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The Pathophysiology of Alpha-1 Antitrypsin Disease and COPD

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Introduction

Chronic obstructive pulmonary disease (COPD) is the number one disease process treated in the Pulmonary Department at the Chalmers P. Wylie VA Ambulatory Care Center (VAACC). The medical staff includes doctors, nurses, and respiratory therapists. The team works together to ensure the veteran gets the best care available. Smoking is very popular in the military, and this puts veterans at a higher risk for COPD, compared to the general public. COPD can develop at a much younger age if the patient has alpha-1 antitrypsin deficiency (AATD). Janciauskiene, Ferrotti, Laenger, Jonigk, and Luisetti (2011) point out that patients who develop COPD with certain genotypes of AATD start showing severe signs of emphysema between the ages of thirty and fifty. Cigarette smoking greatly increases this risk (Janciauskiene, Ferrotti, Laenger, Jonigk, & Luisetti, 2011).

Steps taken at the VAACC to detect and treat AATD:

- Pulmonary function testing completed
- AATD serum lab test for all COPD patients
- Smoking cessation education with nicotine replacement or medication
- Infusion therapy provided
- COPD inhalers and medications are prescribed
- Pulmonary rehabilitation encouraged and available on site
- Oxygen is supplied at no cost

Early detection of AATD, COPD can be avoided. However, if detected after the patient has COPD, treatment will add quality years to the patient's life.



Puett, W. (Photographer). (no date). *World War II & Korean War veteran*. [digital image]. Retrieved from <http://www.inogen.com/blog/salute-veterans-day/>

The Genetic Variants of Alpha-1 Antitrypsin Deficiency

Alpha-1 antitrypsin (AAT) as explained by Brode, Ling, and Chapman (2012) is a glycoprotein protease inhibitor encoded by the SERPINA1 gene on chromosome 14. Alpha-1 antitrypsin is synthesized in the liver and secreted into the blood. It travels to the lungs where it diffuses into the interstitium and the alveolar lining fluid. Here it inactivates neutrophil elastase, helping to protect the lungs from protease-mediated damage (Brode, Ling, & Chapman, 2012).

Stoller and Brantly (2013) describe AATD as an autosomal co-dominant condition with over 100 variants (Stoller & Brantly, 2013). Brode, Ling, and Chapman (2012) further explain that not all of the variants are associated with the disease. The most common of these variants is the M allele. The M allele variant poses no risk for liver or lung disease. Most people with severe AATD are homozygous for the Z allele. The Z allele variant protein miss-folds and polymerizes during its production in the endoplasmic reticulum of hepatocytes. The abnormal polymers get trapped in the liver; reducing the amount of AAT released into the blood. As a result, the alveoli allows uncontrolled proteolytic attack and tissue destruction of the lungs. The connective tissue throughout the lungs is damaged, due to the increase in elastase activity. The decrease is AAT in the lungs places the individual at risk for lung disease. However, there has to be environmental or other genetic factors to elicit respiratory symptoms. The buildup of AAT in the liver causes liver disease. The AAT causes a reaction from the hepatocytes including autophagy and apoptosis of hepatocytes (Brode, Ling, & Chapman, 2012).

Treatment

Pini et al. (2014) research indicates that a new treatment should be developed for Z-phenotype AATD patients. AAT is mainly produced by the hepatic cells. However, there is a small amount produced by the bronchial epithelial cells (BEC). Inflammation causes BECs to secrete Z-AAT protein and its polymers. The process may be involved in the pathogenesis of lung emphysema and in BEC dysfunction. A new therapeutic approach for such a finding could be a treatment to prevent polymer formation, thus blocking the destruction of the lung tissue (Pini et al., 2014).

Prolastin infusion therapy, as pointed out by Koepke et al. (2013), has been the treatment of choice for the past 30 years for patients with AATD-related emphysema. The intravenous infusions are weekly for an indefinite amount of time. Prolastin is an augmentation therapy using AAT from purified pooled human plasma. The treatment greatly reduces the sputum elastase activity and levels of leukotriene B4, IL-8, and myeloperoxidase. It also reduces lung consolidation caused by proteolytic attack and destruction of lung tissue. Currently, this is the best therapy available for AATD (Koepke et al., 2013).

At the VAACC Prolastin augmentation therapy is provided for veterans with AATD-acquired COPD, when indicated. Standard medication prescribed for COPD symptom management would be the following:

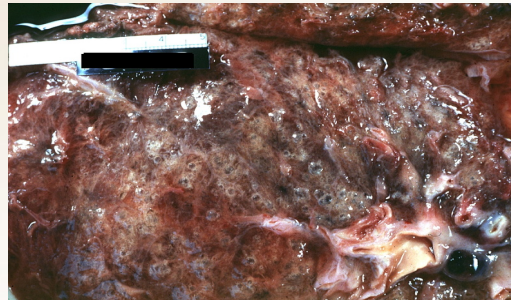
- Albuterol Sulfate: short-acting beta-2 adrenergic agonist bronchodilator (rescue inhaler)
- Budesonide/Formoterol Fumarate Dihydrate: anti-inflammatory corticosteroid/long-acting B2 agonist bronchodilator (twice daily)
- Tiotropium Bromide: long-acting anticholinergic bronchodilator (once daily)
- Montelukast: leukotriene receptor antagonist (once daily)

These medications provide the optimal breathing conditions for the patient. The VAACC also provides Pulmonary Rehabilitation and smoking cessation. All of these options are available to ensure the best tertiary care is provided to the veterans.

