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Antibiotic Therapy in Preventing Exacerbations of Severe Chronic Obstructive Pulmonary Disease

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Abstract

- Chronic obstructive pulmonary disease (COPD) is a progressive disease that has no cure but is treatable. The treatment goal is to have adequate symptom control, decreased exacerbations, prevent hospitalizations and maintain an independent quality of life.
- The review of literature is to determine if the benefits of long-term antimicrobial therapy outweigh the risks in the treatment of severe COPD.
- The gold standard for pharmacotherapy consists of inhaled corticosteroids and bronchodilators (long-acting beta$_2$ agonist (LABA).
- Adding azithromycin to standard therapy for patients with frequent exacerbations showed a 27% reduction in exacerbation frequency.
- With prolonged use of antimicrobials there is an increased risk of bacterial resistance. However, in doing this research, it was found that bacterial resistance was not noticed between azithromycin (52%) versus placebo (57%), p = 0.64.
- Although long-term antimicrobial therapy is becoming a hot topic, it is imperative that we continue to study the detrimental development of bacterial resistance.

Introduction

- COPD is a chronic, slowly developing progressive disease. Symptoms include shortness of breath, wheezing, coughing and frequent respiratory infections.
- Standard pharmacological treatment includes inhaled bronchodilators and corticosteroids (National Heart, Lung, and Blood Institute [NHIBI], 2017).
- In severe cases, would adding a macrolide antibiotic to their standard treatment decrease exacerbations and improve overall health and quality of life? Do the benefits of antibiotic therapy outweigh the risks?
- In an effort to answer the above questions, the chosen studies and review articles included adults (18 years and older), having a history of moderate to very severe COPD, having had one to three acute exacerbations of COPD (AECOPD) in the last year and continuing on standard therapy for COPD.

Statement of the Problem

- Patients with severe COPD that have exhausted all modalities of standard treatment, may still suffer from "flare ups" or exacerbations of symptoms which can alter their quality of life and lead to frequent hospitalizations (NHIBI, 2017).

Research Question

1. In patients with severe COPD, are standard pharmacological methods of therapy enough to prevent exacerbations?
2. In patients with severe COPD, what are the benefits of adding a long-term macrolide antibiotic to standard therapy?
3. In patients with severe COPD, what are the risks and contraindications of adding a long-term macrolide antibiotic to standard therapy?

Literature Review

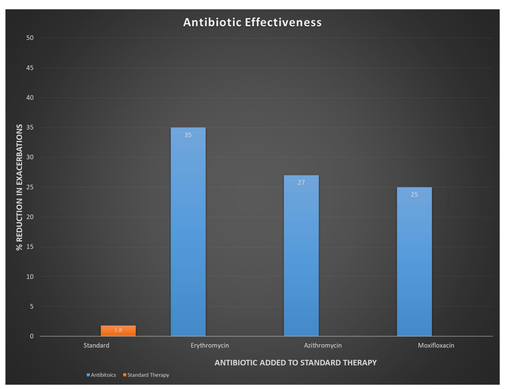
- The literature yielded high-quality studies concerning macrolide antibiotics and their effects, benefits, and challenges in preventing and treating AECOPD.
- **An Overview of COPD -** COPD is the third leading cause of death in the United States (U.S.). In determining the severity of a patient's COPD, the clinician will classify them in a stage based on their pulmonary function tests (PFT) and symptoms.
- *GOLD Stages (Lung Institute, 2016)*

Stage One	Mild COPD with FEV_1 about 80 percent or more of normal. COPD commonly causes slight airflow limitations.
Stage Two	Moderate COPD with FEV_1 between 50 and 80 percent of normal. Usually during this stage, most people seek help for COPD symptoms of coughing, wheezing and shortness of breath.
Stage Three	Severe COPD with FEV_1 between 30 and 50 percent of normal. Typically, in this stage, COPD symptoms worsen, causing decreased quality of life.
Stage Four	Very severe COPD with a lower FEV_1 than stage three, or those with stage three FEV_1 and low blood oxygen levels. Generally, this stage is known as end stage COPD, meaning the disease has progressed, lung function has deteriorated and flare-ups could be life threatening.

- **The Benefits of Macrolide Antibiotics in Preventing and Treating COPD Exacerbations –** An exacerbation is defined as an increase in respiratory symptoms over baseline that usually requires a change in therapy (Miravitlles, 2010).
- Miravitlles (2010) found that bacterial eradication decreases the inflammatory nature of the airways in turn helping reduce exacerbations.
- In one study by Seemungal, Wilkinson, Hurst, Perera, Sapsford, & Wedzicha (2014), erythromycin 250 mg twice daily showed a 35% reduction in exacerbations.
- **The Risks of Macrolide Antibiotics in Preventing and Treating COPD Exacerbations -** Antibiotic resistance is a major public health problem world-wide and an international effort is needed to counteract its emergence.
- In a study by Albert et al. (2011) the percentage of resistance to macrolides in respiratory pathogens isolated from nasopharyngeal swabs was greatly increased in the azithromycin population compared to the placebo arm.
- In a very large cohort of Tennessee Medicaid patients, Ray and colleagues (2012) demonstrated increased cardiovascular and all-cause mortality during azithromycin therapy compared to placebo.

Discussion

- Current research indicates there is significant improvement in symptom exacerbation for the patients using long-term antibiotic therapy.
- **Is standard pharmacological therapy enough to prevent exacerbations?**
- Kew, Mavergames and Walters (2013) found that LABAs are effective for moderate/severe COPD. However, mainly Caucasian males were used in their research.
- **Is there a benefit to adding long-term antibiotics?**
- Seemungal et al. (2014) found a significant reduction in exacerbations for erythromycin versus placebo (35%) (p=0.006). However, the study only had 109 patients.
- Sethi et al. (2010) showed Moxifloxacin given for five days a week reduced exacerbations by 25% and those with mucopurulent sputum had a reduction of 45%.
- **What are the risks of long-term antibiotics?**
- Chronic or long-term use of antibiotics will always bring up a concern for bacterial resistance.
- Albert et al. (2011) found that patients using long-term azithromycin showed more resistance to macrolides in respiratory pathogens compared to placebo. However, Simoens et al. (2013) found no difference in macrolide resistance (azithromycin 52% and placebo 57%)(p=0.64)
- Ray and colleagues (2012) showed an increase in cardiovascular and all-cause mortality with azithromycin versus placebo.
- As discussed, the data is proving the benefit, but it needs to be used in an appropriate patient population. With all patients involved in this therapy, bacterial resistance is the main risk and concern.



Applicability to Clinical Practice

- Long-term antibiotic use for the prevention and treatment of AECOPD is being minimally used at this point.
- In discussing this topic with Val Tomhave, RRT and supervisor of the Sanford Pulmonary Rehab, she states that three of her patients with severe to very severe COPD are currently using long-term azithromycin therapy with great success.
- The majority of COPD patients (up to two thirds) are non-exacerbators, therefore, not candidates for long-term antibiotics.
- Patients suffering from frequent or severe infective exacerbations despite optimal pharmacological and non-pharmacological treatment would be candidates for long-term antibiotic treatment.
- Primary care providers will inevitably play a pivotal role in the use of this therapy.
- Due to the large push for preventative medicine, primary care will be a major factor by helping patients with smoking cessation, eating a healthy diet, getting regular cardiovascular exercise and overcoming psychosocial barriers to accomplish a healthy lifestyle.

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