Inner City Pediatric Asthma: What are we doing about it?

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Presentation Outline

- Overview of asthma
- Pharmacologic treatments
- Role of allergens in asthma
- Omalizumab (Anti-IgE) overview
- Inner City Asthma Consortium and ICATA study results
- Asthma management pearls

Asthma in the U.S.

- Prevalence, morbidity, and mortality are increasing
- Prevalence, morbidity and mortality are highest among the urban poor
Diagnosis of Asthma

- History or presence of episodic symptoms of airflow obstruction
- Airflow obstruction is at least partially reversible
- Alternative diagnoses are excluded

Asthma Pathophysiology

Pharmacologic Therapy
The Medications

Long-Term-Control Medications
Quick-Relief Medications
Patients requiring albuterol > 2 times/week require daily preventive therapy for asthma

Control of Factors Contributing to Asthma Severity
For at least those patients with persistent asthma on daily medications, the clinician should:
- identify allergen exposures and use the patient's history to assess sensitivity to seasonal allergens
- use skin testing or in vitro testing to assess sensitivity to perennial indoor allergens

Seasonal Allergens
*Important causes of "hayfever"

- Tree pollens - early spring
- Grass pollens - late spring
- Weed pollens - late summer to fall
- Outdoor molds - summer and fall
Perrenial Allergens

*Important triggers of asthma*

- Warm-blooded animals
- Cockroaches
- House dust mites
- Indoor molds

How to Control asthma

Triggers!!
Questionably Effective Cat Allergen Control

Terminating Dust Mites
- Encase bedding
- Wash bedding in hot cycle
- Carpet removal

Cockroach Control Measures
- Caulk cracks and crevices
- Chemically treat cockroach runways
- Bait stations
Cockroach Control Measures

- Remove sources of food
- Store all food in sealed containers
- Reduce access to water (leaky pipes)

New Asthma Therapy: Omalizumab or "Anti-IgE"

Omalizumab – Anti-IgE

- Recombinant humanized monoclonal anti-IgE antibody
- Binds IgE at the same site as FceRI
- Decreases free serum IgE
- Is non-anaphylactogenic
- Does not fix complement
The Binding Specificity of Therapeutic Anti-IgE

Known Immunomodulatory Actions of Anti-IgE

- Decreases free IgE and FcεRI expression on basophils and dendritic cells
- Decreases basophil histamine release
- Decreases mast cell responsiveness

Inner City Asthma Consortium

- Goals:
  - Identify forms of immune-based therapy that are most likely to promote control and prevention of asthma
  - Design protocols that will evaluate immune-based therapies in the treatment of asthma in low income inner-city children
  - Determine both the mechanisms of immune-based therapies and the potential unique mechanisms associated with the pathogenesis of asthma in low income inner-city children via mechanistic studies
Inner City Asthma Consortium (ICAC)

- Consists of 10 pediatric asthma centers across the country:
  - Baltimore
  - Boston
  - Chicago
  - Cleveland
  - Dallas
  - Denver
  - New York
  - Saint Louis
  - Tucson
  - Washington, DC
- Administrative center: Madison
- Data coordinating center: Rho, Chapel Hill
- National Institute of Allergy and Infectious Diseases (NIAID)

What we have learned from previous Inner City Asthma Studies...

- Cockroach allergy and exposure to high levels of this allergen may help explain the frequency of asthma-related problems in inner-city children (Rosenstreich et al., 1997 – National Cooperative Inner City Asthma Study – NCIAS)
- Home-based environmental remediation programs appear to offer an effective means of reducing asthma morbidity in this population (Morgan et al., 2004 – Inner City Asthma Study – ICAS)

Inner City Anti-IgE Therapy for Asthma (ICATA) Rationale

- Children with asthma who live in the inner city have
  - Increased morbidity and mortality
  - High prevalence of sensitization to indoor allergens
  - Challenging environments with high levels of indoor allergens and irritants
  - Substantial barriers to adherence with complex medical regimens
Inner City Anti-IgE Therapy for Asthma Rationale (cont.)

- Allergen-specific IgE is the fuel that drives allergic inflammation. The ICATA clinical study provided a unique opportunity to evaluate the spectrum of anti-inflammatory effects of omalizumab (anti-IgE) therapy of asthma
- A key question is the mechanism by which anti-IgE perturbs the allergic inflammatory response

Background and Hypothesis

Because allergen sensitization and exposure is an important determinant of asthma severity and response to therapy, we hypothesized that the addition of omalizumab to guidelines-based treatment would improve disease control in allergic inner-city children with moderate-to-severe asthma and persistent symptoms.

ICATA Clinical Study Overview

- Randomized, double-blind, placebo-controlled, parallel group efficacy and safety trial
- 500 inner-city children age 6-20 years old with moderate-to-severe allergic asthma (250/arm)
- Both arms received standardized specialist asthma care based upon NAEPP guidelines, including basic asthma education
- Treatment group received q2 or q4 week treatment with omalizumab
- Control group received placebo injection at similar intervals
Enrollment characteristics

- 6 to 20 years of age with a diagnosis of persistent asthma
- Allergy to a perennial allergen
- Inner-city resident
- At recruitment, participants had uncontrolled asthma
- Weight and total serum IgE levels were suitable for omalizumab dosing

Study Design

- Enrollment
  - Asthma control assessed
    - Using a Guidelines-based algorithm, treatment was begun or adjusted to achieve asthma control
- Randomization and treatment (60 weeks)
  - Following an adjustment of asthma medications during enrollment, participants were randomized to receive omalizumab or placebo every 2 to 4 weeks for 60 weeks

Primary outcome – Days with asthma symptoms over last 2 weeks

- Wheezing, chest tightness or cough
- Sleep interruption
- Activity limitations
Asthma control of participants at enrollment (n=419)

- Days of asthma symptoms the previous 2 weeks: 4.9 ± 4.2
- Childhood ACIC score in the last month (4 to 11 years): 16.9 ± 4.1
- ACIC score (12 years and over): 18.8 ± 4.2
- FEV1 (% predicted value): 92.1 ± 17.1
- FVC/FVC: 77.1 ± 9.9
- ≥ 1 Hospitalizations/past year: 25%
- ≥ 1 Unscheduled visits/past year: 76%

The effect of omalizumab on the number of days with symptoms in last 2 weeks

The effect of omalizumab on exacerbations
Summary

- Omalizumab significantly improved asthma control in inner-city children with asthma who were receiving guideline-based treatment.
  - 25% reduction in days with asthma symptoms
  - 30% reduction in the percent of patients with an exacerbation
  - 15% reduction in ICS dose
  - Dramatically reduced the seasonal asthma exacerbation pattern
- No safety issues

Asthma Management Pearls

- Have scheduled visits when well
- Perform routine PEFR or spirometry
- Err on side of overtreatment initially
- Don't be "steroidophobic"
- Don't forget about the nose

Asthma Management Pearls

- Reinforce inhaler technique often
- Consider other diagnosis if poor response to treatment
- Intervene early in exacerbations
- Persistent asthma requires daily chronic therapy
- Simplify the treatment regimen
PARTNERSHIP IN ASTHMA CARE

• Develop an Asthma Action Plan with the patient
• Fit the daily medication regimen into the patient's and family's routine
• Identify and address obstacles and concerns
• Ensure regular follow-up with the physician