Peptides 43 (2013) 8–12

Contents lists available at SciVerse ScienceDirect

Peptides

journal homepage: www.elsevier.com/locate/peptides

Elevated plasma visfatin concentrations in patients with community-acquired pneumonia

Wei Hu*, Chang-Wen Liu, Jun Su, Jun Lu, Ying Zhu, Bing-Wei Liu

Department of Intensive Care Unit, The First People's Hospital of Hangzhou, Nanjing Medical University, 261 Huansha Road, Hangzhou 310006, China

ARTICLE INFO

Article history:
Received 1 February 2013
Received in revised form 21 February 2013
Accepted 21 February 2013
Available online 4 March 2013

Keywords:
Community-acquired pneumonia
Visfatin
Outcome
Mortality
Inflammation
Disease severity

ABSTRACT

Visfatin has been associated with some inflammatory disease. This study aimed to compare plasma visfatin levels in patients with community-acquired pneumonia and healthy controls and to furthermore investigate the relationship between their concentrations and 30-day mortality in patients. Plasma visfatin concentrations were measured in 176 patients and 95 healthy controls. The admission visfatin levels were significantly increased in all patients, survivals and non-survivals with community-acquired pneumonia compared with healthy control individuals, associated with pneumonia severity index score, Acute Physiology and Chronic Health Evaluation II score, white blood cell count, and plasma C-reactive protein level, and identified as an independent predictor for 30-day mortality. Its predictive value was similar to those of pneumonia severity index score and Acute Physiology and Chronic Health Evaluation II score. However, visfatin did not statistically significantly improve the predictive values of pneumonia severity index score and Acute Physiology and Chronic Health Evaluation II score. Thus, higher plasma visfatin level correlates with disease severity and markers of system inflammation and represent a novel biomarker for predicting 30-day mortality in patients with community-acquired pneumonia.

1. Introduction

Visfatin, a peptide predominantly expressed in and secreted from visceral fat in both humans and mice, was originally identified as a pre-B colony enhancing factor [2,24]. Gradually, visfatin is thought to play roles in immune response and inflammation, and therefore, mediates pro-inflammatory actions in various metabolic diseases like obesity, type 2 diabetes and cardiovascular disease [21,25,26]. Furthermore, visfatin concentration in the peripheral blood is increased in patients with sepsis, chronic kidney disease and cancer [13,19,20]. Additionally, high visfatin expression in breast cancer tissue is associated with more malignant cancer behavior as well as poor patient survival [14]; high plasma visfatin levels are also closely related to the degree of myocardial damage in patients with ST-elevation myocardial infarction [16] and independently predict the poor clinical outcomes of severe traumatic brain injury [4] and spontaneous intracerebral hemorrhage [8]. Visfatin also plays critical roles in apoptosis of neutrophils [11] and secretion of interleukin-8 from human pulmonary artery endothelial cells [29]. Recent studies have shown that the visfatin level is significantly increased in bronchoalveolar lavage fluid and serum of acute lung injury in a mouse model [7,28]. A few polymorphisms of visfatin gene are associated with increased odds of developing acute respiratory distress syndrome and an increased hazard of intensive care unit mortality among at-risk patients [1]. Moreover, plasma visfatin levels are increased in patients with chronic obstructive pulmonary disease and its enhancement is significantly correlated with tumor necrosis factor-alpha and C-reactive protein [15]. However, little is known about its plasma concentration in patients with community-acquired pneumonia (CAP). Thus, the present study was to determine the plasma visfatin levels in patients with CAP, as well as to investigate the relationship between the visfatin level and 30-day mortality.

2. Materials and methods

2.1. Study population

This prospective study was conducted during the period of February, 2009 to August, 2011 by the Department of Intensive Care Unit, The First People's Hospital of Hangzhou. The inclusion criteria required that patients be admitted for the treatment of CAP, and be diagnosed at the emergency room. Exclusion criteria included younger than 18 years, transferred from another hospital, discharged from a hospital within the past 30 days, active pulmonary tuberculosis, known to be positive for human immunodeficiency virus, or chronically immunosuppressed (defined as immunosuppression for solid organ transplantation, postsplenectomy,

* Corresponding author. Tel.: +86 0571 87065701; fax: +86 0571 87065701.
E-mail address: hzhuweihuwei@163.com (W. Hu).

0196-9781/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.peptides.2013.02.017

receiving ≥10 mg/day prednisolone or equivalent for more than 30 days, treatment with other immunosuppressive agents or neutropenia [$<1.0 \times 10^9$/L neutrophils]). The patients, who had visfatin measurements unavailable or had missing of follow-up, were also excluded.

Subjects were initially evaluated as controls if they presented to our hospital and had blood collected as part of medical examination on May 2011. Exclusion criteria were <18 years of age, existing previous uremia, liver cirrhosis, malignancy, heart and lung disease. The subjects who had the disagreements were also excluded.

Written informed consent to participate in the study was obtained from the subjects or their relatives. This protocol was approved by the Ethics Committee of The First People's Hospital of Hangzhou before implementation.

