Egyptian Journal of Chest Diseases and Tuberculosis 66 (2017) 739–743

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Egyptian Journal of Chest Diseases and Tuberculosis

journal homepage: www.sciencedirect.com

Assessment of serum Retinol-Binding Protein-4 Levels in patients with acute exacerbation of chronic obstructive disease at intensive care unit

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ARTICLE INFO

Article history:
Received 31 August 2017
Accepted 11 October 2017
Available online 6 November 2017

Keywords:
Acute exacerbation of chronic obstructive pulmonary disease
Retinol-Binding Protein-4
Intensive care unit

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a major cause of mortality and morbidity. Retinol-Binding Protein 4 (RBP4), has been recognized as an adipokine implicated in COPD. In this study we assessed the level of serum RBP4 in patients with acute exacerbation of COPD (AECOPD) at intensive care unit and compared to stable patients and healthy controls.
Objective: Assessment of serum RBP4 in patients with AECOPD at intensive care unit and the possibility of its use as a predictive biomarker for mortality in AECOPD.
Patients and method: This study was conducted on Ninety persons divided into 3 groups: *Group 1*: Forty patients with AECOPD admitted to ICU. *Group 2*: Thirty patients with stable COPD. (Group 1 and 2 were classified according to Global Initiative for COPD (GOLD, 2015). *Group 3*: Twenty healthy persons as a control. They were subjected to full history taking, clinical examination, Investigations as liver and kidney functions and serum RBP4 assessment by Enzyme-linked immunosorbent assays.
Samples were collected within first 24 h of admission.
Results: There was a significant decrease in serum RBP4 in patients with AECOPD (mean 71.73 ± 33.43) mg/L admitted in ICU than other 2 groups: stable COPD (mean 177.53 ± 93.24) mg/L and healthy controls (mean 231.21 ± 122.90) mg/L and further decrease in non survivors (mean 48.57 ± 16.26) mg/L than survivors (mean 106.46 ± 18.85) mg/L. ($Z = 5.301$, $p \leq .001$). RBP4 was positively correlated with body mass index and serum albumin, while negatively correlated with serum creatinine, c reactive protein, total bilirubin and APACHE-II score.
Conclusion: Serum-Retinol-Binding Protein-4 can be used as a predictive biomarker for mortality in AECOPD. We recommend that the serum RBP4 should be taken in consideration as a part of the assessment of mortality of AECOPD patients admitted in ICU.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common preventable and treatable disease, characterized by persistent airflow 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 cormorbidities contribute to the overall severity in individual patients [1]. Patients with Acute of Chronic Obstructive Pulmonary Disease (AECOPD) have high mortality rates and usually need admission to intensive care units (ICUs) [2]. Mortality rates with AECOPD in ICU can be up to 50% [3]. Many factors have been identified as predictors of ICU mortality in patients with COPD [4]. Adipose tissue is a potent producer of inflammatory mediators and may contribute to systemic inflammation in COPD [5]. Adipokines are associated with the systemic inflammatory process during exacerbations of COPD [6]. Retinol-Binding Protein-4 (RBP4) is a molecule found in the circulation, thought to be secreted mainly by adipose tissue and the liver, and is a specific transporter for retinol in the circulation [7]. Recently, RBP4 has been extensively studied and is associated with various pathologies [8,9].

Patients and methods

This study included Ninety cases: – forty with (AECOPD) admitted to intensive care unit (ICU), thirty with stable COPD and twenty

Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.
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https://doi.org/10.1016/j.ejcdt.2017.10.009
0422-7638/

healthy elderly persons. All cases were classified according to GOLD [1] and all patients' data were collected from December 2014 to December 2015. Spirometry was used to diagnose COPD, the presence of a post-bronchodilator FEV1/FEV < 0.7 assures the presence of continual airflow limitation and so, for COPD according to the GOLD, [1].

AECOPD patients admitted to the ICU must have at least one of the following indications [10]:

1) Severe dyspnea that not responds adequately to the initial emergency therapy.
2) Disturbances in mental status (lethargy, confusion, coma).
3) Persistent hypoxemia (PaO_2 < 5.3 kPa, 40 mmHg), and/or severe or worsening of hypercapnia ($PaCO_2$ > 8.0 kPa, 60 mmHg), and or severe of respiratory acidosis (pH < 7.25) in spite of additional oxygen and noninvasive ventilation.
4) Indications for invasive mechanical ventilation.
5) Hemodynamic instability and the demand for vasopressors.

