Original Article

Relationship between Patients with Chronic Obstructive Pulmonary Disease and Serum S100B Protein

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a common cause of death and disability worldwide. Brain hypoxia due to acute COPD exacerbation or in chronic course of disease can affect the central nervous system and lead to behavioral and cognitive dysfunction. In addition, hypoxia causes brain injury which increases the serum biomarker of S100B protein excreted from astrocytes. The aim of the study was to assess the effect of hypoxia following COPD exacerbation on the brain by measuring the S100B. **Methods:** Our study consisted of group of COPD patients. These groups had 80 peoples. The serum S100B protein levels of COPD patients who were admitted to the emergency department of a teaching Hospital were measured by the ELISA method, and their correlation with other clinical and laboratory parameters was assessed. Statistical methods consisted of mean ± standard deviation. We assessed the association between two categorical variables of S100B and presence or absence of COPD by Chi-squared test. We used SPSS version 21 with $p<0.05$ considered significant. **Results:** Out of 80 COPD exacerbation patients, 39 (48.8%) were men. The mean age of the patients was 66 ± 12.76 years (range, 30–87). S100B protein was positive in 35 (43.8%) and negative in 45 (56.2%) patients. There were no significant correlations between S100B and other parameters, such as PH, O_2 Saturation, bicarbonate, and clinical findings such as respiratory rate, pulse rate and blood pressure, except for carbon dioxide in arterial blood (PaCO2) (p=0.046). **Conclusion:** Serum S100B protein was higher in acute COPD exacerbation patients and could be a marker of brain injury.

Keywords: COPD Exacerbation; S100B Protein; Dyspnea

Introduction

Chronic obstructive pulmonary disease (COPD), a common preventable and irreversible disease, is characterized by air flow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patient. [1] COPD is one of the most common causes of death worldwide. [2-4] The most common cause of COPD is cigarette smoking; breathing other types of irritant materials, such as dust and chemicals pollutions, can also lead to COPD. [5] Due to an increased smoking rate and the late onset of disease, the prevalence of COPD continues to increase and is expected to remain the seventh cause of decrease quality of life up to 2030. [6]

The diagnosis of COPD is confirmed by spirometry; COPD diagnosis must be considered in patients with symptoms of dyspnea, chronic coughing, sputum for three months in two consecutive years and history of exposure to COPD risk factors. Since the development of COPD is slow, it is more frequently diagnosed in individuals 40 years of age or older. [7] The pulmonary symptoms of COPD are characterized by limitations in airflow that are not fully reversible. This limitation is usually progressive. [8] The base of COPD physiopathology is airway inflammation, which can lead to hypoxia and attacks of breathlessness. [9]

Dyspnea attacks decrease brain cognitive function [10,11] One study showed that cerebral perfusion changes significantly in COPD patients; therefore, hypoxemic patients showed more deterioration in cerebral perfusion and cognitive performance than non-hypoxemic patients. [12] Because Astrocytes secrete S100B protein in response to cerebral damage and stress, S100B protein could be considered as a marker of cerebral damage in plasma and cerebrospinal fluid. [13-15] The term S100B refers to members of a multigenic family of calcium-modulated proteins (S100 proteins), mostly of low molecular mass. [14]

In terms of quality of life, cerebral damage consequent to hypoxia has not been given much attention in COPD patients; moreover, life expectancy is strongly dependent on the health of the central nervous system in these individuals. Due to lack of research in this field, we studied the effect of hypoxic attacks of dyspnea on the brain by measuring S100B protein levels in plasma. Because S100B protein is

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secreted by astrocytes during cerebral damage; we considered it as a suitable marker for assessing changes in the brains of COPD patients.

Material and Methods

Our study included group that consisted of 80 peoples who had COPD. Eighty patients (30–87 years of age) diagnosed with COPD referring to the University Hospital over six months. 76 (95%) of the patients were found with dyspnea and 4 (5%) had other reasons for referring to the center. It is to be noted that the COPD diagnosis was made by a single pulmonologist.

Measurement of S100B

Measurement of serum S100B concentration blood samples (3-5 ml) were collected in a regular exanimation and after obtaining informed consent. Serum was obtained by centrifugation and then frozen at −70°C and were sent to a reference laboratory. Serum S100B concentration was measured using a commercial enzyme-linked immunosorbent assays (ELISA).

Because the half-life of the S100B protein in peripheral blood is one hour [14,15], the blood samples were taken from the patients immediately upon arrival before receiving high-flow oxygen, and were sent to the laboratory within less than 15 minutes. To determine the S100B protein levels, serum samples were kept to maintain the chain and other parameters.

The following data were collected: Age, gender, cardiopulmonary disease status, respiratory rate, heart rate, serum Creatinine, arterial oxygen saturation by pulse oximetry, the amount of carbon dioxide in arterial blood and pH by arterial blood gas laboratory analysis method.

Statistical analysis

The data were statistically analyzed using SPSS version 21 and described with charts, graphs, mean and standard deviation indicators. Kolmogorov–Smirnov test was used to assess the normality of the S100B. We assessed the association between the numerical variable of S100B and presence or absence of COPD using Analysis of Variance (ANOVA) test. In all the tests, the significance level was considered to be 0.05.

