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Prolonged treatment with macrolides in adult patients with non-cystic fibrosis bronchiectasis: Meta-analysis of randomized controlled trials

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ABSTRACT

Background: Infection, resulting in chronic airway inflammation, forms the basis of bronchiectasis pathogenesis. Macrolides possess antibacterial, anti-inflammatory and immunomodulatory properties, and are used to treat patients with non-cystic fibrosis bronchiectasis (NCFB). However, the efficacy and safety of long-term treatment with macrolides in patients with bronchiectasis have been controversial. We performed a meta-analysis to assess the efficacy and safety of macrolides in adults with NCFB.

Methods: We performed electronic search of several databases, including: Pubmed, EMBASE, EBSCO, SCI, and CENTRAL, and also searched references from identified articles for further consideration. Only randomized controlled trials (RCTs) comparing prolonged macrolide treatment with placebo for adult bronchiectasis were included. Data were extracted independently by two reviewers and combined using a fixed-effects model or random-effects with effect size expressed as OR or MD or SMD and 95% CIs for different situations.

Results: 834 studies were identified. Four RCTs met the inclusion criteria. Macrolide treatment significantly reduced pulmonary exacerbation (OR = 0.39, 95% CI 0.25–0.63) and improved lung function (SMD = 0.37, 95% CI 0.16–0.58) as compared to the placebo group. However, macrolide treatment did not significantly improve quality of life (MD = −1.90, 95% CI −7.01 to 3.20). With respect to the total numbers of participants who developed adverse events, there was no significant difference between the macrolides and placebo groups (OR = 0.83, 95% CI 0.50–1.39). Macrolides therapy could have increased the rate of macrolide resistance in adults with NCFB.

Conclusions: Macrolide maintenance therapy was effective in reducing pulmonary exacerbations, and improving lung function in adults with NCFB. However, it did not improve quality of life, and could have led to macrolide resistance.

1. Introduction

Non-cystic fibrosis bronchiectasis (NCFB) is defined as an irreversible and progressive dilatation of bronchi due to chronic bronchial inflammation [1,2]. The clinical presentations may range from no symptoms to chronic cough with frequent sputum production, hemoptysis, dyspnea, decreased exercise tolerance, frequent exacerbations [3,4], respiratory failure, need for lung transplantation in some cases or death. Many pathological conditions can give rise to NCFB, including post-infection, foreign body aspiration, immunodeficiency, congenital abnormalities of the airway, and allergic bronchopulmonary aspergillosis [5,6]. Although the etiologies are variable, the common pathophysiological pathway is a vicious cycle involving inflammation, infection, and repair of the bronchial mucosa. This pathogenic process causes

