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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, 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 by triplicate for each sample. Relative quantification of these different transcripts was determined with the $2^{-\Delta\Delta Ct}$ method using GAPDH as endogenous control and normalized to NP-CRS without asthma group.

All of the data analysis from human samples was performed by nonparametric tests and described as mean ± SEM. Statistical analysis of data between 2 groups or more were performed using the Mann Whitney test or Kruskal-Wallis test respectively using GraphPad Software Inc (San Diego, CA, U.S.A.). Significance was accepted when $P<0.05$.

Results:

Normalizing MUC1 expression to one in NP-CRS without asthma group, we observed that MUC1 gene expression was significantly down-regulated to 0.69±0.11 ($P<0.05$) in asthma and NSAID intolerant NP-CRS patients and to 0.53±0.09 ($P<0.05$) in glucocorticoid-resistant group.

In a similar way, MUC4 and MUC16 were down-regulated to 0.58±0.12 ($P<0.05$) and 0.82±0.24 ($P>0.05$) respectively in asthma and NSAID intolerant NP-CRS patients, and to 0.41±0.16 ($P<0.05$) and 0.28±0.12 ($P<0.05$) respectively in glucocorticoid-resistant group.

In contrast, secreted mucins MUC5AC and MUC5B gene expression was increased to 4.69±1.9 ($P<0.05$) and 1.99±0.91 ($P<0.05$) respectively in glucocorticoid-resistant group.

NP-CRS asthmatic patients did not show significant differences with other groups.

Conclusions:

These results show a decreased expression of MUC1, MUC4 and MUC16 membrane-tethered mucins and an increased expression of 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.