

393 Cytokine Association With Chronic Rhinosinusitis With And Without Nasal Polyps And Efficacy Of Preoperative Oral Steroids

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RATIONALE: Oral steroids are commonly given to patients with Chronic Rhinosinusitis (CRS), however no study has looked into their efficacy in the different disease states of CRS on a large scale.

METHODS: Our study included 176 adult patients of whom 66 were given preoperative oral steroids including 26 non-polypoid CRS (CRSsNP) and 40 CRS patients with nasal polyps (CRSwNP). The steroid naïve cohort included 30 controls, 40 CRSsNP, and 40 CRSwNP. Extracts from sinus tissue were run on a 23-plex Procarta Cytokine Assay. A student's t-test was performed. Pre-op, 1-month, and 3-month post-op SNOT-22 quality of life surveys were completed for each patient.

RESULTS: Cytokines associated with steroid naïve CRSsNP tissue included IL-2, IL-5, IL-7, IL-12(p70), IL-17, IFN-gamma, and MCP-1 compared to control tissue (p<0.05). IL-2, IL-7, IL-12(p70), IFN-gamma, and MCP-1 were significantly lower in steroid exposed CRSsNP (p<0.05). Cytokines associated with steroid naïve CRSwNP tissue included IL-5, IL-10, IL-13, and IL-17, with reduced levels of RANTES and FGF-basic compared to control tissue (p<0.05). IL-5, IL-13, and MCP-1 were lower in steroid exposed CRSwNP (p<0.05). Cytokines not effected by steroids included IL-4, IP-10, IL-10, IL-12(p40), RANTES, GM-CSF, and EOTAXIN. Patients that received preoperative steroids had better SNOT-22 scores at 1 and 3 months post-op. Patients who did not receive preoperative steroids improved at 1 month but had worse SNOT-22 scores at 3 months post-op.

CONCLUSIONS: Different cytokines are associated with CRSsNP and CRSwNP. Oral steroids given before surgery reduce the majority of cytokines and may help in long-term improvement in quality of life.

394 Sensitization to Alternaria as a potential risk factor for Chronic Rhinosinusitis

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RATIONALE: Chronic rhinosinusitis (CRS) is a major cause of morbidity in North America, however, the etiology remains poorly defined. Hypersensitivity to fungi, in particular *Alternaria*, has been proposed to have a putative role. In this study, our objective was to characterize skin prick test (SPT) and human serum reactivity to other common aeroallergens in CRS patients.

METHODS: One hundred and thirty two subjects (18-65 years of age) were recruited into the study. 101 subjects had a confirmed diagnostic history of CRS and 31 subjects were recruited as controls. Enrolled subjects underwent SPT to a panel of perennial, grass, weed, tree, and fungal aeroallergens. A blood sample was collected by venipuncture for hematological analysis. Atopic status to selected common environmental allergens (grass, mold, and tree species) was determined using Phadia ImmunoCap. Specific-IgG was also quantified to *Cladosporium herbarum*, *Alternaria alternata*, *Stachybotrys atra*, and *Aspergillus versicolor*. Differences between CRS and control patients were determined by analysis of variance (ANOVA) and chi-squared analysis.

RESULTS: No statistically significant differences were observed between mean specific IgE and IgG titers in CRS and control patients in the ANOVA analysis. Chi-squared analysis of SPT data revealed similar statistically insignificant results, however, positive SPT reactivity to *Alternaria* was identified as a risk factor for having CRS (OR 3.58, p < 0.0487).

CONCLUSIONS: Sensitization to common perennial, grass, weed, and tree aeroallergens were not associated with CRS. This study supports recent data which suggests that in predisposed individuals, *Alternaria* sensitization is associated with increased risk of having CRS.

395 Alpha-1-Antitrypsin Deficiency: A New Clinical Entity in CRS?

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RATIONALE: Alpha-1-antitrypsin (AAT) is a serine proteinase inhibitor which protects the lower respiratory tract from proteolytic damage by neutrophil elastase. AAT deficiency, an inherited disorder with an incidence of 1 in 2,500 individuals (0.04%), is associated with an increased risk of emphysema or hepatic disease yet frequently remains undiagnosed. While AAT deficiency is not associated with chronic rhinosinusitis (CRS), in previously reported results from genetic association studies of severe CRS, we have identified SERPINA1, the gene coding for the AAT protein, to be associated with a severe form of CRS, suggesting that AAT deficiency may be present in CRS. We wished to determine whether AAT deficiency is present in patients with severe CRS.

METHODS: Prospective study of all patients seen in our tertiary care institution for assessment of CRS with or without nasal polyposis not responding to surgery. Assessment included measurement of the serum level of AAT.

RESULTS: During an 18 month period 199 patients with refractory CRS were screened for AAT deficiency. Eight patients (4.0%) were identified with low levels of AAT (Range: 0.10 - 0.98, Normal: 1.00- 2.00mg/dL). All of these patients were asthmatic under therapy, and all responded well to standard management protocols using irrigation with saline and corticosteroids.

CONCLUSION: AAT deficiency is more frequent in individuals with refractory CRS than the general population, thus screening for AAT deficiency should probably be routinely performed in cases of severe CRS. Additionally, this finding suggests a novel mechanism of pathogenesis of CRS and offers potential avenues for therapy of selected cases of CRS.

396 Efficacy of Antifungal Therapy in Chronic Rhinosinusitis: A Systematic Review

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RATIONALE: Chronic rhinosinusitis is a common disease, but its pathophysiology is still unclear. It has been suggested that an exaggerated immune response to fungi is crucial in the pathogenesis of this disease, however, studies on the effectiveness of antifungal therapy have been controversial. Our study evaluates the effectiveness of antifungal therapy for chronic rhinosinusitis.

METHODS: We performed a systematic review by searching MEDLINE, EMBASE, and the Cochrane Collaboration Database for randomized controlled trials from 1966 to January 2009 examining the efficacy of antifungal therapy in chronic rhinosinusitis patients.

RESULTS: We identified 7 randomized placebo-controlled trials: 6 examined the efficacy of intranasal amphotericin B, one examined the efficacy of oral terbinafine. Studies varied widely in patient populations and methodology, especially with respect to therapy delivery and outcome measurements. Only one study found statistically significant improvements in computed tomography (CT) results, endoscopy scores, and intranasal eosinophil-derived neurotoxin (EDN) levels after treatment. Another study found a worsening of symptom scores and quality of life scores in the treatment group. All other outcomes, including measurements of inflammatory markers besides EDN, revealed no statistically significant differences between placebo and active treatment, including in patients observed to have intranasal fungus before but not after treatment.

CONCLUSIONS: There was no convincing evidence that antifungal therapy had an effect on clinical outcomes or inflammatory marker levels in chronic rhinosinusitis. However, larger studies with more uniform study methodology and outcome measures are needed.