

Investigation serum procalcitonin in patients with exacerbation of obstructive pulmonary disease

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a disease of chronic diffuse irreversible airflow obstruction. Due to the relatively high prevalence of the disease, paying attention to the treatment of these patients helps a lot in controlling the disease and reducing its cost. This study aimed to investigate the presence of serum procalcitonin in patients with an acute attack of COPD.

Methods & Materials: This cross-sectional study was performed on 65 patients with an acute COPD attack in Imam Reza Hospital in 2019 by the convenience sampling method. Three ccs of blood samples were taken from patients to check serum procalcitonin levels from hospitalization to 24 hours after that. Patients with an acute COPD attack were selected based on American thoracic society criteria. Also, demographic information such as age, sex, hospitalization time, and duration of the disease was recorded. Patient complaints, disease exacerbation, and type of ventilation were recorded. Data were analyzed with SPSS software (version 16). Man-Whitney and Kruskal Wallis tests were used to analyze the data. The significance level was <0.05. Informed consent was received from all participants.

Results: According to data, 65 patients (36 men and 29 women) were examined and the mean age of the patients was 66.72 (± 12.65) years. Dyspnea was the most common complaint in patients. Serum procalcitonin levels were higher in patients with invasive ventilation ($P = 0.007$). Also, serum procalcitonin levels were lower in patients with non-invasive ventilation ($P = 0.008$). Besides, serum procalcitonin levels increase with increasing disease exacerbation from mild to moderate ($P < 0.001$). According to the results of the post hoc test, there was a significant difference between mild and severe ($P < 0.001$) and moderate and severe groups ($P < 0.001$). There is also a significant correlation between procalcitonin serum levels and exacerbation ($R=0.6$, $P < 0.001$) and age ($R=0.2$, $P = 0.01$). serum procalcitonin levels were higher in patients with the use of invasive ventilation

Conclusion: According to the results, serum procalcitonin levels are associated with acute COPD attacks. Measurement of procalcitonin levels in patients with acute COPD attacks can help diagnose and perform timely care.

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Introduction

According to the latest definition of the World Health Organization, chronic obstructive pulmonary disease (COPD) is a chronic pulmonary disorder associated with irreversible restriction of airflow(1). Sustainable reduction in expiratory flow rate is the most prominent feature of chronic pulmonary obstructive pulmonary disease(2, 3). Also, an increase of residual volume, the ratio of residual volume to total lung capacity, non-uniform distribution of ventilation, and a mismatch between ventilation and blood supply are other characteristics of this disease(4). Three hundred million people have COPD globally(5). About 16 million Americans have chronic obstructive pulmonary disease, and it is estimated to be the sixth leading cause of death in the United States. In Iran, in the age group of 15 to 49 years, the number of people with chronic obstructive pulmonary disease is 105 people per 100,000 people, and in the age group over 55 is 1057 people per 100,000 people(6, 7). The life expectancy of these patients is 5-10 years. The estimated direct and indirect cost to them is \$ 45 billion annually. Many of these patients' activities are limited and reduces their quality of life(8). Increased serum level of procalcitonin in acute patients with chronic obstructive pulmonary disease enhances the COPDs re-attacks and hospitalization, and its positivity is used to initiate antibiotic therapy as well as the course of treatment(9, 10). Exacerbation of COPD is usually characterized by an increase of breath shortness, cough, and changes in the amount and type of sputum (11). In COPD patients, quality of life is related to the frequency of exacerbations. Patients with moderate to severe airway obstruction usually have one to three attacks per year. Patients with moderate to severe COPD will have more severe and prolonged symptoms during exacerbations (12). Exacerbations are the main reason for patients to be hospitalized with stable COPD, and especially after the first hospital stay, is a factor for subsequent hospitalizations. Previous studies have shown that enhancement of procalcitonin has been associated with an increase in disease

attacks and hospitalization time for chronic obstructive pulmonary disease(13). But the results have not been described in detail and conflict. According to this information, this study aims to determine the serum level of procalcitonin in patients with an acute attack of chronic obstructive pulmonary disease.

