Egyptian Journal of Chest Diseases and Tuberculosis (2014) **63**, 689–693

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

www.elsevier.com/locate/ejcdt
www.sciencedirect.com

ORIGINAL ARTICLE

Hepatocyte growth factor and the risk of pulmonary embolism

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Received 27 December 2013; accepted 4 February 2014
Available online 30 April 2014

KEYWORDS

Hepatocyte growth factor;
Pulmonary embolism

Abstract *Background:* Diagnosis of pulmonary embolism (PE) in early stages by conventional laboratory methods is difficult because the currently available tests lack sufficient sensitivity and specificity. Hepatocyte growth factor (HGF) was originally regarded as specific to hepatocytes, but has been found to be identical to the scatter factor affecting a wide range of tissues including the lungs.

The aim of this work is to study the relationship between HGF and PE.

Patients and methods: This study included 40 patients with PE, 40 stable angina (SA) patients, and 10 healthy controls. HGF and D-dimer were measured in all patients of this study.

Results: Mean HGF was significantly higher in the PE group (788.8 ± 361.5 pg/ml) compared to the SA group (262.4 ± 158.1 pg/ml) and control group (215.5 ± 18.5 pg/ml) ($P = 0.0001$). The predictive values of D-dimer in the diagnosis of PE were as follows: 100% sensitivity and negative predictive value, 80% specificity, 83.3% positive predictive value and 90% accuracy, while those of HGF were: 97.5% sensitivity, 97.4% negative predictive value, 92.5% specificity, 92.9% positive predictive value and 95% accuracy. When used both D-dimer and HGF together the values improved to: 100% sensitivity and negative predictive value, 97.5% specificity, 97.6% positive predictive value and 98.8% accuracy.

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

Production and hosting by Elsevier

 http://dx.doi.org/10.1016/j.ejcdt.2014.02.001

Conclusions: Our observations suggest that the plasma HGF level may be a useful biological marker of pulmonary ischemia, and a valuable tool for early diagnosis of PE. Clarification of the mechanisms, characteristics, and biological significance of HGF elevation is important for clinical use in diagnosing and treating pulmonary ischemia. The use of both D-dimer and HGF increases the predictive power of both tests when used together. The clinical significance of the role of HGF in PE opens a new therapeutic area in treating acute ischemic pulmonary disease that would be able to prolong the time frame for the application of reperfusion–thrombolytic therapy.

Introduction

Pulmonary embolism (PE) is a common and often fatal postoperative complication. Late diagnosis and delayed management of this condition are associated with pulmonary infarction. The common clinical manifestations in pulmonary embolisms are frequently inconsistent and often vague. Routine laboratory examinations are also nonspecific. A chest film, arterial saturation, and electrocardiogram may be helpful in excluding other cardiorespiratory diseases, but are frequently unreliable in establishing an objective diagnosis of pulmonary embolism. Although pulmonary arteriography is the gold standard for the diagnosis of pulmonary embolism, it requires expensive equipment and trained radiologists, and the patient could show sensitivity to the contrast agents used. Therefore, it is necessary to use a more convenient and reliable method of diagnosing pulmonary embolism [1].

Hepatocyte growth factor (HGF) was initially thought to be liver-specific, but it has become clear that HGF acts on a variety of epithelial cells and organs such as mitogen, motogen and morphogen [2,3]. HGF may also be involved in vascular proliferation and regeneration, as it is a principal mediator of mesenchymal, epithelial, and endothelial interactions that contribute to wound healing and angiogenesis. It is likely that HGF plays an important role in ischemic lung injury [4].

It is unclear whether high HGF levels are a risk factor for ischemic pulmonary disease or a result of it. To address these issues, we conducted this study to evaluate the association between circulating HGF levels and pulmonary embolism and whether it could serve as an indicator of this disease in the early period of pulmonary ischemia.

Patients & methods

This study included 40 patients with pulmonary embolism (PE group 1), 40 stable angina patients (SA group 2), and 10 healthy controls (group 3).

All patients and controls were recruited from patients attending Intensive care unit, Menoufiya University Hospital, Shebin El-Kom and Critical Care Unit, Alexandria University Hospital. All studied subjects underwent a detailed clinical history and physical examination. An informed consent was obtained from all subjects enrolled in the study. This study was approved by our Ethics Committee of Faculty of Medicine.

Exclusion criteria were patients whose medical history was consistent with systemic metabolic disorders (other than DM), systemic vasculitis, or apparent liver disease.

The control group consists of 10 examinees of the same age and sex.

Laboratory assessment:

1- Liver enzymes (SGOT, SGPT) were done on autoanalyser SYNCHRON CX5 from Beckman.
2- Lipid profile.
3- D-Dimer: was considered positive if >500 ng/ml FEU (fibrinogen expressed unit by using latex agglutination test).
4- Hepatocyte growth factor (HGF) was measured in all patients and controls within 24 h of onset of pulmonary embolism and before giving heparin. HGF is relatively stable and that a single measurement at baseline may reflect an individual's long-term exposure to this growth factor. It was estimated by ELISA kit based on standard sandwich enzyme-linked immune-sorbent assay provided by biorbyt. We did not research the time course of HGF concentration in patients with pulmonary thromboembolism who received heparin treatment for 3–7 days after the admission, because Matsumori et al. found that serum HGF concentration increased immediately after heparin use [5].

Pulmonary embolisms were diagnosed by using computed tomography pulmonary angiography.

Statistical analysis

Data input to the computer was done followed by tabulation and analysis. Analysis was done using SPSS-9 (Statistical Package for Social Sciences version 12). We represent the data in arithmetic mean, standard deviation, frequency and percentage. The following tests were used to analyze the results: analysis of variance (ANOVA), least significant difference, Student "*t*" test, Chi square test and correlation coefficient test. Statistical analysis was done at level of significance of $P \leqslant 0.05$.

Results

There were no significant differences between the 3 studied groups as regards age, gender and body mass index (Table 1).

There were no significant differences between both patient groups as regards systolic and diastolic blood pressure ($P = 0.321$ and $=0.167$, respectively).

There were no significant differences between the PE group and SA group as regards liver enzymes (ALT, AST), renal