2.2. Clinical assessment

Demographic characteristics, co-morbidities, symptoms and signs of pneumonia, and laboratory results were recorded upon admission. The diagnostic criteria for CAP were based on the guidelines of the Infectious Disease Society of America/American Thoracic Society [17]. The guidelines for diagnosis of CAP included a typical infiltration change on chest X-ray films within 1 day of symptom occurrence and at least one clinical manifestation, such as cough, yellow and thick sputum or high fever (>37.8 °C); or at least 2 minor criteria, including tachypnea, dyspnea, pleural pain, chest pain, confusion or disorientation, lung consolidation or white blood cell counts of >12,000 cells/μL. Pneumonia severity was assessed by the two doctors through the pneumonia severity index (PSI) [6], and Acute Physiology and Chronic Health Evaluation (APACHE) II [12]. The endpoint of this study was 30-day mortality.

2.3. Immunoassay methods

The informed consents were obtained from study population or family members in all cases before the blood were collected. Venous blood in the healthy individuals or the CAP patients was drawn at study entry or on admission. The blood samples were immediately placed into sterile EDTA test tubes and centrifuged at $1500 \times g$ for 20 min at 4 °C to collect plasma. Plasma was stored at −70 °C until assayed. The concentration of visfatin in plasma was analyzed by enzyme immunoassay using commercial kits (Phoenix Pharmaceuticals, Belmont, CA) in accordance with the manufactures' instructions. The blood samples were run in duplicate. Researchers running enzyme immunoassay were blinded to all patient details.

2.4. Statistical analysis

Statistical analysis was performed with SPSS 15.0 (SPSS Inc., Chicago, IL, USA) and MedCalc 9.6.4.0 (MedCalc Software, Mariakerke, Belgium). The normality of data distribution was assessed by the Kolmogorovor–Smirnov test or Shapiro–Wilk test. The categorical variables are presented as percentages, and the continuous variables are presented as mean ± standard deviation. Comparisons were made by using (1) chi-square test or Fisher exact test for categorical data, (2) unpaired Student *t*-test for continuous normally distributed variables, and (3) the Mann–Whitney *U*-test for continuous non-normally distributed variables. The correlations of visfatin with APACHE II score and PSI score were assessed by Spearman's correlation coefficient. The relations of visfatin to 30-day mortality were assessed in a logistic-regression model with odds ratio (OR) and 95% confidence interval (CI). Variables showing $P < 0.1$ in univariate analysis were included in the multivariate model. The receiver operating characteristic (ROC) curves were used to determine the best threshold for on admission values of visfatin to predict 30-day mortality. Assessment of the predictive performance of on admission values of visfatin was analyzed by calculating the sensitivity and specificity. The area under curve (AUC) was calculated based on the ROC curves. AUC ranges from 0.5 to 1.0. An AUC closer to 1 indicates a higher predictive power. In a combined logistic-regression model, we estimated the additive benefit of visfatin to APACHE II score and PSI score. A *P*-value of less than 0.05 was considered statistically significant.

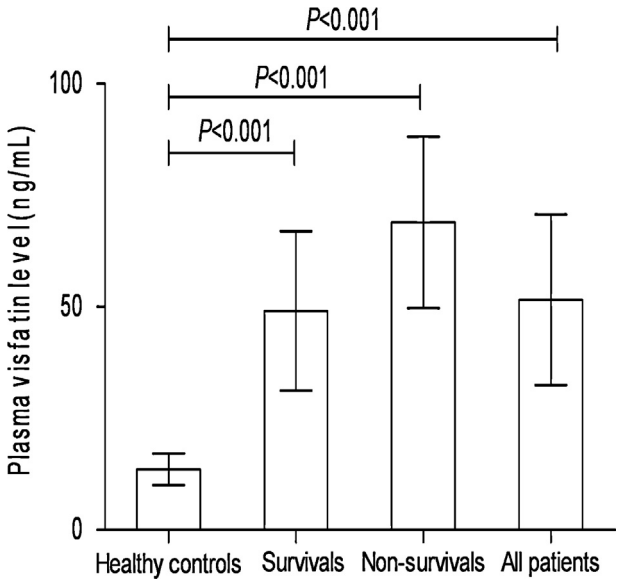

Fig. 1. Graph showing the change of plasma visfatin concentration in patients with community-acquired pneumonia. Data are expressed as mean ± standard deviation.

3. Results

3.1. Study population's characteristics

Finally, 176 CAP patients and 95 healthy controls were enrolled in this study. The intergroup differences in age, gender and body mass index were not statistically significant (all $P > 0.05$). The demographic, clinical and laboratory data of patients were provided in Table 1.

3.2. The change of plasma visfatin level in CAP patients

The admission visfatin levels were significantly increased in all patients (51.6 ± 19.1 ng/mL), survivals (49.1 ± 17.9 ng/mL) and non-survivals (69.0 ± 19.2 ng/mL) with CAP compared with healthy control individuals (13.6 ± 3.5 ng/mL, all $P < 0.001$) (Fig. 1).

3.3. Correlations of plasma visfatin level with disease severity

A significant correlation emerged between plasma visfatin level and PSI score ($r = 0.549$, $P < 0.001$) as well as between plasma visfatin level and APACHE II score ($r = 0.584$, $P < 0.001$) (Fig. 2).

3.4. Correlations of plasma visfatin level with markers of system inflammation

A significant correlation emerged between plasma visfatin level and white blood cell count ($r = 0.294$, $P < 0.001$) as well as between plasma visfatin level and plasma C-reactive protein level ($r = 0.418$, $P < 0.001$) (Fig. 3).