Materials and Methods

In this cross-sectional study, which was conducted at Mashhad University of Medical Sciences, Iran in 2019, 65 patients (According to the Ergon et al study (9), the sample size was calculated: $N = (z_{(1-\alpha/2)} + z_{(1-\beta)})^2 p(1-p) / d^2 = (1.96 + 0.84)^2 * 0.238 * 0.762 / (0.15)^2 = 64.3$, With alpha of 0.05 and power of 80% and accuracy of estimation of 0.15, the sample size of 64.3 people was calculated. Which was considered 64 people) with acute COPD attacks referred to (Imam Reza Hospital were examined. Inclusion criteria include patients with an acute COPD attack (based on the American Thoracic Society criterion) who do not have another underlying disease that increases procalcitonin. Non-entry criteria include Antibiotic use for the past three months. Patients with acute COPD attack were selected by the convenience sampling method and procalcitonin serum level were measured. Demographic information such as age, sex, smoking, comorbidities, history of previous hospitalization, duration of hospitalization, duration of illness, and medications were recorded by checklist at the beginning of the study. The acute attack of COPD was defined by a sudden increase of breath shortness and exacerbation of cough and sputum, which led to hospitalization in the emergency department, lung ward, and ICU based on guidelines and other studies (2). Clinical signs and complaints of the patient, severity of the disease (mild, moderate, and severe), type of ventilation, routine examination, respiration and heart rate, PH, cyanosis, systemic blood pressure, and body temperature were identified and recorded. Blood samples were taken in 3ml volume from eligible patients for examining procalcitonin serum levels. Blood sampling was performed from the time of hospitalization to 24 hours after hospitalization and was sent to the same laboratory for examination.

The consent form was filled by patients before entering the study.

Statistical analysis

Data were entered into SPSS software (version 16) and were analyzed. Data were expressed as mean \pm standard deviation and in the form of appropriate tables. **Mann-Whitney U** and Kruskal Wallis were used to comparing the data. To figure out the relationship between smoking history and opium consumption with patients' gender, Chi-squared and Fisher's exact tests were used. The post-Hoc test (Tukey's-b) was used to compare groups ($P < 0.05$ was considered statistically significant). To investigate the relation between serum procalcitonin levels and other variables, spearman test was used.

Results

In this study, 65 patients were included in the study and their mean age was 66.72 ± 12.65 years. According to patient data, 36 patients in the study were male and 29 were female. Also, 23 patients were under 60 years old, 16 were aged 61-70 years and 26 were over 70 years old.

According to the results in table 1, sixty-six percent of patients had a history of smoking and 56.9 percent had a history of using opium. Patients' complaints during hospitalization were: shortness of breath in 32 people, cough in 5 people, and consciousness disorder in 28 people, respectively. The duration of chronic obstructive pulmonary disease was 1-5 years

In 36 people, 6-10 years in 17 people, 11-15 years in 7 people, and more than 15 years in 5 people. The duration of hospital stay in 36 people was 1-5 days, in 16 people 6-10 days, in 3 people 11-15 days, in 6 people 16-20 days and in 4 people more than 20 days.

According to data in table 2, serum procalcitonin levels were higher in patients with invasive ventilation ($P = 0.007$). Also, serum procalcitonin levels were lower in patients with non-invasive ventilation ($P = 0.008$). The results of the Kruskal-Wallis test showed that Serum procalcitonin levels increase with increasing disease exacerbation from mild to moderate ($P < 0.001$) and the median of serum procalcitonin levels were higher in patients with more exacerbation. Post Hoc test was used to compare the two groups. According to the results, there was a significant difference between mild and severe ($P < 0.001$) and moderate and severe groups ($P < 0.001$).

