Alpha-1 Deficiency: Better Detection May Improve Outcomes for COPD Patients

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Alpha-1 antitrypsin deficiency (AATD) is an autosomal co-dominant condition resulting in decreased or absent levels of alpha-1 antitrypsin (AAT) which is produced primarily in the liver. This allows the uninhibited proteolytic action of neutrophil elastase to overtake the lungs resulting in degradation of lung tissue and early onset (prior to the fourth or fifth decade) emphysema and chronic obstructive pulmonary disease (COPD) (Hatipoglu, Umur & Stoller, 2016). Exposure to environmental pollutants and cigarette smoke greatly increase neutrophil elastase activity and therefore exacerbate lung destruction in AATD individuals. It is thought that similar inflammatory reactions occur in the skin resulting in vasculitis and panniculitis. In addition, intrahepatic accumulation of the defective protein may cause cirrhosis or primary liver cancer. This condition is present for 2%-5% of chronic obstructive pulmonary disease cases in America (Diaz, J.A., Minami, 2017) and is thought to be most common in individuals of Northern European descent (Hatipoglu, Umur & Stoller, 2016).

**Introduction**

Alpha-1 antitrypsin deficiency (AATD) is an autosomal co-dominant condition resulting in decreased or absent levels of alpha-1 antitrypsin (AAT) which is produced primarily in the liver. This allows the uninhibited proteolytic action of neutrophil elastase to overtake the lungs resulting in degradation of lung tissue and early onset (prior to the fourth or fifth decade) emphysema and chronic obstructive pulmonary disease (COPD) (Hatipoglu, Umur & Stoller, 2016). Exposure to environmental pollutants and cigarette smoke greatly increase neutrophil elastase activity and therefore exacerbate lung destruction in AATD individuals. It is thought that similar inflammatory reactions occur in the skin resulting in vasculitis and panniculitis. In addition, intrahepatic accumulation of the defective protein may cause cirrhosis or primary liver cancer. This condition is present for 2%-5% of chronic obstructive pulmonary disease cases in America (Diaz, J.A., Minami, 2017) and is thought to be most common in individuals of Northern European descent (Hatipoglu, Umur & Stoller, 2016).

**Literature Review**

A search of peer reviewed journal articles was performed utilizing electronic databases including: PubMed, Cochrane, and Clinical Key. Several articles published between 2002 and 2017 were retrieved and reviewed including those regarding the physiopathology and prevalence of alpha-1 deficiency, guidelines for testing and management of patients with AATD, current and emergent therapies for AATD, barriers to diagnosis, and strategies for improved diagnosis. One systematic review of articles published between January 2002 and December 2014 regarding practice guidelines for diagnosis and management of AATD patients was reviewed. An observational study published in 2012 provides a type 1 genetic counseling report by assessing the level of knowledge of AATD among internal medicine house officers and respiratory therapists was included. Three observational studies published between 2009 and 2014 aimed at analyzing processes for improving detection of alpha-1 antitrypsin deficiency were included. Information was also obtained from the Alpha-1 Foundation website and personal interviews with Ronald Reilkoff, M.D. (University of Minnesota Pulmonary, Allergy, Critical Care & Sleep Medicine) and Mary Davis (Sales Director, Grifols USA).

**Discussion**

**Potential Barriers to Detection of AATD:**

- Lack of knowledge regarding A1A among providers and patients.
- Perception among providers that treatment is ineffective.
- Patient fear that diagnosis will affect their ability to obtain life or health insurance or fear of emotional impact.
- Cost associated with testing.

**Addressing the Barriers and Exploring Strategies to Overcome Them:**

**Knowledge of AATD**

Taelierio, Chatter, and Stoller, 2010, conducted a study assessing the knowledge of AATD among internal medicine house officers and respiratory therapists (RTs) at the Cleveland Clinic. There was no statistically significant difference between the physicians and RTs mean scores of 54% and 52%, P=.25. Half of physician scores were below 55% with that being the median for the group. The median for RTs was 50%. Those who rated themselves as “somewhat knowledgeable” on self-assessment scored highest with physician scores of 60% correct and RT scores of 56%, P=.001. Physician scores did not change based on post-graduate educational level (P=.94), but RTs with 4-year degrees had a higher mean score than those graduating from 2 years program (56% vs 50%) (Taelierio, Chatter, & Stoller, 2010).

