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Title: Downregulation of Th 17 response after low dose clarithromycin in non-CF bronchiectasis patients

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Body: INTRODUCTION: Th17 lymphocytes and, particularly, IL-22-secreting Th17 cells play a crucial role in neutrophilic inflammation and tissue injury. It has been shown that clarithromycin (CAM) has antiinflammatory and immunoregulatory effects. However, the effect of CAM administration on Th17 response in the setting of non-CF bronchiectasis has not yet been studied. AIM: To evaluate the effects of CAM prophylaxis on the inflammatory process and Th17 response in patients with steady-state non-CF bronchiectasis. METHODS: Ten adult patients received CAM 500mg per day p.o. for 12 weeks. Peripheral blood Th17 cells were analyzed by flow cytometry using antibodies against CD4, IL-17 and IL-22. IL-17 concentrations in exhaled breath condensate (EBC) were quantified using a commercially available ELISA. Pulmonary function tests (PFT) and clinical data were recorded during the treatment period. RESULTS: Post treatment CD4+IL17+ count (cells/ μ l) and EBC IL-17 levels (pg/ml) decreased significantly (mean 3.2016 ± 2.7280 vs 2.8181 ± 1.9426 , $p=0.001$ and 4.3560 ± 1.5899 vs 3.2990 ± 0.74311 , $p<0.001$, respectively). Mean pO₂ (mmHg) improved significantly (72.8 ± 6.477 vs 79.3 ± 10.242 , $p<0.001$), while PFT and pCO₂ remained unaltered. Notably, the decrease in CD4+IL17A+ cell count correlated with the decrease in exacerbations ($r: 0.618$, $p=0.057$) and the pO₂ increase ($r: 0.648$, $p=0.043$), while the decrease of IL-22+IL-17+ effectors correlated with the decrease in EBC IL-17 levels ($r: 0.852$, $p=0.002$). CONCLUSION: We report for the first time that low dose CAM in patients with non-CF bronchiectasis appears to reduce lung inflammatory process potentially via downregulating the Th17 response.