Clarithromycin suppresses airway hyperresponsiveness and inflammation in mouse models of asthma.


Source
GlaxoSmithKline Research Centre Zagreb Limited, Zagreb, Croatia.
oboska.y.hrvacic@gsk.com

Abstract
Macrolide antibiotics, a class of potent antimicrobials, also possess immunomodulatory/anti-inflammatory properties. These properties are considered fundamental for the efficacy of macrolide antibiotics in the treatment of diffuse panbronchiolitis and cystic fibrosis. In patients with asthma, macrolide antibiotics have been reported to reduce airway hyperresponsiveness and improve pulmonary function. However, their beneficial actions in asthmatics possibly could be attributed to antimicrobial activity against atypical pathogens (e.g. Chlamydia pneumoniae), corticosteroid-sparing effect (inhibition of exogenous corticosteroid metabolism), and/or their anti-inflammatory/immunomodulatory effects. In order to investigate whether efficacy of macrolide antibiotics in asthma results from their immunomodulatory/anti-inflammatory activity, the influence of clarithromycin pretreatment (2 h before challenge) was examined on ovalbumin-induced airway hyperresponsiveness and airway inflammation in the mouse. Clarithromycin treatment (200 mg/kg intraperitoneally) decreased IL-4, IL-5, IL-13, CXCL2 and CCL2 concentrations in bronchoalveolar lavage fluid and markedly reduced inflammatory cell accumulation in bronchoalveolar lavage fluid and into the lungs, as revealed by histopathological examination. Furthermore, clarithromycin-induced reduction in inflammation was accompanied by normalization of airway hyperresponsiveness. In summary, in ovalbumin-induced mouse models, clarithromycin efficiently inhibited two important pathological characteristics of asthma, airway hyperresponsiveness and inflammation. These data suggest that the efficacy of clarithromycin, as well as of other macrolide antibiotics, in asthmatic patients could be attributed to their anti-inflammatory/immunomodulatory properties, and not only to their antimicrobial activity or exogenous corticosteroid-sparing effects.

PMID:19560456