**Effectiveness of Augmentation with Human Plasma Derived Alpha-1 Protein**

The American Thoracic Society currently recommends augmentation therapy with Alpha-1 antitrypsin derived from human plasma for mild to moderate COPD (FEV1 of 35%-65%) and alpha-1 antitrypsin deficiency. Despite early randomized control trials that failed to prove improvement in lung function of AATD individuals receiving augmentation therapy while using sputometry and FEV1 as measures, more recent studies have noted reductions in the loss of lung density when subjects were assessed with Computed Tomography rather than spirometry. In addition, observational benefits such as: decreased mortality, reduced rates of hospitalization, reduced rates of development of other pulmonary disease, and panniculitis. In addition, researchers have been investigating the use of augmentation therapy as an approach to improving the quality of life for those affected.

**Utilizing Respiratory Therapists and Automated EMR Algorithms to flag patients for testing:**

Rahaghi et al. (2009) analyzed the effects of a physician for AATD testing generated by respiratory therapists following abnormal PFT results. During the pre-acute period, 6% of included patients underwent testing for AATD compared to 13% in the physician alert phase (p<0.04). In 2011, Alzaid, Moulla, and Stoller conducted a similar study at the Cleveland Clinic in Ohio utilizing an EMR based flag for testing. The study included 979 subjects during a pre-acute period, 4.7% were referred for testing resulting in 8.9% found to have AATD based on serum liver enzymes. Phenotyping of those with low serum levels, resulted in 3.2% with genotype PI ZZ. During the alert period, 642 patients were determined eligible and the rate of testing increased substantially to 15%. Based on their results, they concluded that utilizing respiratory therapists and EMR flags to identify individuals for testing based on PFT result substantially increased rates for testing individuals clinically indicated at risk for AATD (Rahaghi et al., 2009).

**The Genetic Information Nondiscrimination Act (GINA)**

The Genetic Information Nondiscrimination Act of 2008 protects those diagnosed with genetic disorders from discrimination when applying for health insurance and employment (NII, 2013).

**Overcoming the Cost of Testing and Providing Patient and Provider resources regarding diagnosis and management of AAT:**

The Alpha-1 Foundation and many of the pharmaceutical manufacturers of augmentation offer free testing kits for evaluation of AAT serum level and genotype using dried blood spot (DBS). Alpha-1 Foundation offers genetic counseling services for those identified with AATD. In addition, the foundation provides and array of educational offerings regarding AATD diagnosis and treatment to clinicians (Alpha-1 Foundation, n.d.)

**Applicability to Clinical Practice**

Primary care is often the first point of entry for many patients with obstructive airways diseases making it an ideal environment in which to implement new strategies for improved detection of alpha-1 antitrypsin deficiency. Fromer (2017) states that primary care settings may improve diagnosis and management of AATD in the primary care setting.

**Statement of the Problem**

Despite guidelines from the American Thoracic Society and the European Respiratory Society regarding testing for AATD, the disorder remains highly under-diagnosed. Furthermore, individuals report long delay times (averaging 5-7 years) and visits to multiple providers between onset of symptoms and diagnosis which delays opportunities for lifestyle modifications and potential therapeutic treatments that may improve prognosis(Hatipoglu, Umur & Stoller, 2016).

**Research Questions**

- What are the barriers to detection of AATD?
- Are there effective strategies that may be implemented to overcome barriers to recognition and decrease diagnostic delays allowing for interventions that may decrease progression of lung function in COPD patients with AATD?

**References**


**Acknowledgements**

I would like to thank my loving husband and sons for their support through this journey. In addition, I would like to thank Mary Davis (Grifols, USA) and Ronald Reilkoff M.D. (University of Minnesota Pulmonary, Allergy, Critical Care & Sleep Medicine) for their willingness to share their knowledge of alpha-1 antitrypsin deficiency and opening my eyes to the serious need for improved recognition. Lastly, I would like to express my thanks to the UND PA program staff for their guidance throughout my PA education.