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Aquaporin 3 Expression in Respiratory Mucosa is Down-Regulated in Bronchiectasis *in vivo*

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Introduction: Bronchiectasis is characterized pathologically by permanent abnormal bronchial dilation, and clinically by chronic sputum production. Aquaporin 3 (AQP3), a recently described water channel that is also found in large airway cell membrane, could play a role in the pathogenesis and particularly that of bronchorrhea in bronchiectasis. However, little is known of its *in vivo* distribution and physiological role in human airways.

Methods: We have, therefore, performed this quantitative immunohistochemistry study on endobronchial biopsies to evaluate the expression and clinical relevance of AQP3 in patients with idiopathic bronchiectasis (n=25, 15F, 64.3 ± 11.5 yrs) and control subjects (n=14, 5F, 57.5 ± 12.0 yrs). Quantitative image analysis was performed to evaluate the expression of AQP3 in the bronchial epithelial cells.

Results: The intensity of AQP3 immunoreactivity in the epithelial cells of the bronchiectatic was significantly lower than that for the control sections (median 58.26 ± 10.6, mean 59.57 ± SD 10.57, range 46.80–82.50; 51.60, 23.07–70.20, 50.07 ± 10.80; p=0.009; Figure 2). Among the bronchiectasis patients, the intensity of AQP3 immunoreactivity in the entire epithelium for sputum producers was significantly lower than that obtained from the non-producers (60.96, 47.14–82.50, 60.70 ± 12.41; 54.10, 46.80–63.10, 54.81 ± 5.54, p=0.04). While there was a significantly lower intensity of AQP3 immunoreactivity in the entire epithelium for sputum producers than that in control airways (51.60, 23.07–70.20, 50.07 ± 10.81, p=0.004), there was no such difference between sputum non-producers and control subjects (p=0.24).

Conclusion: Our findings suggest that AQP3 could have an important role in the pathogenesis of increased mucus production in bronchiectasis. Further evaluation of these water channels could lead to better understanding of the pathogenesis in bronchiectasis. (Supported by a University Department of Medicine Mini-Grant 2000).

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Inhaled Fluticasone Therapy Reduces Exacerbation Frequency and Sputum Production in Bronchiectasis (BX)

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Introduction: Despite its efficacy in asthma, inhaled steroid therapy has not properly tried on BX patients, who also suffer from chronic airway inflammation. Although we have previously demonstrated reduction in sputum pro-inflammatory mediator levels in patients treated with inhaled steroid therapy, the clinical efficacy of such therapy has not been studied in bronchiectasis.

Methods: We have performed a double-blind randomized study on 87 stable BX patients, who received either fluticasone 500µg BID (FG, n=42, 20F, 57.7 ± 14.6 yr) or matched placebo (PG, n=45, 33F, 58.9 ± 14.2 yr) administered via the Accuhaler device for 52 weeks.

Results: At 52-week, 38 and 42 patients in FG and PG completed the study. Significantly less patients in FG reported cough (p=0.03) but the two groups had no difference in dyspnoea, wheezing, chest pain or fatigue (p>0.05). Although there was no significant difference in the exacerbation frequency (EF) between FG and CG (2.8 ± 1.8, 3 ± 2.9/yr; p=0.39), significantly more patients in the FG had EF<4/yr than PG (10.5 and 19%, p<0.05). Clinical response in 52-week EF, was “improvement” (<20% of 0-week) in 19, stable in 12, and deterioration (≥20% of 0-week) in 7 of FG patients, which was significantly different from PG (12, 15, 15; p=0.03). Similarly, FG patients were significantly different from their counterparts in improvement, stable disease and deterioration (24, 4, 10; and 14, 13, 15; p=0.004) for clinical response in 24h sputum volume. There was no significant difference in the sputum purulence score, FEV₁% or FVC% between the treatment groups at 52-week (p>0.05). 0-week EF of ≥4 predicted an improved outcome in 52-week EF for patients in FG (OR 10.5, 95%CI 2.3-47.2), but not PG. Neither 0-week 24h sputum volume or sputum purulence score predicted treatment. The only reported adverse reaction was sore throat, which occurred in 17.5 and 2.4% of patients from FG and PG respectively (p=0.03).

Conclusion: We conclude that inhaled fluticasone therapy reduces sputum volume and exacerbation frequency in patients with active bronchiectasis. Our results, for the first time, demonstrate the efficacy of anti-inflammatory therapy in bronchiectasis, and are vital to future management these patients.