

516 Carbon Dioxide Inhibits Mast Cell Degranulation And Histamine Release

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RATIONALE: Intranasal delivery of carbon dioxide (CO₂) has been shown to be efficacious in the symptomatic treatment of seasonal and perennial allergic rhinitis in clinical trials. The goal of this study was to determine whether administration of 100% CO₂ could inhibit degranulation and histamine release from isolated mast cells in response to compound 48/80, an agent known to activate mast cells.

METHODS: Mast cells labeled with the fluorescent dye sulfardodamine-B were isolated from the peritoneal cavity of adult Sprague Dawley rats. Mast cell cultures were left untreated, treated with 48/80, treated with CO₂ alone, or treated with CO₂ prior to addition of stimulatory agents. Phase and fluorescent microscopy were used to study mast cells degranulation, while an immunoassay was used to directly measure the amount of histamine released into the culture media.

RESULTS: While treatment with 48/80 caused >90% of mast cells to degranulate and caused a significant increase in the amount of dye detected in the media, this stimulatory effect was greatly inhibited by pretreatment with CO₂ prior to addition of 48/80. Histamine levels in the media were increased several-fold in response to 48/80. However, CO₂ treatment decreased the amount of histamine detected in the culture media in response to 48/80 to near baseline levels.

CONCLUSIONS: Results from this study provide the first evidence of a unique regulatory mechanism by which CO₂ inhibits mast cell degranulation and histamine release. Our data may help explain the reported therapeutic benefit of non-inhaled intranasal delivery of 100% CO₂ to treat allergic rhinitis.

517 Association Between Interleukin-10 Promoter Polymorphism And Aspirin-Intolerant Asthma

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RATIONALE: The molecular genetic mechanisms of the AIA with rhinosinusitis are still unknown. The goal of this study was to investigate the association of *IL10* gene polymorphism with an AIA phenotype with rhinosinusitis in the Korean population.

METHODS: Three promoter polymorphisms of interleukin-10 (*IL-10*) gene, -1082 A/G, -819 T/C, -592 A/C, were genotyped in 498 asthmatics including 176 AIA and 268 patients with aspirin-tolerant asthma (ATA), and 455 normal controls (NC) by the SNaPshot primer extension method and the functional effects of three promoter polymorphisms were analyzed using a luciferase reporter assay.

RESULTS: The frequency of rare genotype (AG or GG) of *IL-10* -1082 A/G polymorphism was significantly higher in AIA than in ATA ($P = 0.008$, $P_c = 0.024$) and furthermore, the *IL-10* -1082 A/G polymorphism showed a significant association with the prevalence of rhinosinusitis ($P = 0.042$). Gene-gene interaction of the *IL-10* -1082 A/G polymorphism with TGF β 1 -509C/T polymorphism was observed. When stratified by the presence of rhinosinusitis, the frequency of rare allele carriers (CT or TT genotype of TGF β 1 -509C/T, AG or GG genotype of *IL-10* -1082 A/G) was significantly higher in AIA (15.6%) compared to ATA (6.5%, $P = 0.020$, OR = 3.750, 95% CI = 1.485~9.466). The reporter plasmid that carried the -1082 G allele exhibited significantly higher promoter activity compared with the promoter activity of the -1082A allele in a human mast cell (HMC-1) and T lymphocyte cell (Jurkat) ($P < .001$).

CONCLUSIONS: Our results show that the *IL-10* promoter polymorphism may contribute to the development of the AIA phenotype with rhinosinusitis by genetically interacting with TGF β 1.

518 Sex Hormone Levels are Not Associated with Asthma in Pubertal Children

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RATIONALE: The prevalence of asthma switches from a male to female predominance around the time of puberty. This suggests the influence of sex steroids.

METHODS: Children involved in the 1995 Manitoba Birth Cohort attended study visits at 8-10 yrs (visit 1), 10-12 yrs (visit 2) and 12-13 yrs (visit 3). Children were assessed by a pediatric allergist at visits 1 and 3. Serum estrogen and testosterone levels were drawn at visits 2 and 3. Logistic regression was used to examine the relationship between asthma and sex hormone levels, with adjusting for potential confounders (weight, height, maternal asthma, breast-feeding, socio-economic characteristics).

RESULTS: For this analysis, 271 children (148 [54.6%] boys) were assessed at all study visits. At visit 1, 104 (59 [56.7%] boys) had asthma; at visit 3, 85 (45 [52.9%] boys) had asthma. Serum hormone levels were not normally distributed; thus, log values of these continuous data were used for all analyses. There were no significant gender differences in testosterone ($p = 0.344$) or estrogen ($p = 0.534$) at visit 2 (mean age 10.5 ± 0.38 yrs), while estrogen was higher in girls ($p < 0.001$) and testosterone ($p < 0.001$) was higher in boys at visit 3 (mean age 12.35 ± 0.37 yrs). No associations were identified between hormone levels at visit 2 or visit 3 and asthma at visit 3 (all p -values > 0.05).

CONCLUSIONS: In this cohort of pubertal children, no associations were identified between asthma and sex hormones. Factors other than sex hormone levels may play a role in the gender switch in the prevalence of asthma around puberty.

519 The Effect of Body Mass Index, Fat Percentage, and Fat-free Mass Index on Pulmonary Function Test

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RATIONALE: Sex specific cross sectional reference values for the lung function indices usually employ a linear model with a term for age and height. The purpose of this study was to determine the effects of the body mass index (BMI), the fat percentage of the body mass and the fat-free mass index (FFMI) on the forced expiratory volume curve.

METHODS: A total of 300 subjects, 150 men 150 women (mean age: 45 ± 13 years), with a normal lung function were enrolled in the study sample. This study measured the FEV₁, FVC and FEF_{25-75%} from the forced expiratory volume curve by a spirometer and the body composition by a bio-electrical impedance method in all subjects. Multiple regression analysis was used in order to examine the effects of the body composition on the parameters derived from the forced expiratory volume curve.

RESULTS: After adjusting for age, the BMI and Fat percentage improved the descriptions of the FVC ($p < 0.05$, $r^2 = 0.491$) and FEV₁ ($p < 0.05$, $r^2 = 0.654$) in women. In contrast, the FFMI contributed significantly to the FVC ($p < 0.05$, $r^2 = 0.432$) and FEV₁ ($p < 0.05$, $r^2 = 0.567$) in men. The FEF_{25-75%} correlated with the fat percentage in women ($p < 0.05$, $r^2 = 0.337$).

CONCLUSIONS: These results suggest that the BMI, the fat percentage and the FFMI are significant determinants of the forced expiratory volume curve. The pulmonary function test, when considering the BMI, the fat percentage and the FFMI, might be useful in clinical applications.