A Comparison of Bronchodilator Expressions to Identify the Asthmatic Child

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RATIONALE: The asthma guidelines 2002 recommend spirometry including the bronchodilator response (BDR) to short acting beta agonists to establish an asthma diagnosis. The purpose of this observational study was to determine which BDR expression and cut point best differentiates asthmatic from non-asthmatic children.

METHODS: Controller naive children were evaluated by clinical criteria alone to establish both an asthma diagnosis and severity classification, which was then compared to pre and post bronchodilator forced expiratory volume 1 second (FEV1). BDR expressions evaluated were change in volume (∆ FEV1, % vol.), percent change from initial FEV1 (∆ FEV1, % initial), and change from predicted FEV1 (∆ FEV1, % predicted). Receiver operator curve analysis determined the best cut point (positive response) based on sensitivity, specificity, and positive likelihood ratio (+LR) for each expression to differentiate asthmatic from non-asthmatic children.

RESULTS: Three hundred forty six asthmatics, 51 non asthmatics, predominantly Hispanic children, ages 4 to 17 years were evaluated. All BDR expressions were significantly greater in the asthmatics regardless of severity (P < .001), and increased with severity. Positive BDR values established for ∆ FEV1, % vol. was ≥ 100 ml, and for ∆ FEV1, % initial and ∆ FEV1, % predicted were ≥ 20% with sensitivity of 56.6%, 42.5% and 36.2%, specificity of 70.09%, 86.3% and 90.2%, +LR of 1.89, 3.10 and 3.69 respectively.

CONCLUSIONS: At the best cut point (≥20%) the ∆ FEV1, % predicted had similar sensitivity and specificity combination to ∆ FEV1, % initial, but had higher +LR, and was less dependent on initial FEV1 and lung size factors. We suggest that the BDR expression ∆ FEV1, % predicted be a routine part of evaluating childhood asthma regardless of baseline FEV1.

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Adrenergic β2 Receptor Genotyping in Asthma: Case Reports

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RATIONALE: Recent publications have suggested a possible relationship between a specific polymorphism of the β2 adrenergic receptor gene (ADRB2) and adverse effects of regular β₂-agonist use in subjects with asthma. Thus, individuals who are homozygous for arginine at codon 16 (ADRB2) and adverse effects of regular use of short or long-acting bronchodilators, with or without concomitant use of inhaled corticosteroids (Wechsler et al, Am J Respir Crit Care Med. 2006;173:519).

RESULTS: Poorly controlled asthmatic patients seen in the Pediatric Allergy and Immunology clinic at our center underwent genotyping of codon 16 of the ADRB2 gene using PCR with gene and polymorphism-specific primers.

RESULTS: We report 3 cases of asthma in subjects with the Arg/Arg ADRB2 genotype who had poorly controlled asthma while on maintenance therapy with a combination of a high-dose inhaled corticosteroid and a daily long-acting β₂ agonist (LABA). All three patients had significant improvement in their pulmonary function tests as well as clinical symptoms and decreased use of rescue bronchodilator medications within one month of discontinuing treatment with LABA. FEV1 pre- and post- LABA were as follows: 51% vs 102%, 66% vs 87%, and 59% vs 92%, respectively.

CONCLUSIONS: Prospective randomized controlled studies are needed to confirm the possible relationship between the Arg/Arg ADRB2 genotype and potential adverse effects of regular use of β₂-agonist medications.

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Effect of Budesonide and Formoterol Administered Via One Pressurized Metered-dose Inhaler on Lung Function in Adults and Adolescents With Moderate to Severe Persistent Asthma

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RATIONALE: To compare treatment effects on lung function of budesonide and formoterol in one pressurized metered-dose inhaler (pMDI) with budesonide pMDI, formoterol dry powder inhaler (DPI), budesonide and formoterol in separate inhalers (budesonide pMDI + formoterol DPI), and placebo.

METHODS: This 12-week randomized, double-blind, double-dummy, placebo-controlled, multicenter study (SD-039-0717) included 596 patients aged ≥12 years with moderate to severe asthma previously treated with inhaled corticosteroids. After a 2-week run-in period on 2 inhalations budesonide pMDI 80 µg bid, patients were randomized to receive 2 inhalations of one of the following: budesonide/formoterol pMDI 160/4.5 µg, budesonide pMDI 160 µg + formoterol DPI 4.5 µg, budesonide pMDI 160 µg, formoterol DPI 4.5 µg, or placebo. Lung function variables included morning predose forced expiratory volume in 1 second (FEV1), 12-hour mean postdose FEV1 (serial spirometry), and morning and evening peak expiratory flow (PEF).

RESULTS: Mean changes from baseline in predose FEV1 at end of treatment and 12-hour FEV1 at week 2 were greater (P ≤ .049) for budesonide/formoterol pMDI (0.19 L and 0.34 L, respectively) versus budesonide pMDI (0.10 L and 0.15 L), formoterol DPI (0.12 L and 0.19 L), and placebo (-0.17 L and -0.03 L) but similar versus budesonide pMDI + formoterol DPI (0.14 L and 0.32 L). Improvements in morning and evening PEF were greater with budesonide/formoterol pMDI versus all groups (P < .001) except budesonide pMDI + formoterol DPI.

CONCLUSIONS: Twice-daily budesonide/formoterol pMDI provides improvements in lung function significantly greater than its monocomponents or placebo and similar to that of budesonide pMDI + formoterol DPI.

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Efficacy and Safety of Intravenous Aminophylline in Children with Acute Exacerbation of Asthma: A Multicenter Randomized Trial

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RATIONALE: Use of aminophylline or theophylline as an additional treatment for acute asthma is controversial. IV aminophylline is a “classical” bronchodilator but may have therapeutic advantages in its putative anti-inflammatory effect and availability to peripheral airways where inhaled drugs may inadequately reach. The study was performed to assess if the addition of IV aminophylline to standard treatment for acute exacerbation of asthma would enhance the recovery without serious adverse events.

METHODS: Children aged 2 to 15 years with acute asthma who did not respond to repeated inhalations of beta2 agonists were enrolled. All subjects were treated with inhaled salbutamol and IV methylprednisolone/hydrocortisone and were randomized to receive additional IV aminophylline (Group A) or none (Group B). Asthma symptom score and time when wheeze disappeared were compared.

RESULTS: Fifty subjects were enrolled with 26 randomly allocated to group A and 24 to B. The groups were well matched at baseline. One in Group A and 7 in B dropped out because of exacerbation or non-compliance and outcome was analyzed in 24 from A and 17 from B. Faster improvement in symptoms were seen in Group A and there was a significant difference in symptom score at 24 h after treatment between the groups (p<0.05). The time to resolution of wheezing was significantly shorter in Group A than in B (median 46 h and 70 h, respectively; p<0.01). Four minor adverse events were observed in Group A but all completed the treatment.

CONCLUSIONS: Addition of aminophylline may be a beneficial therapeutic option for children with acute asthma.

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