According to results in table 3, the results of the correlation test showed that there was a significant relationship between serum procalcitonin levels and exacerbation ($P < 0.001$) and age ($P = 0.01$) that serum procalcitonin levels were directly related to exacerbation and age. However, there was no relationship between serum procalcitonin levels and duration of obstructive pulmonary disease ($P = 0.23$) and hospital stay ($P = 0.1$).

Table 1: Demographic variables

Variables		Frequency	Percentage
History of smoking		43	66.1
History of using opium		37	56.9
Chief complaint	Shortness of breath	32	49.2
	Cough	5	7.7
	Awareness disorder	28	43.1
Duration of the disease (years)	1-5	36	55.4
	6-10	17	26.2
	11-15	7	10.8
	>15	5	7.6
hospitalization time (Days)	1-5	36	55.4
	6-10	16	24.6
	11-15	3	4.6
	16-20	6	9.2
	>20	4	6.2

Table 2: Serum levels of procalcitonin in patients were studied by gender, blood pH, respiratory status, cyanosis, and exacerbation.

Variables		N	Median	IQR	P-value	
gender	Male	36	0.2	0.18	0.37	
	Female	29	0.2	0.40		
Blood PH	Normal	38	0.2	0.30	0.1	
	Abnormal	27	0.22	0.44		
Respiratory status	Use of oxygen	Yes	20	0.2	0.84	
		No	45	0.2		0.32
	IV*	Yes	13	0.56	2.05	0.007
		No	52	0.2	0.17	
	NIV**	Yes	35	0.2	0.02	0.008
		No	30	0.30	1.19	
Cyanosis	Yes	44	0.2	0.22	0.5	
	No	21	0.2	0.58		
Exacerbation	Mild	23	0.2	0.00	<0.001	
	Moderate	23	0.2	0.02		
	Severe	19	0.98	7.07		

*IV: invasive ventilation

**NIV: noninvasive ventilation

Table 3: Correlation between serum procalcitonin levels and study variables

Variables	Exacerbation	Hospitalization time	Duration of the disease	Age	
Procalcitonin (N=65)	R*	0.6	0.2	0.15	0.29
	P value	<0.001	0.1	0.23	0.01

*The correlation coefficient, Spearman test

Discussion

Chronic obstructive pulmonary disease is one of the most serious health problems and common lung diseases and is the fourth leading cause of death in patients. The American Thoracic Society has defined COPD as a disease in the form of progressive and chronic airway obstruction due to chronic bronchitis, emphysema, or both. These diseases are progressive and limit the respiratory capacity, reducing airflow through the airways, and their prevalence is increasing day by day. On average, 15% of adults over the age of 55 have COPD, a large percentage of them are female. COPD is observed in 15-20% of smokers, and approximately 45% of patients have some degree of limitation in their activities. Therefore, due to its chronic nature, this disease has a profound effect on the life process of patients, affecting their health, family life, social support, and economic

progress. According to similar studies, increasing of Procalcitonin serum level in patients with an acute attack of chronic obstructive pulmonary disease increases COPDs re-attacks and hospitalization, and its positivity is used to initiate antibiotic therapy and treatment(14).

This study aimed to investigate the presence of procalcitonin in patients' serum with an acute attack of obstructive pulmonary disease. The mean age of patients was 66.72±12.65 years. The results of the statistical analysis showed that there is a significant difference between procalcitonin serum level and age of patients and with increasing of patient's age, the average procalcitonin serum level increases, which corresponds to the age of adults with COPD. In the study, conducted by Chang et al. (6), Looked at Procalcitonin as a differentiation factor in distinguishing between virus and infection in patients with COPD, and also the

