Utility of routine screening for alpha-1 antitrypsin deficiency in patients with bronchiectasis

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ABSTRACT

Alpha-1 antitrypsin deficiency (AATD) is a cause of bronchiectasis. Guidelines for bronchiectasis from the British Thoracic Society do not recommend to routinely test patients for AATD. In contrast, guidelines for AATD recommend routine screening. This contradiction, in part, results from the lack of data from large studies performing comprehensive screening. We screened 1600 patients with bronchiectasis at two centres in the UK from 2012 to 2016. In total, only eight individuals with AATD were identified representing 0.5% of the overall population. We conclude that routine screening for AATD in bronchiectasis in the UK has a low rate of detection. Further studies are required in different geographical regions, which may have a higher prevalence of AATD.

Bronchiectasis is a heterogeneous airway disease characterised by chronic respiratory symptoms and permanent dilatation of bronchi. Guidelines from the European and British Thoracic Societies recommend systematic investigations for underlying causes, since there is specific treatment for some diseases that could have clinical and prognostic impact.1 2

Alpha-1 antitrypsin deficiency (AATD) is a potential cause of bronchiectasis and augmentation therapy is licensed in several countries, particularly in cases of severe disease with airway obstruction.3 Prevalence of PiSZ and PiZZ phenotypes, the two most common phenotypes associated with lower serum alpha-1 antitrypsin (A1AT) levels and increased risk of lung disease, has been estimated to be 1:900 and 1:15.388, respectively, in the overall population.3 4

We, therefore, investigated if routine measurement of serum A1AT in the aetiological assessment of bronchiectasis was clinically useful in two large populations of UK adults.

New patients attending the Bronchiectasis Clinics at Ninewells Hospital and the Royal Brompton Hospital, London (RBH) for initial investigation of bronchiectasis aetiology were included in the study. All patients had documented bronchiectasis by high-resolution CT (HRCT) scans. Standardised testing for aetiologies of bronchiectasis was performed including A1AT testing, but also testing for allergic bronchopulmonary aspergillosis (ABPA), immunoglobulins, functional antibodies and serum electrophoresis. Serum A1AT level was measured according to the local laboratory standard procedures and in cases where the serum level was low, phenotyping was performed. At the Ninewells laboratory, the level for phenotyping was 1.0 g/L and at RBH it was 1.3 g/L.

Between January 2012 and December 2016, 675 people with bronchiectasis were investigated at Ninewells Hospital and 925 patients were investigated at RBH. Characteristics of patients at both centres have been previously reported and are predominantly elderly females (median 67 years, 60% female).

At the Scottish centre, we identified 17 patients (2.52%) with A1AT levels <1 g/L who went on to have phenotyping performed. In those with an abnormal A1AT level, the mean was 0.79 g/L (+/-0.18). Phenotypes were PiMZ in 13 patients (average 0.86 g/L+/-0.09), PiSZ in three patients (average 0.7 g/L+/0.06) and PiZZ in one patient (0.2 g/L). We, therefore, identified one patient with severe AATD disease (PiZZ) from 675 screened and three patients with moderate AATD disease (PiSZ).

The minimum protective level of A1AT has been reported as 0.8 g/L. On this basis we identified six individuals with deficient A1AT levels.

From the 925 patients screened at RBH 254 patients had phenotyping performed due to a level <1.3 g/L of which 21 had levels <1 g/L equating to the Ninewells cut-off. From phenotyping we...
identified seven patients with PiZZ with an average level of 0.23 g/L (0.05), three patients with PiSZ or PiS where the second allele could not be identified with an average of 0.93 (0.23). Twenty-eight patients were identified with PiMZ with an average of 1.01 g/L (0.16). Eight patients had A1AT levels below the protective threshold of 0.8 g/L. Results are summarised in figure 1.

Augmentation therapy is recommended only to non-smoking patients with pulmonary emphysema and reduced or progressive decline on lung function. Non-smoking PiMZ individuals are not known to have increased risk of lung disease and PiSZ phenotype is not usually an indication for augmentation therapy, therefore, in 673 bronchiectasis patients, only one (0.15%) patients in Scotland and 7 (0.8%) in England had severe AATD that could possibly benefit from augmentation therapy. The slightly higher prevalence in England may reflect true differences as the reported prevalence is higher in England, or differences in the characteristics of patients referred to each centre.

In the UK, National Health System, A1AT serum assay and phenotyping costs were £2.45 and £35.50, respectively, which permits others to distribute, remix, adapt, build upon this work non-commercially and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

REFERENCES