Ethical considerations

We obtained informed consent the patients who participated in this study. The patients were informed about the privacy and confidentiality of their medical information. In order to maintain the confidentiality concept, the all data of the patient were coded. The blood test for S100B was free of charge.

Results

Gender distribution in COPD patients of the 80 COPD exacerbation patients, 39 (48.8%) were male and 41(51.2%) were female. The mean age of the patients was 66 ± 12.76. S100B protein was positive in 35 (43.8%) cases of COPD patients.

The detail of descriptive data for COPD patients showed the following mean ± SD for the following variables: Respiratory rate: 28 ± 8; pulse rate: 101 ± 22; systolic blood pressure: 137 ± 21; diastolic blood pressure: 84 ± 11; O2 saturation: 78 ± 13; PCO2: 45 ± 13; blood sugar: 158 ± 59; BUN: 24 ± 14; creatinine: 1.3 ± 1; WBC: 9074 ± 3267; bicarbonate: 31 ± 7. In the case group of COPD patients, twelve patients had concurrent congestive heart failure (CHF), 28 had another lung disease, and four (5%) had both lung and heart diseases. Only 29 patients had COPD alone.

Table 1: Characteristics of COPD patients.

Characteristics	COPD group (n=80)
Female/male	41 / 39
With cardiovascular disease	12
With other respiratory disease	28
With heart and lung disease	4
Loss of consciousness	11
S100B	
Positive	35
Negative	45

Table 2: Number and percentage of positive and negative S100B based on presence or absence of respiratory and cardiovascular diseases.

COPD patients	Number	S100B Positive (%)	S100B Negative (%)
Without heart and lung disease	29	40	63
With cardiovascular disease	12	0	23
With other respiratory diseases	28	60	2
With heart and lung disease	4	0	12
Loss of consciousness	11	0	0
With cardiovascular disease*	4		
Without heart and lung disease	7		
Total	80	100	100

*Among COPD patients with cardiovascular disease, there were four patients who lost their consciousness.

Statistical descriptions of some variables were assessed in the COPD patients [Tables 1 and 2]. Number and percentage of positive and negative S100B based on presence or absence of respiratory and cardiovascular diseases has been shown in Table 2.

There were no significant relationships between S100B protein and other laboratory parameters, such as PH, O2 saturation, respiratory rate, systolic blood pressure, mean arterial pressure, bicarbonate, and respiratory rate.

No significant relationships were observed between S100B protein and age or gender. However, there was a significant relationship between PCO2 and S100B (p=0.046).

Discussion

We studied 80 patients with previously diagnosed COPD that was confirmed by a pulmonologist. S100B protein levels were positive in 55% of the patients. A previous study also reported a significant difference in S100B levels between groups. In a study, the S100B protein levels were measured in patients with COPD who suffered from pulmonary encephalopathy and authors concluded that the observed increase in serum S100B protein levels could be caused by hypoxia. Consistent with that study, we found that the relationship of S100B protein and carbon dioxide of arterial blood was significant. They showed that S100B protein level was inversely related with blood pH and partly correlated with arterial blood oxygen and carbon dioxide.

Ueno et al. reported that the S100B protein levels in patients with loss of consciousness or seizures after surgery were higher than in individuals without those disorders. [16] Their findings could be considered as a confirmation for our results in terms of decreasing brain function and elevated S100B protein.

Hung et al. assessed the cognitive function of patients with COPD over six years. Correspondingly, they showed that the disease might reduce brain performance, which was directly associated with illness severity. [17] Li and Fei found that serum S100B concentration is higher in COPD patients compared with control subjects. The possible explanation is

that changes in hippocampal structure and volume appear to arise from a reduction in neural processes and synapses, rather than from neuronal loss.[18]

In our study, there was a significant association between S100B protein and respiratory system disorders in patients with lung disease. However, due to a higher average level of S100B protein in these patients compared to the total study population, this was a direct and positive relationship. In addition, as mentioned before, the S100B protein level of CHF patients was significantly lower than patients with COPD alone or with other lung diseases.

Protein S100B can be an indirect marker for hypoxic brain damage in exacerbated attacks of COPD. Therefore, it could be one of the reasons that cause fluctuation in consciousness levels in these patients.

Limitations and Suggestion

There was no peak flow meter and capnogram in the Emergency Department to evaluate the association of protein S100B with the severity of COPD attacks. For future applications, we suggest evaluation of S100B and severity of COPD attacks in the presence of peak flow meter. Another suggested research is to compare S100B in COPD exacerbation before and after treatment.

Conclusion

Serum S100B protein was higher in acute COPD exacerbation patients and could be a marker of brain injury. Therefore, oxygen therapy is the best way to minimize brain damage.

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This study is thesis presented to achieve the degree of specialist in Emergency Medicine by Dr Alireza Movahedan in the school of medicine of Mashhad University of Medical Sciences under supervision of Dr Amir Masoud Hashemian.

Conflict of Interest

The authors disclose that they have no conflicts of interest.

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