 26]. Thus, interventions, such aspirin and statins, with beneficial effects on resolution of the prothrombotic state and inflammation, should arguably be investigated to improve the long-term outcomes after pneumonia [25].

The study can help into understanding the physiological mechanisms in patients with CAP with and without parapneumonic effusion and may help to define new diagnostic and therapeutic approaches.

REFFERENCES

1. Arslan S., Ugurlu S, Bulut G.Akkurt I. The association between plasma D- dimmer levels and community- acquired pneumonia. Clinics 2010; 65(6): 593–7.
2. Milbrandt EB, Reade MC, Lee M, et al. Prevalence and Significance of Coagulation Abnormalities in Community-Acquired Pneumonia. Molec Med 2009; 15(11–12): 438–445.
3. Querol- Ribelles JM, Tenias JM, Grau E, et al. Plasma D- dimer levels correlate with outcomes in patients with community- acquired pneumonia Chest, 2004; 126(4): 1087–1092.
4. Freyburger G, Trillaund H, Labrouche S, Gauther P, Javorschi S, Bernard P, et al D dimmer strategy in thrombosis exclusion- a gold standard study in 100 patients suspected of deep venous thrombosis or pulmonary embolism: 8 DD metods compared. Thromb Haemost 1998; 79: 32–7.
5. Levi M, Keller TT, Van Gorp E, Ten Cate H. Infection and inflammation and the coagulation system Cardiovasc. Res. 60(2003) 26–39.
6. Yende S, D'Angelo G, Mayr F, et al. Elevated Hemostasis Markers after Pneumonia Increases One-Year Risk of All-Cause and Cardiovascular Deaths. Bozza PT, ed. PLoS ONE. 2011; 6(8): e22847.
7. Light RW Parapneumonic effusions and empyema Proc Am Thorac Soc. 2006; 3(1): 75–80.
8. Chapman SJ, Davies RJO The management of pleural space infection. Respitology 2004; 9: 4–11.
9. Light RW. Pleural diseases, 4th ed Baltimore: Lippincott, Williams and Wilkins; 2001.
10. Medford AR, Maskell N. Pleural effusion. Postgrad Med J 2005; 81: 702e10.
11. Costa Vaz MA, Vargas FS, Marinho FCA, D'Amico EA, Rocha TRF, Teixeira LR. Does the evaluation of coagulation factors contribute to etiological diagnosis of pleural effusions?. Clinics. 2009; 64(9): 891–5.
12. Kabrhel C, Courtney DM, Camargo CA, et al. Factors associated with positive D-dimer results in patients evaluated for pulmonary embolism. Academic emergency medicine: 2010; 17(6): 589–597.
13. Nguyen HB, Loomba M, Yang JJ, et al. Early lactate clearance is associated with biomarkers of inflammation, coagulation, apoptosis, organ dysfunction and mortality in severe sepsis and septic shock. Journal of Inflammation. 2010; 7: 6.
14. Barthwal M.S. Intrapleural fibrinolytic therapy in complicated parapneumonic effusion and empyema: present status. Indian journal of chest diseases and allied sciences 50.3 (2008): 277.
15. Satoshi G, Toshiaki I., Yutaka I, et al A multicenter, prospective validation of disseminated intravascular coagulation diagnostic criteria for critically ill patients: Comparing current criteria Critical Care Medicine: 2006; 34(3): 625–631.
16. Kale S, Yende S, Kong L, et all The effects of age on inflammatory and coagulation-fibrinolysis response in patients hospitalized forpneumonia. PLoS One. 2010; 5(11): e 13852.
17. Lee MH, Nahm CH, Choi JW. Thrombin-antithrombin III complex, proinflammatory cytokines, and fibrinolytic indices for assessing the severity of inflamemation in pleural effusions. Ann Clin Lab Sci. 2010 Fall; 40(4): 342–7.
18. Chalmers JD, Singanayagam A, Murray MP, et all. Risk factors for complicated parapneumonic effusion and empyema on presentation to hospital with community-acquired pneumonia. Thorax. 2009 Jul; 64(7): 592–7.
19. El- Habashy M, Elmahalawy I.I, Sonobol A. Value of D-dimer and alkaline phosphatase in the diagnosis of pleural effusion Egyptian Journal of Chest diseases and tuberculosis 2014; 63: 869–872.
20. Dikensoy O., Stathopoulos G.T., Zhu Z, Light R.W. D-dimmer levels in leural effusion Respiratory Medicine 2006; 100: 1337–1341.
21. Seligman R, Ramos-Lima LF, do Amaral Oliveira V, Sanvicente C, Pacheco EF, Rosa KD. Biomarkers in community-acquired pneumonia: A state-of-the-art review. Clinics. 2012; 67(11): 1321–1325.
22. Christ-Crain M, Opal SM Clinical review: the role of biomarkers in the diagnosis and management of community-acquired pneumonia. Crit Care. 2010; 14(1): 203.
23. Rohacek M, Szucs- Farkas Z., Pfortmüller C.A. et all Acute Cardiac Disorder or Pneumonia and Concomitant Presence of Pulmonary Embolism. PLoS One. 2012; 7(10): e7418.