Cases were subjected to:

1) Full History: focusing on: – history of smoking, exposure to risk factors of COPD, having any exclusion criteria as – bronchial asthma, bronchiectasis, interstitial pneumonia, pulmonary tuberculosis, pulmonary fibrosis, and lung cancer [11].
2) Clinical examination: including general examination, vital signs and local chest examination.
3) Investigations as chest X-ray, laboratory analysis as liver and renal functions, CRP, ABG. Serum RBP4 assessment by Enzyme-linked immunosorbent assays: Using enzyme immunoassay for the measurement by RBP4 (Sandwich) ELISA kits.
4) Acute Physiology and Chronic Health Evaluation (APACHE) II Score.
5) Body Mass Index: using the Quetelet's index; weight (kg)/[height(m)]^2 [12].

Samples collected within the first day after ICU admission, with an ICU stay of ≥72 h.

All patients were scheduled for a follow-up visit till being discharged from the ICU (survivors) or they died in the ICU (non-survivors).

Statistical analysis of the data

Data were put to the computer and analyzed using IBM SPSS software package version 20.0. Comparison between different groups regarding categorical variables was tested using Chi-square test. Correlations between two quantitative variables were assessed using Spearman coefficient. Significance of the obtained results was judged at the 5% level [13].

Results

Descriptive parameters between the three studied groups:

The results of the present study revealed a significant decrease in serum RBP4 in patients with AECOPD admitted in ICU than other 2 groups: stable COPD and healthy controls Fig. 1. There was no statistically significant difference in age. FEV_1% of predicted, FVC % of predicted and FEV_1/FVC% were decreased significantly in AECOPD patients than the stable COPD patients and healthy controls. The BMI decreased significantly in AECOPD patients in comparison to stable COPD patients and healthy controls. Table 1. In AECOPD patients admitted in ICU were divided more into 2 groups:– survivors group (discharged) and non survivors group (died).

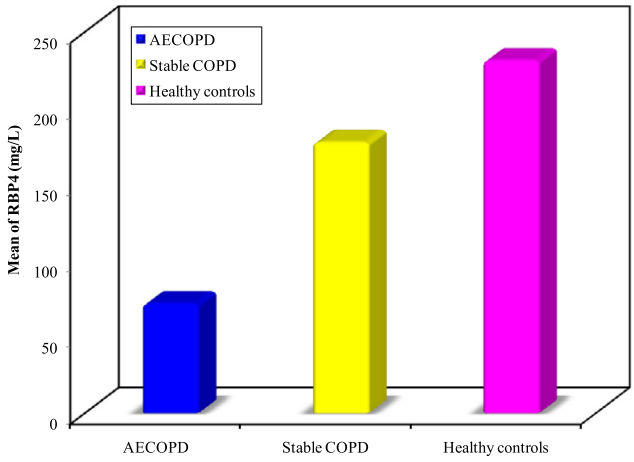

Fig. 1. Comparison between the three studied groups according to RBP4.

Comparison between the Non survivors and survivors

There was no significant statistical difference in age between survivors and non survivors, however; BMI, RBP4, PH, PaO_2, serum albumin and ICU stays were decreased significantly in non survivors than survivors. on the other hand, the results showed significant increase in $PaCO_2$, serum creatinine, blood urea, serum albumin, total bilirubin, APACHE 2 score, white blood count, erythrocyte sedimentation rate and C-reactive protein in non survivors than survivors. Table 2.

Factors affecting serum RBP4

RBP4 was directly related to BMI and serum albumin while inversely related to APACHE 2 score, total bilirubin, serum creatinine and CRP. Table 3 and Fig. 2.

Discussion

The mean age in AECOPD patients was 61.03 ± 3.17 years and in Stable COPD it was 61.33 ± 2.90 years while in healthy controls it was 61.70 ± 4.19 years. Furthermore, the mean age in non survivors patients was 61.21 ± 2.98 while in survivors it was 6o.75 ± 3.51. There was no statistically significant difference in age among the participants included in the study and serum RBP4 ($F = 0.279$, $p = .757$). These results were similar to [14] who studied the relation between mortality and serum RBP4 in ICU of 100 AECOPD patients [14]. In AECOPD: 17 males were non survivors and 12 survivors, while in females 7 were non survivors and 4 survivors. So, there was no significant relation between sex and mortality ($\chi^2 = 0.084$, $p = 1.00$). BMI decreased significantly in non survivors than in survivors. The mean BMI was (19.38 ± 1.70) m^2/kg and (24.86 ± 1.57) m^2/kg respectively, ($t = 10.280$, $p \leq .001$). It is evident that lower values of BMI were associated with increased severity and mortality, giving a negative relation. This is in agreement with Cao et al. [15]. These results reflect the importance of the BMI as a nutritional parameter in assessing the disease severity, as the nutritional depletion, hypoxia and weight loss are included during COPD exacerbation. This is in agreement with a study done by [16] who found that low BMI associated with many risk diseases as osteoporosis and peripheral arterial diseases [16].