285 Immunomodulation of roxithromycin for *Dermatophagoides farinae*(Df)-induced IL4, IFN-γ production in PBMCs from patients with bronchial asthma (BA)

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Roxithromycin, a new member of the macrolide family of antibiotics, which is recently reported to inhibits a bronchial response and improves airway hyperresponsiveness in patients with bronchial asthma. We tested effect of roxithromycin on T cell growth, IL4 and IFN-γ production by Df-stimulated peripheral blood mononuclear cells (PBMCs) from patients with mite-sensitive BA. Roxithromycin have suppressive activity against cell proliferation as measured by responsiveness of Df-activated cells to IL2 and subsequently induced IL4 production by Df-stimulated patient PBMCs. In contrast, by the same treatment, specifically reduced IFN-γ production by Df-stimulated patient PBMCs was increased in a dose-dependent manner beyond normal levels. The results indicate that roxithromycin was capable of functioning as an immunomodulator to inhibit lymphocyte responses to allergen, resulting in suppression of Df-specific IgE production in patients with BA.

286 Effect of Scheduled Albuterol Inhalation on Spirometry, Lung Volumes and Bronchial Hyperreactivity.

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Previous studies revealed no improvement in bronchial hyperreactivity (BHR) despite 3 months of therapy with inhaled and systemic glucocorticoids in children with moderately severe asthma in residential care (JACI 1993,91:169). Since those subjects also receive inhaled albuterol (B_2) the possibility of high use of B_2 contributing to BHR was considered. In a residential unit, a 1 week B_2 washout was followed by baseline PFT and methacholine challenge (MC). Nine subjects then received 2 weeks of nebulized B_2 or placebo given 4 times daily, followed by PFT and MC. Patients continued to receive methyxanthines, inhaled and systemic corticosteroids as needed.

	Baseline	B_2	p-value	Placebo	p-value
FEV_1/FVC	76.4%	72.8%	0.44	69.5%	0.88
FEF 1% 25-75 predicted	53.3%	49.4%	0.39	59.5%	0.91
RV/TLC	31.3%	37.5%	.28	30.44%	.88
PC20 mg/ml	1.1	0.08	.69	4.2	.29

These results illustrate that regularly scheduled inhaled B_2 do not adversely affect PFT parameters of large airway obstruction ,small airway flow or air trapping. Avoidance of B_2 may permit improvement of BHR.

287 Albuterol MDI cumulative dose-response in asthmatic children.

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The safety and efficacy of cumulative doses of albuterol aerosol (A) were studied in a placebo-controlled short term trial. Atopic asthmatics, aged 7-17 years, with baseline FEV_1 < 80% predicted were assigned to receive either albuterol (n=10) or placebo (n=9) inhaled through a 500 ml Volumatic spacer. A doses were increased sequentially from 1 up to 5 puffs at 15 minutes interval (0.1 mg to 1.5 mg). Blood pressure and heart rate were recorded after each set of puffs. Tremor was subjectively assessed. Mean baseline FEV_1% was 63.1 ± 5.4 for A and 69.2 ± 6.4 for placebo (p>0.05). Both FEV_1 and FEF25-75% improved significantly with 1 puff albuterol as compared with baseline values; FEV_1% increased to 93.1 ± 6.6 and FEF25-75% from 34.7 ± 4.2 up to 88.6 ± 10.4 with 15 cumulative puffs or approximately 1,5 mg A. Results are expressed as means ± SEM.

Mean % increase in FEV_1 was 21 with 0.1 mg and reached a 53% increase with 1.5 mg A. FEV_1 % change with placebo varied between 6.4 and 8.6% as compared to baseline values.

Heart rate and blood pressure did not change significantly throughout the study.Tremor was not reported with 3 puffs of A but it was in 6/10 with the final 1.5 mg dose.

In conclusion, cumulative doses up to 1.5 mg A by MDI are safe and effective in children.

288 Long Term Effect of Fenoterol (F) and Fenoterol + Ipratropium Bromide (F+IB) in Asthmatic Children

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The aim of this study was to compare the clinical efficacy and the long term effect of F and F+IB on airway hyperresponsiveness in children with asthma. In a double-blind, crossover study, 50 children with mild asthma and positive skin test to dust mite were randomly assigned, after a 2 week baseline period, to receive either F (200 mcg TID) or F+IB (200 mcg + 80 mcg TID) by meter dose inhaler, for eight weeks, with a washout period of four weeks between each treatment. Methacoline challenge was performed every two weeks before, during and after the treatment period. Methacoline responsiveness was mesured as the provocative dose (PD_{20}) that caused a 20 percent decrease in FEV_1. There was no significant difference in PD_{20} during the treatment period when compared with the baseline and washout period (p=0.748). Clincal scores improved significantly during the treatment period in 69.6% of the patients (95% CI) when compared with the baseline period. There was no significant difference on the clinical scores between the two treatment groups (p=0.9001). There was no side effects in both treatment groups. Our study suggests that prolonged use of F or F+IB is safe and clinically improved children with mild asthma without increasing bronchial hyperractivity.