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Evaluation correlation of Plasma Fibrinogen Concentration with Severity of Acute Community Acquired Pneumonia Disease

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A B S T R A C T

Community Acquired Pneumonia is an important clinical problem that had high morbidity and mortality rates despite the development of antibiotics included. So that the sixth leading accounted for cause of death in the United States. Late diagnosis and inappropriate treatment increases the mortality rate. The aim of this study was to investigate the relationship between plasma fibrinogen concentrations with severity of acute community acquired pneumonia. In a descriptive study that performed in infectious diseases department of Tabriz on patients with acute pneumonia, correlation of the plasma fibrinogen concentration with severity of community acquired pneumonia evaluated. Of 56 patients with community acquired pneumonia, 34 of them were male and 22 of them were female. Mean age of male patients was 68.73 ± 15.97 year and mean age of female patients was 68.86 ± 20.07 year. Mean of the plasma fibrinogen concentration in patients at before treatment was 579.06 ± 207.54 and mean of the plasma fibrinogen concentration in patients at after treatment was 470.50 ± 127.94. Mean of the plasma fibrinogen concentration in patients at after treatment was significantly lower than mean of the plasma fibrinogen concentration in patients at before treatment that indicated the level of fibrinogen in patients with pneumonia significantly reduced after treatment. Significant liner correlation was not found between age, respiratory rate, systolic and diastolic blood pressure and blood urea with the plasma fibrinogen concentration at before and after treatment in the studied patients. Significant liner correlation was not found between CURB-65 score with the plasma fibrinogen concentration at before and after treatment in the studied patients.

Introduction

CAP is one of the major problems which, despite the development of many types of antibiotics, include high rates of clinical morbidity and mortality, so that it is the sixth leading cause of death in the United States. Late diagnosis and inappropriate treatment can increase the mortality rate (1).

Acute phase reactants secreted as the physiological response in inflammatory infections are increased in infections, malignancies and physical traumas. CRP, Fibrinogen, haptoglobin and ESR are some of the most important of acute phase reactants (2-3).

It has been shown that increased ESR level is useful for monitoring inflammatory diseases, increased CRP level is a sensitive marker for pneumonia. CRP is also useful in determining the severity of inflammatory diseases and the efficacy of treatment (2-3).
In a study by Kolsuz et al in 2006, 160 CAP patients, divided into 4 groups according to the severity of the disease based on the ATS guidelines, were examined in terms of acute phase markers including CRP, Fibrinogen and ESR. 53 patients had another underlying chronic disease including obstructive pulmonary disease and diabetes. 10 cases had hospital deaths. The severity of disease at the time of hospital admission had a statistically significant relationship with the levels of CRP and WBC; however, no relationship with the concentration of fibrinogen and ESR was observed (3).

In a study by Yetkin et al on19 patients with pneumonia in 2008, including 7 females and 12 males, the viscosity of plasma and levels of fibrinogen and ESR were measured and analyzed before and after antibiotic treatment. Averagely 10±4 days after starting treatment, there has been a significant reduction in the levels of fibrinogen and ESR and viscosity of plasma. Also in this study, a statistically significant correlation (R=0.7) was observed between serum levels of fibrinogen and viscosity of plasma (4).

In a study by Takizwa in 2006, measuring the concentration of fibrinogen has been a contributing factor in the accurate diagnosis and clinical judgment to determine the status of patients with acute inflammatory respiratory diseases on admission, and it has had a significant relationship with the inflammation of the respiratory tract (5).

According to the above mentioned statements, CAP is one the most important infectious diseases; and determining the status and severity of disease on admission and during treatment is an important factor in the good prognosis of these patients.

Factors with anticipation value presenting the information about status of the patients will be significantly helpful in determining the right treatment. Fibrinogen is an acute phase reactant which increases in the cases of acute inflammatory response. Based on the previously mentioned studies, there have been some controversies regarding the role of this acute-phase reactant with severity of pneumonia. The aim of this study was to investigate the relationship between level of plasmatic fibrinogen and severity of pneumonia, and the changes in the level of fibrinogen with the treatment performed on patients with a diagnosis CAP admitted in Imam Reza and Sina hospitals. The aim of this study is to investigate the relationship between plasmatic concentrations of fibrinogen with the severity of CAP.

