Mucin expression in nasal polyps of glucocorticoid-resistant patients.

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Introduction:
Nasal polyposis associated to chronic rhinosinusitis (NP-CRS) is a chronic inflammatory disorder which may develop resistance to glucocorticoid therapy. This upper airway respiratory disease is estimated to affect 2-4% of general population, 10-15% of asthmatic patients and over 90% of asthmatic patients with nonsteroidal anti-inflammatory (NSAID) intolerance.

Mucus hypersecretion is a hallmark of nasal polyposis and increased mucin expression is a feature of this disease. Glucocorticoids are the main anti-inflammatory therapy for NP-CRS. As part of their anti-inflammatory activity, glucocorticoids have been described to increase membrane-tethered while decrease secreted mucin expression in nasal polyps.

This study explores both membrane-tethered and secreted mucin expression in glucocorticoid-resistant patients with NP-CRS.

Methods:
A total of 38 patients were included in this study. The patients’ diagnosis was fulfilled, according to the European Consense Document EP3OS (Fokkens W et al, Rhinology 2007), with computed tomography (CT) and nasal endoscopy.

Patients included in this study were in treatment with the following intranasal steroids (63% mometasone, 5% budesonide, 24% fluticasone or 8% none) and oral steroids (47% deflazacort, 11% betametasone, 18% none, 24% other).

Patients were classified into the following groups: NP-CRS patients 1) without asthma (n=9), 2) with asthma (n=6), 3) with asthma and NSAID intolerance (n=13) and 4) glucocorticoid-resistant (n=10).

Nasal polyps were removed by biopsy and total RNA was isolated with TriZol reagent. mRNA relative expression of membrane-tethered mucins (MUC1, MUC4 and MUC16) and secreted mucins (MUC5AC and MUC5B) was measured by real-time PCR.

Results:
MUC1 and MUC16 gene expression decreased in nasal polyps of patients with asthma and asthma and NSAID intolerance compared to non-asthmatic patients. This effect was markedly evident in the glucocorticoid-resistant group, reaching a 55% of reduction compared to non-asthmatic patients.

In contrast, MUC4 gene expression was increased by 2-fold in the glucocorticoid-resistant group compared to non-asthmatic patients.

MUC5AC and MUC5B gene expression increased in nasal polyps of patients with asthma and asthma and NSAID intolerance compared to non-asthmatic patients. This increase was evident in the glucocorticoid-resistant group, where MUC5AC and MUC5B reached a 3-fold and 2-fold increase respectively compared to non-asthmatic patients.

Conclusions:
These results show a decreased expression of MUC1 and MUC16 membrane-tethered mucins and an increased expression of MUC4 and secreted mucins MUC5AC and MUC5B in polyps from glucocorticoid-resistant patients. Results evidence mucin participation in glucocorticoid-resistance in NP-CRS.
Mucin expression in nasal polyps may have an important clinical implication in glucocorticoid non-responder patients.