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EDITORIAL

Study of the level of stem cell factor in patients with bronchial asthma



KEYWORDS

Bronchial asthma;
 Stem cell factor;
 Eosinophils

Abstract *Aim of the work:* The aim of this study was to assess serum level of stem cell factor in asthmatic patients and its relation to disease severity.

Methods: This case control study was carried out on 70 individuals classified into 20 healthy control subjects and 50 asthmatic patients that were admitted in Chest Department, Benha university hospital in the period between March 2013 and December 2014. Asthma diagnosis (history and PFT) and assessment of its severity were conducted according to the guidelines of Global Initiative for Asthma (GINA, 2011). Eosinophil percentage in the sputum of asthmatic patients was done. Measurement of stem cell factor (SCF) in the sera was done by Enzyme-Linked Immunosorbent Assay.

Results: Our results found a statistically significant difference (P value < 0.001) between asthmatic patients and control subjects in the mean values of SCF (1192.34 ± 789.89 versus 326.29 ± 274.38 respectively). There was a statistically significant difference (P value = 0.001) between eosinophilic and non eosinophilic phenotype (1457.77 ± 648.83 versus 130.59 ± 83.27 respectively). There was a statistically significant difference in the level of SCF among different degrees of asthma severity ($P = 0.001$). Also, there was a significant negative correlation ($r = -0.288$) between SCF levels and FEV1% and significant positive correlation between SCF levels and sputum ($r = 0.712$) and blood ($r = 0.548$) eosinophils% in asthmatic patients.

Conclusion: This study demonstrated that the serum level of SCF was higher in asthmatic patients especially among eosinophilic phenotype than among healthy control subjects. Also there was a significant association between higher SCF and higher levels of asthma severity, sputum and blood eosinophil%.

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Introduction

Bronchial asthma is a common chronic disease of the respiratory system that affects approximately 300 million people worldwide. It is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation [1]. Stem cell factor (SCF) is a dimeric molecule that exerts its biological functions by binding to and activating the receptor tyrosine kinase c-Kit. Activation of c-Kit leads to its autophosphoryla-

tion and initiation of signal transduction. Activation of c-Kit signaling has been found to mediate cell survival, migration, and proliferation depending on the cell type. Signaling from c-Kit is crucial for normal hematopoiesis, pigmentation, fertility, gut movement, and some aspects of the nervous system. Deregulated c-Kit kinase activity has been found in a number of pathological conditions, including cancer and allergy [2]. SCF can exist both as a transmembrane and a soluble protein. The soluble form of SCF contains a proteolytic cleavage site in exon 6. Cleavage at this site allows the extracellular portion of the protein to be released. The transmembrane form of SCF is formed by alternative splicing that excludes exon 6. Both forms of SCF bind to c-Kit and are biologically active [3]. Although SCF was initially described as a mast cell growth factor; it appeared to be a pleiotropic cytokine exerting its role

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at the first stages of bone marrow stem cell development, inducing eosinophil activation and basophil chemotaxis and survival [4]. SCF appears to play a significant role in eosinophil associated inflammation in allergic airway inflammation. SCF can play an important role in eosinophil activation, inducing degranulation, leukotriene, and chemokine production [5].

Aim of the work

This study was carried out to assess serum level of stem cell factor in asthmatic patients and to evaluate its relation to disease severity.

Subjects and method

This case control study was carried out on 70 individuals, 20 healthy control subjects and 50 asthmatic patients that were admitted in Chest Department, Benha University hospital in the period between March 2013 and December 2014. Subjects were divided into 2 groups: *Group I*: 50 patients with bronchial asthma and *Group II*: 20 apparently healthy individuals as a control group. *Group I* was further divided according to severity of asthma into: group Ia; mild persistent, group Ib; moderate persistent and group Ic; severe persistent asthma [6]. *Group I* was further divided into eosinophilic and non eosinophilic asthma according to percent of sputum eosinophil [7].

Inclusion criteria for group I

- Stable asthmatic patients with airway obstruction (FEV1/FVC < 70%) and with degree of reversibility in FEV1 of $\geq 12\%$ or 200 ml from pre bronchodilator value [6].
- Stopping corticosteroids 12 h before laboratory tests for severe persistent asthmatic patients.

Exclusion criteria

- Patients receiving high dose systemic corticosteroid (prednisone 1 mg/kg/day).
- Patients known to have systemic inflammatory diseases.

All subjects were subjected to the following:

- I. Thorough history taking and clinical examination.
- II. Plain chest X-ray (P-A view).
- III. Pulmonary function test (spirometry pre and post bronchodilator) [8].
- IV. Laboratory investigations:
 1. Complete blood count.
 2. Erythrocyte sedimentation rate.
 3. Liver functions tests.
 4. Kidney function tests.
 5. Eosinophil percentage in the sputum of asthmatic patients. All patients gave sufficient sputum samples with no need for induced sputum technique. Sputum

was treated by adding equivolume N-acetylcysteine, then it was spread on a slide then fixed with methanol 10%, the slide was stained with Leishman stain, then eosinophil percentage in the sample was calculated [9].

6. Measurement of serum level of stem cell factor by Enzyme-Linked Immunosorbent Assay (ELISA).

Principle of the Assay

SCF in standards and samples was sandwiched by the immobilized antibody and the biotinylated polyclonal antibody specific for SCF, which was recognized by a streptavidin-peroxidase conjugate. All unbound material was then washed away and a peroxidase enzyme substrate was added. The color development was stopped and the intensity of the color was measured [10].

Statistics

The data were entered into a personal computer. The statistics were performed using SPSS statistical program (version 20).

Results

Among the patients group, there were 43 (86%) females and 7 (14%) males. The ages of the patients ranged between 25 and 67 years (mean = 47.04 ± 12.08) and their BMI ranged from 19.53 to 47.61 kg/m². Among the control group, there were 15 (75%) females and 5 (25%) males. Their ages ranged between 36 and 68 years (mean = 45.15 ± 7.58). The patients and control groups were matched for sex, age and BMI ($P > 0.05$) (Table 1). Out of 50 asthmatic patients, 2 (4%) patients were mild persistent, 19 (38%) patients were moderate persistent and 29 (58%) patients were severely persistent (Table 2). And among asthma phenotype, 40 (80%) patients were eosinophilic and 10 (20%) patients were non eosinophilic (Table 3). There was a statistically significant difference (P value < 0.05) in the mean value of eosinophil percentage in sputum among asthma severity as it was higher among patients with severe asthma compared with the mild and moderate persistent. While percent of eosinophil in blood increased with increasing asthma severity with no statistically significant difference (Table 4). There was a highly statistical significant difference in the mean level of SCF between case and control group (1192.34 ± 789.89 versus 326.29 ± 274.38 respectively) (Table 5). There was a highly statistical significant difference in the level of SCF among different degrees of severity in asthmatic group as it was significant higher in severe persistent asthmatics compared with mild and moderate persistent (Table 6). There was a statistically significant difference in the level of SCF between eosinophilic and non-eosinophilic asthma (1457.77 ± 648.83 versus 130.59 ± 83.27 respectively) (Table 7). A significant positive correlation was found between SCF and eosinophil percent in sputum ($r = 0.71$) (Table 8 and Fig. 1) and blood ($r = 0.55$) (Table 8 and Fig. 2) as well as age ($r = 0.37$) (Table 8), also there was a significant negative correlation between SCF level and FEV1% predicted of asthmatic patients ($r = -0.29$) (Table 8 and Fig. 3).

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