Methods and Materials

In a descriptive-analytical study performed on patients with CAP in Department of Infectious Diseases of Tabriz, the relationship between the plasmatic concentration of fibrinogen and the severity of CAP was examined.

In this study, the study sample consisted of patients with CAP admitted in Imam Reza and Sina hospitals of Tabriz University of Medical Sciences during 2011-2012.

The sample size of the study was set as covering all of the patients diagnosed with pneumonia during the implementation of the study in the mentioned period, which included 56 cases in the study.

Inclusion criteria included willingness to participate in this study, having the clinical and radiographic symptoms of pneumonia, diagnosed with certain pneumonia, not receiving any medical treatment before admission to the health center and having no Immunosuppressive diseases and malignancy.

Exclusion criteria included patients who have received prior antibiotic therapy, having chronic pneumonia, pulmonary embolism, heart disease, vascular collagen diseases and HAP cases.

In this study, patients with CAP referring to Imam Reza and Sina Hospitals and qualified with the inclusion criteria were studied.
At first, the study cases got clinical examination and clinical evidences were recorded. Front chest radiography was taken from all cases and severity of the disease determined based on the CURB-65 score. On this score, Cunfusion, Urea>7mmol/lit, Respiratory-Rate, BP and finally, the patient's age determine the severity of pneumonia, and patients with any of this cases were categorized in three groups.

After admission and prior to treatment, 2ml blood sample was obtained to determine the plasmatic fibrinogen level along with other tests. Before treatment, in all of the patients, the target lab factors, including WBC, ESR and CRP were also measured. Numerical Cut-off-point of the plasmatic fibrinogen level was considered as greater than or equal to 400mg/dl.

After receiving antibiotic therapy and at the full recovery before discharge, the lab factors were rechecked and the manner of the changes based on the treatment applied was compared in each of the above mentioned cases.

Statistical Analysis

The collected data were analyzed by SPSS-17 statistical software. The collected data were expressed as percentage and mean ± SD. Continuous (quantitative) variables were compared by Independent samples, Paired T test and ANOVA test. Categorical (qualitative) variables were compared by contingency tables and Chi-square test or Fisher's exact test. P-value ≤ 0.05 was considered statistically significant.

Ethical considerations

In this study, patients admitted to Imam Reza and Sina Hospitals were studied and no additional intervention or treatment was performed and the standard treatment of pneumonia was applied. The patients didn't pay any cost, got the necessary information prior to the study and were presented with the informed consent form adjusted in accordance with the study goals. All of the information of the patients are absolutely confidential and their name and address will not be published anywhere.

Result and Discussion

In this study, 56 patients with CAP were examined and the following results obtained:

Out of 56 patients, 34 were male and 22 were female. The mean age was 68.73±15.97 years for males and 68.86±20.07 years for females (P=0.979). The mean body weight was 79.16±8.74kg for males and 72.81±10.51kg for females (P=0.020). The mean height was 1.75±0.06m for males and 1.66±0.06m for

females (P<0.001). The mean BMI was 25.83±2.86 for males and 26.18±3.33 for females (P=0.769).

The mean pre-treatment Level of fibrinogen was 548.22±206.78 in males and 632.72±193.74 in females (P=0.132). The mean post-treatment Level of fibrinogen was 467.78±108.42 males and 474.76±156.65 in females (P=0.847).

The mean Level of fibrinogen in the patients under study before and after treatment was 579.06±207.54 and 470.50±127.94 respectively. The mean post-treatment Level of fibrinogen was significantly lower, indicating that the level of fibrinogen in patients with pneumonia significantly decreases after treatment (P<0.001).

CURB-65 Scores of the patients under study are shown in Table 1. The frequency of CURB-65 scores of the patients in each gender under study is shown in Table 2. Laboratory findings in patients before and after treatment are shown in Table 3. CRP levels in patients before and after treatment are shown in Table 4. The ranges of fibrinogen levels in the patients before and after treatment are shown in Figure 1.

