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Efficacy and safety of anti-interleukin-5 therapy in patients with asthma: A pairwise and Bayesian network meta-analysis

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ABSTRACT

Introduction: Anti-interleukin-5 therapy has been proposed as a novel and promising treatment option in asthma treatment. However, the optimum monoclonal antibodies for asthma treatment remain uncertain.

Methods: We searched the PubMed, EMBASE and Cochrane databases from their inceptions to June 2018 for randomized controlled trials that reported pulmonary function, adverse events, Asthma Quality of Life Questionnaire (AQLQ) scores, and asthmatic exacerbations resulting from anti-interleukin-5 therapy in asthma patients. Extracted data were analyzed by pairwise and network meta-analysis.

Results: Twenty-one randomized studies were identified for this analysis. By pairwise meta-analysis using a placebo as the reference, patients treated with monoclonal antibodies were associated with significantly improved forced expiratory volume (FEV1) values (standard mean difference [SMD], 0.18; 95% confidence interval [CI], 0.12–0.23; $P < 0.001$), lower rates of adverse events (risk ratio [RR], 0.93; 95% CI, 0.90–0.97; $P < 0.001$) and significant improvements in the AQLQ scores (SMD, 0.20; 95% CI, 0.13–0.26; $P < 0.001$). There were no significant differences in exacerbations risks (RR, 0.68; 95% CI, 0.11–4.14; $P = 0.097$). According to network meta-analysis, adverse events-related benefits were seen only with reslizumab, while AQLQ scores benefits, and pulmonary function benefits were still seen with all three monoclonal antibodies. The assessment of rank probabilities indicated that reslizumab presented the greatest likelihood of having benefits for pulmonary function, reducing adverse events and improving AQLQ scores when compared with the placebo, and mepolizumab presented the best benefits for reducing asthmatic exacerbations.

Conclusions: Anti-interleukin-5 therapy appears to be a safe and effective treatment for asthma patients with respect to pulmonary lung function, adverse events and AQLQ scores, and do not increase asthmatic exacerbations. Our network meta-analysis in patients with asthma suggests that reducing adverse events benefits due to reslizumab, and pulmonary lung function benefits as well as good AQLQ scores are seen with respect to the three antibodies. Network meta-analysis indicates the probability that the best anti-interlukin-5 therapy for asthma patients might be reslizumab, but further trials are required to determine the most effective asthma treatment drug.

1. Introduction

Asthma is a problem worldwide, with an estimated 300 million affected individuals, characterized by bronchial inflammation, airway hyper-responsiveness induced by specific and nonspecific stimuli, and reversible bronchial obstruction [1]. The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach to asthma control, with treatment being stepped up until control is achieved and maintained [2]. However, there are some cases of persistent asthma that are not adequately controlled by combination therapy with ICS and LABA. The quality of life for Patients with persistent uncontrolled asthma is under strain from high risk of asthma-related hospitalization and mortality. Persistent eosinophilic airway inflammation in asthma is believed to increase the risk of subsequent exacerbation [3]. Over the last 2 decades, specific targeting of cytokines has been developed through high-affinity monoclonal antibodies (and in some cases other molecules) that block the binding of cytokines to their receptors, block the receptors, or deplete cells responding to the cytokines. These biologics are now entering clinics, and one group specifically targets IL-5. It is known that interleukin (IL)-5 is central to eosinophil maturation, release from the bone marrow, and subsequent accumulation, activation, and persistence in the tissues. Thus, specific targeting of IL-5 has been an attractive drug target in asthma [4].