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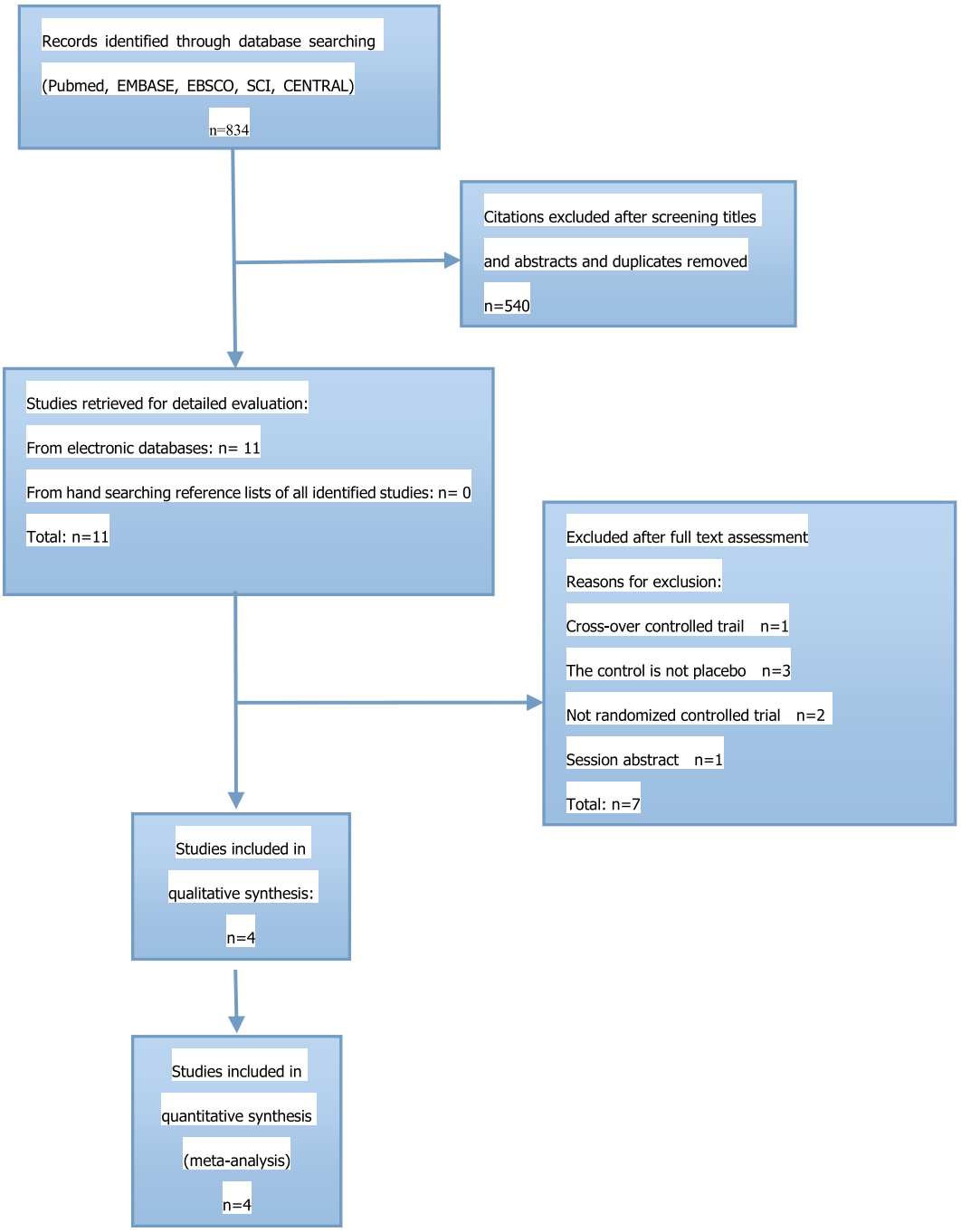

Fig. 1. Flowchart for identification of studies.

destruction of the bronchial ciliated epithelium, loss of structural elements of the bronchial airway wall, such as elastin, and lesions in smooth muscle layers. The damaged airway ciliated epithelium impairs mucociliary clearance, and results in retention of secretions, which in turn attracts bacterial colonization, and predisposes the patient to repeated infections [1,3,7–9]. So the ultimate goal of bronchiectasis treatment is to break this vicious cycle, and prevent or retard progressive inflammatory lung damage.

Macrolides have been known for their antimicrobial activity since 1952, and are widely used to treat respiratory and soft tissue infections caused by Gram-positive bacteria, such as *Streptococcus pneumoniae* and *Haemophilus influenzae*, also rickettsiae, chlamydiae, and *Mycoplasma pneumoniae*, as well as some Gram-negative bacterial pathogens [10,11]. Emerging evidence has shown that macrolides also have anti-inflammatory and immunomodulatory properties [10,12,13]. The benefits of macrolides in the treatment of diffuse panbronchiolitis and cystic fibrosis are well known [14,15]. Several studies have also demonstrated the benefits of macrolides in bronchiectasis [16,17]. But the efficacy and safety of long-term treatment with macrolides in patients with bronchiectasis have been controversial [18,19]. The purpose of our study was to summarize the efficacy and safety of macrolide treatment in adults with NCFB through a meta-analysis of RCTs comparing prolonged macrolides therapy (for four or more weeks) with placebo.