There was a significant inverse linear relationship between the pre-treatment CRP level and the pre-treatment Level of fibrinogen in the patients under study (P=0.008 and r=-0.376).

Overuse of antibiotics is common in all societies and especially in our hospitals, leading to antibiotic resistance and increased nosocomial infections.

These drug resistances include new strains of penicillin-resistant *Pneumococcus* and methicillin-resistant *Staphylococcus* in the community. Reduced overuse of antibiotics by people and their lesser prescription by doctors can play an effective role in the use of antibiotics and reduction of drug resistance and the other side effects such as diarrhea following antibiotic therapy of infections caused by difficile Clostridium. CAP is one of the main reasons of the use of antibiotics.

Despite the presence of imaging techniques and guidelines, and culturing the samples of patients' fluids, due to some impediments and also time consuming procedure of the methods of direct vision and culture, several biochemical markers have recently been proposed for the detection of infection. Some of these tests are specific and some are non-specific. Among the available biochemical markers, CRP, Procalcitonin, and recently, fibrinogen are crucial and make up a great volume of studies.

Besides the fact that these markers are helpful in starting antibiotic therapy, they are also very valuable in controlling the response to treatment and indication of complications particularly in patients with CAP.

Given the importance of the issue and the challenges in diagnosis and treatment of CAP, level of plasmatic fibrinogen was examined in patients with CAP.

Several biomarkers increase in bacterial infections. Some of these biomarkers are ESR, CRP and Procalcitonin. Procalcitonin is the early marker of infection in CAP, and increased level of 0.25-0.5mg/ml is the indication for commencing antibiotic therapy. In addition, reduction of level of fibrinogen is useful in determining the duration of antibiotic therapy, and also helpful in predicting the mortality rate (6). In the study by Stolz et al, the sensitivity and specificity of the signs and symptoms of

bacterial infection of the lower airways in the decision to start antibiotic therapy was low (7).

A prospective cohort study has shown that physicians overestimate the risk of death in patients with CAP, and this leads to unnecessary admissions to hospital (8).

In the study by Muller et al in 2007 in Switzerland, the results showed that along with other signs and symptoms of pneumonia, including radiographic and clinical findings, application of Procalcitonin is very valuable (5).

In a similar study in the University Of Basel, Switzerland, on the role of biomarkers in the diagnosis and treatment of CAP, Mirjam et al concluded that Procalcitonin alone is not useful in the diagnosis CAP and should be interpreted along with other symptoms and findings of the disease (9).

Lacoma et al suggested that the CRP level was significantly higher in patients with pneumonia (8). In our study, a significant inverse linear relationship between the pre-treatment levels of CRP and fibrinogen in the patients under study (P=0.008 & r=-0.376). In a study by Faran et al, they suggested that the use of inflammatory biomarkers is of particular importance in the diagnosis of pneumonia, and in this study, it is proposed that CD14 and fibrinogen are not a reliable marker for the diagnosis of CAP, and the level of fibrinogen in patients with pneumonia was less than the control group (10).

In another study by Faran et al, examining the level of fibrinogen in patients with pneumonia and pulmonary edema, they suggested that in the first 48-72 hours the level of fibrinogen in patients with pneumonia and pulmonary edema was significantly higher than in healthy people in the control group (11). In our study, the mean fibrinogen levels in patients before and after treatment in patients were 579.06±207.54 and 470.50±127.94 respectively.

The mean post-treatment level of fibrinogen is significantly lower, indicating that the post-treatment level of fibrinogen in patients with pneumonia significantly decreases.

In a study by Hedlund et al in Sweden, examining the level of CRD and IL6 in patients with pneumonia, they suggested that high level of CRP and IL6 in patients with pneumonia is associated with prolonged hospital stay, prolonged and severe fever, and also increased hospital mortality in these patients (12). In a study by Ranzanir et al in ICU ward of the Hospital of University of São Paulo in 2013, indicated that the level of CRP is associated with hospital mortality in these patients (13).

In 2006, in a study by Lagerstrom et al in the Department of Family Medicine, University of Orebno, Sweden, examining the levels of CRF and ESR in patients with pneumonia, they suggested that the levels of CRP and ESR in patients with pneumonia increases compared to those in healthy people, and also, there was no significant relationship between the levels of CRF and ESR with different etiologies of CAP (14). In our study, there was a significant inverse linear relationship between the pre-treatment levels of CRP and fibrinogen in the patients under study.

