Expression of Granulocyte/Macrophage-Colony-Stimulating Factor, Interleukin-8 and RANTES in the Bronchial Epithelium of Mild Asthmatics Is Down-Regulated by Inhaled Beclomethasone Dipropionate

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Key Words

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Introduction

Material and Methods

Recent studies have demonstrated that bronchial epithelial cells of asthmatics are capable of expressing proinflammatory cytokines, including granulocyte/macrophage-colony-stimulating factor (GM-CSF) interleukin (IL)-6 and IL-8, which may play a role in the aetiology of allergic airway disease, possibly by attracting and activating inflammatory cells [1, 2]. In this study, we have investigated the expression of GM-CSF, IL-8 and RANTES and activation of eosinophils in the bronchial epithelium of mild asthmatics and assessed their associations with bronchial responsiveness. We have also assessed the effects of inhaled beclomethasone dipropionate (BDP) on GM-CSF, IL-8 and RANTES and activated eosinophils in the bronchial epithelium, in a randomised, placebo-controlled double-blind manner.

25 mild-asthmatic volunteers were randomised to two parallel treatment groups to receive either BDP 500 µg twice daily or matched placebo for 4 months. The PC20 FEV₁ was determined and bronchial biopsies were collected from each subject prior to commencing treatment and at the end of the treatment period. All biopsies were processed immunocytochemically and analysed for the total number of EG2-staining cells (activated eosinophils), GM-CSF, IL-8 and RANTES. EG2-staining cells in the epithelium were counted and expressed as the number of cells/mm². Expression of GM-CSF, IL-8 and RANTES was quantified by computerised colour image analysis [3] and the results expressed as the percentage of the total epithelial area staining for these cytokines.

Results

Discussion

Staining for GM-CSF, IL-8 and RANTES in biopsies was mainly localised in the epithelium. However, some inflammatory cells and endothelial cells in the biopsies were also stained. EG2-staining cells were also abundant in the bronchial epithelium. Epithelial expression of GM-CSF was correlated weakly but significantly with both PC2 $\dot{U}$ FEV₁, to histamine ($r = -0.462$, $p < 0.05$) and EG2-staining cells in the epithelium ($r = 0.484$, $p < 0.05$). BDP treatment significantly decreased the percentage staining for GM-CSF (from 24.7 to 12.8%; $p = 0.008$), IL-8 (from 27.1 to 14.7%; $p = 0.014$) and RANTES (from 17.1 to 4.2%; $p = 0.042$) in the epithelium. The number of EG2-staining cells was also significantly reduced after BDP treatment (from 790.1 to 203.3/mm²; $p = 0.003$). The changes in the expression of GM-CSF, IL-8 and RANTES were independently correlated with changes in EG2-staining cells following treatment ($r = 0.789$, $p < 0.01$; $r = 0.653$, $p < 0.02$, and $r = 0.60$, $p < 0.05$, respectively).

The findings of our present study suggest that the expression of inflammatory cytokines, particularly GM-CSF in the bronchial epithelium of asthmatics, may influence at least partly, both the number of activated eosinophils and bronchial hyperresponsiveness, in these individuals. This is in agreement with the findings of other studies [4, 5].

Our finding that treatment with 500 μ g BDP twice a day for 4 months significantly decreased the expression of GM-CSF, IL-8 and RANTES in the bronchial epithelium of the asthmatic individuals, and that changes in the expression of GM-CSF, IL-8 and RANTES were correlated with EG2-staining cells suggests that BDP may attenuate the activation and/or infiltration of the airways by eosinophils partly by down-regulating the expression of these cytokines in the bronchial epithelium.

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