Three previous meta-analyses reported that anti-IL-5 therapy might

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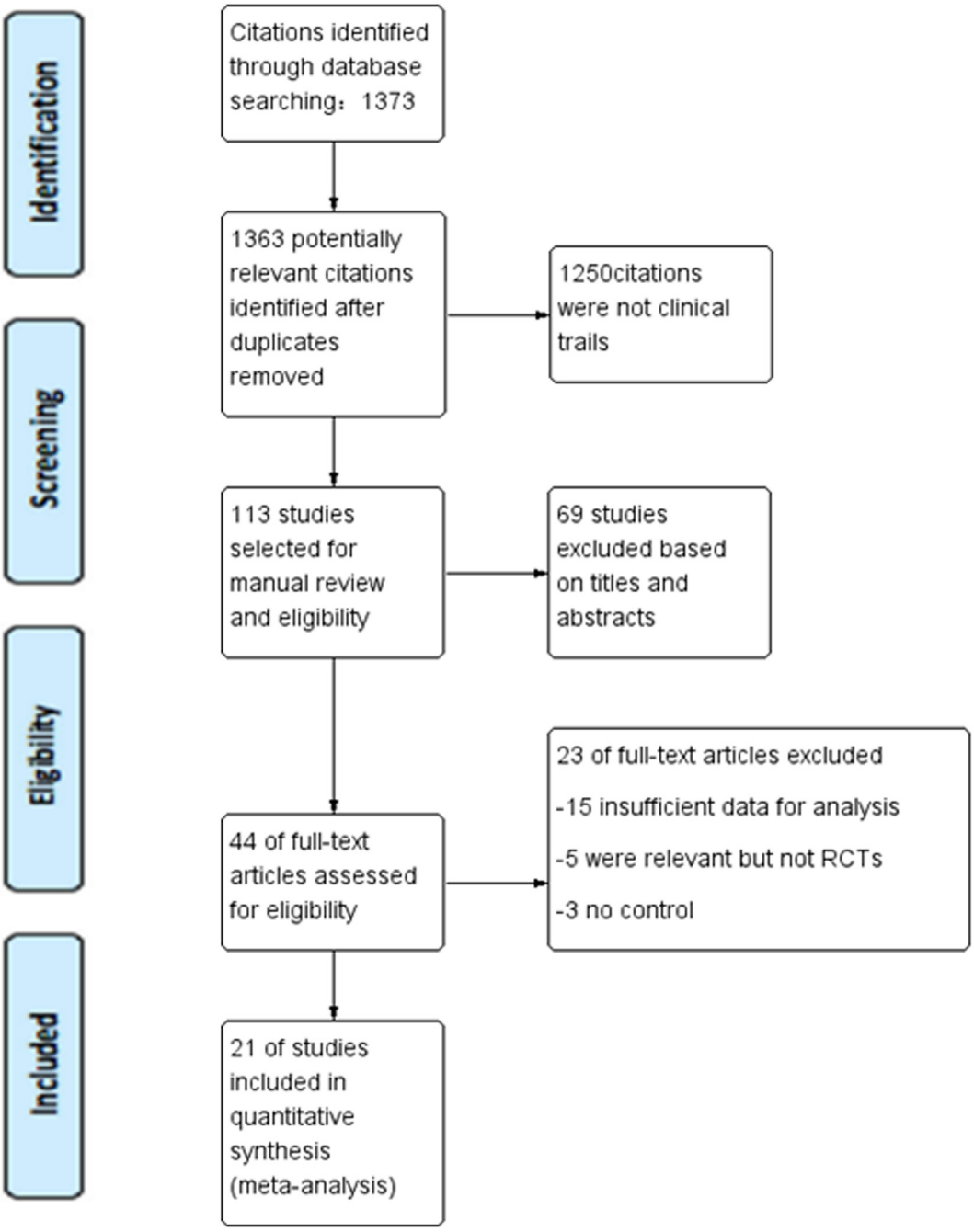

Fig. 1. Study flow diagram.

be beneficial in the treatment of asthma [5–7]. However, two studies were traditional pairwise meta-analyses compared anti-IL-5 antibodies with placebo, which didn't made comparisons among the anti-IL-5 antibodies. The only network meta-analysis (NMA), a method for concurrent comparison of multiple treatments in a single meta-analysis [8], only included trials published up to September 2015, which limited the power of the tests [6].

In the present study, our objective was to update the evidence to systematically evaluate the effect of anti-IL-5 antibodies in asthma patients on pulmonary function, adverse events, AQLQ scores and exacerbation rates and we also used a network meta-analysis approach, which enabled us to assess three anti-IL-5 antibiotics by indirect comparison to determine their efficacy.

2. Methods

2.1. Search strategy

We searched the PubMed, EMBASE, and Cochrane databases from inception to June 2018, to identify potentially relevant studies. Search terms included several parameters: 1.) anti-IL-5 OR anti-interleukin-5 OR monoclonal antibody OR mepolizumab OR benralizumab OR reslizumab; 2.) asthma. Publication type of randomized controlled trials (RCTs) was limited. We also evaluated the reference lists of the relevant clinical trials to identify additional studies.

Studies were included if they met several criteria: 1.) patients which included a study population that was diagnosed with asthma; 2.) intervention which included use of anti-IL-5 antibodies for treatment of asthma compared to placebo; and 3.) reported at least one of the