In a study by Mantinot et al at the Department of Infectious and Tropical Diseases of the University of Hopitaux, Strasbourg in 2001, examining the levels of CRP and PCT in patients with CAP, they suggested that the levels of CRP and PCT increases in these patients (15).

Table.1 CURB-65 Scores of the patients

	Sex		Total
	Male	Female	
Confusion	12	7	19
Urea≥ 20 mg/dl	34	20	54
RR≥ 30	8	12	20
BP(SBP ≤ 90 or DBP ≤ 60)	9	4	13
Age≥ 65	20	17	37

Table.2 The frequency of CURB-65 scores of the patients in each gender

	Sex		
	Male	Female	Total
CURB-65-0 score	0	1	1
CURB-65 1 score	7	3	10
CURB-65 2 score	10	2	12
CURB-65 4 score	12	11	23
CURB-65 5 score	5	5	10

Table.3 Laboratory findings in patients before and after treatment

	Sex		P
	Male	Female	
Urea	67.97± 40.35	53.27 ± 25.10	0.099
WBC –Before	13941.18 ± 5096.71	12177.73 ± 7217.07	0.288
Hb – Before	53.89 ± 221.56	17.58 ± 28.32	0.449
ESR – Before	60.58 ± 30.34	64.82 ± 33.46	0.638
WBC - After	9635.19 ± 4354.49	7900.00 ± 5633.32	0.208
Hb - After	11.89 ± 1.80	15.65 ± 19.64	0.381
ESR - After	54.21 ± 23.62	56.48 ± 30.00	0.759

Table.4 CRP levels in patients before and after treatment

		Sex		P
		Male	Female	
CRP Before	0	1	0	0.008
	1+	20	7	
	2+	13	11	
	3+	0	4	
CRP After	0	1	0	0.412
	1+	19	10	
	2+	11	9	
	3+	3	2	

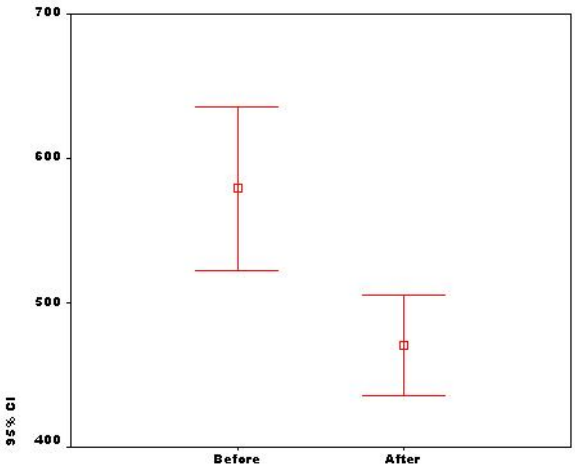

Figure.1 The ranges of fibrinogen levels in the patients before and after treatment

The results obtained in our study suggest that the patients with CAP had higher level of fibrinogen on admission, which had no significant relationship with the severity of disease in patients; however, there was an inverse relationship between the pre-treatment levels of CRP and fibrinogen in the patients under study.

Conclusion

Out of 56 patients with CAP, 34 were male and 22 were female. The mean pre-treatment level of fibrinogen was significantly lower than the mean post-treatment level of fibrinogen in the patients under study, indicating that the level of fibrinogen in patients with pneumonia significantly decreases after treatment. There was no significant linear relationship between age, respiratory rate, systolic and diastolic blood pressure and blood urine of patients with fibrinogen levels before and after treatment. There was no significant linear relationship between CURB-65 scores of patients with fibrinogen levels before and after treatment. There was a significant inverse linear relationship between the pre-treatment level of CRP of patients and fibrinogen levels before and after treatment. There was no significant linear relationship between the post-treatment level of CRP of patients under study with fibrinogen levels before and after treatment. There was no significant linear relationship between the pre-treatment level of CRP of patients under study with fibrinogen levels before and after treatment.

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