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Serum Alpha 1 Antitrypsin and Pulmonary Emphysema

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Abstract

Using isoelectric focusing (IEE) and radial immunodiffusion (RID) techniques, serum samples from 100 normal healthy adults and 21 patients with pulmonary emphysema were analysed to identify various alpha 1 antitrypsin phenotypes and the Serum concentrations. Ten percent of the patients had low serum values. The normal or most common genetic form, MM, is the predominant phenotype in both controls and patients (JPMA 46:102, 1996).

Introduction

Emphysema is generally defined as an anatomical disorder of the lungs characterized by increase beyond the normal in the size of the air spaces distal to the terminal bronchioles with destructive changes in their walls. Chronic bronchitis is mostly associated with it. Together, they form chronic airway obstructive disease.

Protease - antiprotease imbalance plays a major role in the development of emphysema. Elastase, a serine protease has the ability to cleave native elastin. Inflammation in the lung results in the release of elastase, which in the tissue is inactivated by complex formation with the protease inhibitors. Alpha 1 antitrypsin (alpha 1 AT)is the most potent serine protease inhibitor. It’s primary site of action is the lower respiratory tract, where it protects the alveolar walls against destruction. Normally, the inactivation of elastase is so efficient that no activity is left in the pulmonary tissue. However, deficiency of alpha 1 AT may leave some of the elastase uninhibited, resulting in destruction of the elastic tissue in the alveolar wall and subsequent development of emphysema of the lungs. Apart from alpha 1 AT deficiency, other factors such as cigarette smoking, asthma, lower respiratory tract infections contribute to the serious clinical course.

This study was undertaken to determine the serum concentration and to identify the various alpha 1 AT phenotypes in the local population, comprising of healthy subjects and patients with emphysema.

Patients and Methods

Twenty-one patients with pulmonary emphysema and one hundred healthy adults, with no history of pulmonary disease were selected for the study.
Patients complaining of dyspnoea on exertion, were subjected to physical examination. Those with increased percussion note and reduced air entry in both lungs with signs of airway obstruction were x-rayed. The patients with flattened or low diaphragm, hyperlucent lung fields with diminished lung markings with or without bullae had spirometry and only those with compromised lung function not reversible after bronchodilators were included in the study. No arterial blood gases were done. Most of the patients were either smokers or ex-smokers.
Patients age varied from 7-70 years, with a mean age of 48.5 years (median: 41 years). There were 20 males and 1 female. In the control group the age range was 18-82 years (mean age: 33.4 years). There
were 52 males and 48 females. 

**All sera were stored at -70°C until analysed.**

Quantitative measurement of senun alpha 1 AT was came out by single radial immunodiffusion (RID) technique using M partigen immunodiffusion plates (Behring Diagnostic, MaEburg, Germany). Phenotyping was performed by ultra thin layerpolyacrylamide gel isoelectric focusing (IEF), using gels containing 2% ampholytes in the pH range 4.2-4.9. Further corifinnation of alpha 1 AT phenotypes was done by immunofixation. 

**Results**

The mean value of serum alpha 1 AT concentration in healthy subjects was 2.47+0.08 g/l (range: 0.52-5.0 g/l) and in patients with pulmonaiy emphysema 2.68+0.14 g/l (range: 1.46-3.95 g/l). Amongst the control, mean serum alpha 1 ATmn non-smokers was 2.56+0.075 g/l (range:1.46-5.0 g/l), whereas in smokers the mean serum concentration was 2.1+0.21 g/l (mnge: 0.52-3.95 g/l). It was observed that 13% of the control subjects and 10% of the patients manifested low levels. Any value of less than 2.0 g/l was considered as lower than normal. But these low levels appear to have no diagnostic significance as none of these sera exhibited abnormal patterns when subjected to IEF. Isoelectric focusing is now considered as a procedure of choice in evaluating the various phenotypes and evolves a more correct assessment of serum alpha 1 AT levels in normal population as well as in disease conditions.

![Figure](image)

Figure represents a typical pattern of alpha 1 AT on IEF. Seventy percent of healthy subjects have a phenotype resembling MM, followed byM 1M2(28%) and FM3 (2%). Inpatients with pulmonary emphysema also MM was predominant followed by M1 M2.

**Discussion**

Alpha 1 antitrypsin deficiency is the most common genetic cause of emphysema in adults and liver disease in children. Although a severe deficiency is clearly a risk factor for the development of emphysema, most individuals with the said disease have normal serum concentration of this anti-
elastase. In the present study, serum concentrations were lower than normal values in 10% of the patients, but they too had the normal phenotype M. Clinical findings also show that there was no difference between the patients manifesting low concentrations versus those with normal values. It is the phenotype and not the serum concentration alone that is apparently of some importance in predisposing to lung disease. Persons who are PI type M and yet have moderately reduced concentrations of alpha 1 AT, probably have ample reserve capacity to increase their alpha 1 AT concentration during times of infection, when more alpha 1 AT might be required to protect the lungs from proteolysis. The Z gene product apparently cannot respond with increased production. The increased risk for heterozygotes of PI MZ could be due to this lack of response of the Z allele or to some other effect of the abnormal Z protein in circulation.

For most people, it is cigarette smoking and not severe alpha 1 AT deficiency, that is the major risk factor for the development of emphysema. The present observations accords with the findings of others where most of the patients had a history of smoking.

Exposure of the lungs to tobacco smoke markedly increases the number of pulmonary alveolar macrophages which become activated to give increased proteolytic activity and also to secrete a chemotactic factor which attract leucocytes to the lung. There is an increase in the elastolytic load in the lungs and at the same time the inhibitory activity of alpha 1 AT in the alveoli greatly decreases. This decrease is the result of direct oxidation of its reactive centre by free radicals in the smoke and also by oxygen radicals released from the activated leucocytes. This increased production of elastase, together with a decrease in inhibitory activity, results in an attack on the elastic tissue of the lower respiratory tract and the development of emphysema.

References