age of patients and its relationship with serum levels of procalcitonin was evaluated. The researchers concluded that as patients got older, the average serum levels of Procalcitonin in patients with COPD increased, which is consistent with the results of the present study. Thirty-six (55.4%) of the patients in this study were male and 29 (44.6%) were female. The results showed that there was no significant difference between procalcitonin serum level and sex of patients, but procalcitonin serum levels were higher in female patients than in male patients. One study found that high serum levels of procalcitonin were a stronger predictor of women's deaths than men (13). Which is consistent with the results of our study. The results showed that there was a significant relationship between the history of smoking and the history of opium consumption with the sex of patients, and the history of smoking and opium consumption was higher among men than women. Patients' complaints at the time of hospitalization included: shortness of breath in 32 people (49.2%), cough in 5 people (7.7%), and consciousness disorder in 28 people (43.1%). The duration of chronic obstructive pulmonary disease in 36 people (55.4%) was 1-5 years, in 17 people (26.2%) was 6-10 years, in 7 people (10.8%) was 11-15 years and 5 people (7.6%) had this disease for over 15 years old. Also, the duration of hospitalization in 36 people (55.4%) was 1-5 days, in 16 people (24.6%) 6-10 days, in 3 people (4.6%) 11-15 days, in 6 The person (9.2%) was 16-20 days and the 4 people (6.2%) stayed at the hospital for over 20 days. The results of the statistical test also showed that there was no significant difference between procalcitonin serum level and time of hospitalization. In a study by Ergan et al. (9), procalcitonin was evaluated as a determinant factor of hospitalization time and mortality rate of COPD patients in the hospital. The researchers concluded that the procalcitonin serum level was a contributing

factor in predicting and estimating hospital mortality rates in patients with COPD that matched the results of the present study.

The results of the present study showed that there was a significant difference between procalcitonin serum level and exacerbation and procalcitonin serum level was higher in patients with high exacerbation. In a 2017 study by Yanyan et al. (12), serum levels of procalcitonin in patients with acute COPD were investigated as a prognostic factor. In this study, the researchers found that in patients with an acute COPD attack, increased serum levels of procalcitonin reduced clinical improvement and correspond with the results of our study. In a study by Stolz et al. (15), procalcitonin was studied as a determinant factor of mortality in COPD patients. The researchers concluded that procalcitonin serum level was associated with patients' survival. Other results of the present study showed that there was no significant difference between procalcitonin serum level and hypoxemia levels of patients and procalcitonin serum levels were higher in patients without cyanosis. There was also no significant difference between procalcitonin serum level and patients' blood pH, and procalcitonin serum level was higher in patients with abnormal blood PH. Also, results showed that there was no significant difference between procalcitonin serum level and oxygen utilization, and procalcitonin serum level and were higher in patients who did not use oxygen. The results of statistical analysis showed that there is a significant difference between procalcitonin serum level and invasive ventilation and higher procalcitonin serum level was observed in patients who had invasive ventilation. There is also a significant difference between the serum levels of procalcitonin and NIV for patients. In a 2017 study by Giorgi et al. (13), the serum levels of procalcitonin in patients with acute COPD attack was investigated as a prognostic factor. In this study, the researchers found that in

patients with an acute COPD attack, procalcitonin serum level alone could not be a definitive predictor of COPD in patients with ventilation. Which is inconsistent with the results of our study. According to the study and comparing the results of this study with other studies, the examination of the procalcitonin serum level in COPD patients can help us to early diagnosis and timely treatment and can reduce many of the complications in patients with COPD.

Limitations

There are also limitations in our study that can be mentioned. Also, the sample size was lower compared to similar articles in other places. Based on the mentioned points, it is recommended that further studies be conducted to confirm the findings of this study. Due to the fact that the test is performed from the time of hospitalization to 24 hours after hospitalization, the next studies should be performed in series and with a longer test duration.

Conclusion

Overall, based on present study results and comparison with other studies, it is concluded that evaluating procalcitonin level while patients with an acute attack of obstructive pulmonary disease refer to the hospital, can be helpful in early diagnosis and care, and considering that the increased mortality in patients with high procalcitonin levels, more intensive care and hospitalization in the ICU may be needed during this time.

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