24. Woodhouse PR, Khnaw K T, Plummer M, Foley A, Meade TW. Seasonal variations of plasma fibrinogen and factor VII activity in the elderly: winter infections and death from cardiovasucalre disease. Lancet; 1994:19; 343: 435–439.
25. Serhan CN, Chiang N, Van Duke TE Resolving inflammation: dual anti-inflammatory and pro-resolution lipid mediators. Nat Rev Immnol 2008; 8: 349–361.
26. Kasal J, Jovanovic Z, Clermont G, Weissfeld LA, Kaplan V, et al. Comparison of Cox and Gray's survival models in severe sepsis. Crit Care Med; 2004: 32: 700–707.

Резиме

УЛОГАТА НА СЕРУМСКИТЕ КОАГУЛАЦИОНИ ФАКТОРИ ВО ДИФЕРЕНЦИЈАЛНАТА ДИЈАГНОЗА КАЈ ПАЦИЕНТИ СО ПНЕВМОНИЈА И ПАРАПНЕВМОНИЧЕН ИЗЛИВ

Сања Петрушевска-Маринковиќ[1], Ирена Кондова-Топузовска[1], Звонко Миленковиќ[1], Бисерка Каева[2]

[1] Универзитетска клиника за инфективни болести, Медицински факултет, Скопје, Р. Македонија
[2] Универзитетска клиника за пулмологија и алергологија, Медицински факултет, Скопје, Р. Македонија

Цел на оваа студија е да се идентификуваат факторите на коагулација и фибринолиза кои имаат придонос во диференцијална дијагноза на пациенти со вонболнички здобиена пневмонија без излив, пациенти со некомплициран и со комплициран парапневмоничен излив.

Коагулациониот систем кој е фундаментален за одржување на хомеостазата учествува и во воспалителниот процес кој се јавува кај вонболнички здобиена пневмонија и парапневмонични изливи. Факторите на коагулација и фибринолиза учествуваат во клеточната пролиферација и миграција, како и во синтеза на инфламаторни медијатори.

Евалуиравме лабораториски профил на коагулација и фибринолиза во серум кај 148 пациенти со вонболничка пневмонија без излив, 50 пациенти со некомплициран парапневмоничен илзив и 44 со комплициран парапневмоничен излив. Ги одредувавме коагулационите тестови кои го мерат времето поминато од активација на коагулационата каскада со осврт на различните начини на генерација на фибрин. Како последица на оваа активација на фибринолитичкиот систем се зголемува нивото на Д-димери во плазма кое е одредувано во сите три групи пациенти.

Пациентите беа со средна виозраст ±SD (53,82 ± 17,5) мин.-макс. 18–93 години. Сигнификантно повисоки вредности на тромбоцити беа во групата со комплициран парапневмоничен излив со медијана 412 × 0^9/L (ранг 323–513 × 10^9/L). Продолжено активирано протромбинско време (аПТТ) беше сигнификантно со повисоки вредности во истата група пациенти со медијана 32 сек. (ранг 30–35 сек.). Средни вредности на Д-димери во плазмата беа 3266,5 ± 1292,3 ng/ml кај пациенти со комплициран парапневмоничен излив, кај оние со вонболничка пневмонија без излив 1646,6 ± 1204 ng/ml и кај пациенти со некомплициран парапневмоничен излив 1422,9 ± 970 ng/ml.

Коагулациониот систем и фибринолиза имаат значајна улога во развојот и патофизиологијата на вонболничка пневмонија и парапневмоничните изливи.

Клучни зборови: коагулациони фактори, фибринолиза, вонболничка пневмонија, парапневмоничен излив, некомплициран парапневмоничен излив, комплициран парапневмоничен излив, Д-димери