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Title: The effect of long-term macrolides therapy for acute exacerbation of chronic obstructive pulmonary disease: A meta-analysis

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Body: Introduction: Chronic obstructive pulmonary disease (COPD) exacerbations are associated with frequent hospital admission reduction of lung function, and decreased quality of life. Macrolides have airway antiinflammatory actions and may reduce the frequency of COPD exacerbations. Methods: we searched PubMed and Embase databases to identify randomized controlled trials (RCTs) that assessed the effect of long-term macrolides therapy for COPD. The primary outcome assessed was frequency of acute exacerbations during follow-up. Both the fixed and random-effects models were used to obtain the hazard ratio of exacerbations associated with the use of macrolides versus controls or placebo depending on the heterogeneity of effects among studies. Results: Combining six studies (N=1485), use of macrolides showed can decrease relative risk of experiencing acute exacerbation of COPD [point estimate=0.592, 95%CI(0.423, 0.829), P <0.05], but the effect on number of patients with at least one exacerbation was not so sure (RR=0.58, 95%CI[0.33, 1.04], P=0.07). However, subgroup analysis found that prolonged treatment period to more than 6 months can decrease not only relative risk of experiencing acute exacerbation of COPD (with Point estimate=0.569, 95% CI [0.416, 0.778], P<0.05), but also number of patients with at least one exacerbation(RR=0.50, 95%CI (0.27, 0.90), P=0.02). Five studies reported adverse events, and adverse events were more frequent with macrolides (RR=1.35,95%CI(1.09,1.67),p=0.007). Conclusions: Long-term macrolide therapy in patients with COPD can decrease exacerbations, but the safety is not sure.