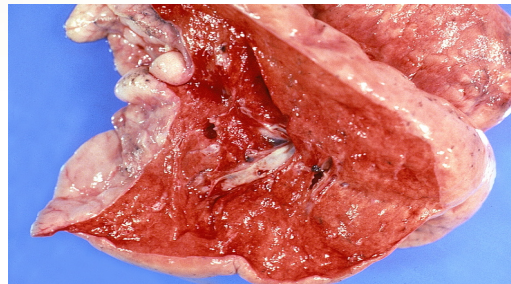
Signs and Symptoms of Alpha-1 Antitrypsin Deficiency with COPD

Janciauskiene et al. (2011) explain that 10% of children with the Z-protein phenotype AATD identified through newborn screening have abnormal liver function. The identified babies have prolonged obstructive jaundice and 2% of these children will have liver failure and require a transplant. Since the disease is identified early the opportunity to avoid smoking and environmental exposures are paramount. Avoiding unnecessary exposure will lessen the chance of developing the COPD aspect of this illness (Janciauskiene et al., 2011).

Strange (2013) points out that AATD is a genetic condition that predisposes individuals to an early onset of pulmonary emphysema. Also, within this population of AATD patients, asthma and bronchiectasis have been reported. The reports of asthma are thought to be misdiagnosed. Possibly because of the age of the patient or a non-smoking history. The symptoms associated with this disease process is the same for emphysema without the AATD component. Patients present with a cough, wheezing, dyspnea, and excessive sputum production. They may also have a lower oxygen saturation. Another sign is frequent exacerbations and lung infections. The diagnosis of AATD is usually identified after the patient has COPD. Generally, the Pulmonologist will order a blood test to see if the patient has the genetic disorder, especially if they are exhibiting symptoms at a younger age than what is typical for a COPD patient (Strange, 2013).



Anderson, P. (Photographer). (2013, August 1). *Lung: Emphysema: Gross fair but not the best photo case of alpha-1 antitrypsin deficiency* [digital image]. Retrieved from <http://peir.path.uab.edu/library/index.php?search/9186>



Anderson, P. (Photographer). (2013, August 1). *Lung: Normal* [digital image]. Retrieved from <http://peir.path.uab.edu/library/picture.php?/12218/category/93>

Implications for Nursing Care

Wewers and Crystal (2013) make a point in saying that AAT augmentation therapy is a triumph over a genetic disease. They go on to mention that it is the only genetic lung disease with effective therapy for all affected people (Wewers & Crystal, 2013). With this being the case; nurses should be advocates for testing these individuals. Detection is the biggest challenge health care professional's face.

Stoller and Brantly (2013) discuss reasons for the lack of AATD detection. The medical and health care staff are undereducated on the subject of AATD. They also lack the awareness to recognize the clinical manifestations adequately. Some of these patients will never see a Pulmonologist and many primary care providers seem to lack the basic knowledge to assess this disease. A questionnaire regarding signs and symptoms of AATD was given to a group of Respiratory Therapists, as well as, internal medicine trainees and the average score was 53% (Stoller & Brantly, 2013). There is a need for education of healthcare professionals in identifying this disease.

The role of the Pulmonary Advanced Practice Nurse (APN) at the VAACC should be to educate staff. Week there is a Primary Care Provider and Nurse meeting at the VAACC. A presentation at these meetings, regarding AATD, would be prudent. Engaging with the "first line" providers and nurses would be a good start in educating the staff. Also, the Pulmonary APN would provide information to the Registered Respiratory Therapists (RRTs) who perform Pulmonary Function Testing (PFT) about AATD and ask them to inform the physicians when they suspect AATD. Since many of these patients are underdiagnosed; most of them probably don't see a Pulmonologist. Educating RRTs would be an excellent way in identifying potential AATD patients.

Conclusion

Alpha-1 antitrypsin deficiency has many different genetic mutations. The most damaging of these mutations is the Z-homologous AAT allele. Even with this genetic mutation, it takes environmental exposure for COPD to occur. If detected at a younger age the patient would understand the risk factors associated with smoking and environmental exposures and could avoid COPD completely. AATD-acquired COPD is treatable. Prolastin therapy reduces symptoms and lessens exacerbations. The biggest challenge with this disease is the lack of knowledge and under-diagnosing of AATD. Providing education to providers, nurses, and respiratory therapists regarding this very treatable lung disease is important to help these patients prosper.



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