Inner-City Severe Asthma and Anti-IgE

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Disclosures

• Employment
  – Cincinnati Children’s Hospital

• Financial Interests
  – Consultant: GSK, Regeneron, TEVA, MERCK
  – Honoraria: GSK, Regeneron, TEVA, MERCK

• Organizational Interests
  – ATS, AAP

• Research Interests
  – NHLBI, Luther Foundation, Verizon Foundation

• Gifts
  – Nothing to Disclose

• Other Interests
  – UpToDate Royalties
Epidemiology
Epidemiology

• Most children with asthma achieve control with low-medium doses of inhaled steroid (ICS; <500mcg/day fluticasone)
• 5% children have sustained symptoms despite high dose ICS
  – Accounts for 50% expenditures

Lang A Allergy 2008
Definition

• ATS/ERS revised definition
  – Difficult to treat
    • Incorrect diagnosis, co-morbidities, or poor adherence
  – Severe therapy-resistant
    • Severe asthma despite addressing other factors

Chung KF Eur Respir J 2014
Epidemiology

- These children demonstrate symptoms in early life
  - Decreased lung function in early life
  - Atopic disease
  - Reversible airway obstruction and bronchial hyperresponsiveness
  - High FeNO

Fitzpatrick AM JACI 2006;
Bossely CJ Eur Respir J 2009
Inner-City Children

- High exposure to:
  - Medical care barriers
  - Environmental risk factors
  - Social and psychological factors

- Successful treatment of inner city asthma in children often requires interventions in multiple domains
Management
Management

- Small particle and standard ICS
- Oral Corticosteroids
- LABA
- Antileukotrienes
- Methylxanthines
- Specific Allergen Immunotherapy
- Omalizumab
- Emerging: tiotropium, azithromycin, new biologics?
Omalizumab
Immunomodulation: Omalizumab

• Omalizumab is humanized monoclonal Ab (mAb) to IgE

• Binds free circulating IgE, preventing it from binding to rec.

• First biologic agent approved for clinical treatment of allergic dz.

• In clinical use since 2003

Ballow M. JACI 2006;118:1209-15
Clinical Effects

• Early RCT of 525 subjects with severe asthma on daily ICS:
  ↓ Exacerbations in treatment group

• Observational study of 250 asthmatics receiving ~450 mg q Mo
  → ↓ Daily symptoms by 76%,
  → ↓ Nocturnal symptoms by 84%
  → ↓ Exacerbations by 82%
  → ↓ Hospitalizations by 78%
  → ↑ Asthma related quality of life scores (from 2.9 to 4.5) after 6 mos

Immunomodulation: Omalizumab

Add-on omalizumab reduced the rate of clinically significant asthma exacerbations in children (6 to <12 years) with uncontrolled moderate-to-severe persistent allergic asthma despite medium to high doses of ICS

Adverse Reactions

• 0.4% incidence of anaphylaxis (compared to 0.07% in controls)
• Current data do not support ↑ risk of neoplasia or ↓ platelets

Ballow M. JACI 2006;118:1209-15
Omalizumab in Inner-City Children

• 419 Inner-city ages 6-20 yrs with moderate-severe persistent asthma in a multi-center RDBPCT by ICAC
• Effectiveness of omalizumab, as compared with placebo, when added to guidelines-based therapy x 60 weeks
• Primary outcome was symptoms of asthma.

Omalizumab added to guidelines-based therapy for inner-city children improved asthma control (↓ 24.5%). Lung function didn’t change.

Omalizumab added to guidelines-based therapy for inner-city children decreased exacerbations (↓37.9%). Greater reductions seen in children sensitized and exposed to cockroach allergen.

Improved asthma control with omalizumab was achieved with significantly lower doses of inhaled glucocorticoids (p<0.001) and LABA (p = 0.003)

Omalizumab decreased seasonal peaks in exacerbations, post-hoc analysis (p<0.001)

Omalizumab in Clinical Practice
CCHMC Severe Asthma clinic

- Track population outcomes and discuss cases pre-clinic conference
- Multi-disciplinary clinic: Pulmonary, Allergy, SW, adherence specialist, intensive asthma education, coordination with schools, & omalizumab, started June 2014
- Systematic workup to assess co-morbidities & airway inflammation
- Standardized approach
Difficult to Treat (DTT) Asthma

- Children with asthma that despite being treated with high dose inhaled steroids (≥ 2 prescriptions) or > 30 days of oral steroids in last year and have 2 of the following:
  - Requirement for second daily controller
  - Urgent care visit for asthma (UC/ED visit or hospitalization)
  - Low lung function
Difficult to Treat (DTT) Asthma

- Prednisone ≥ 3 times in past year
- Low Asthma Control Test (ACT) scores
- Required Xolair (anti-IgE)

• Defined population using electronic algorithms
  - Identification of population ~ 200
  - Tracking of outcomes over time
Conclusions

• Omalizumab role in children with high IgE and/or large body habitus unclear
• Unclear best treatment duration or when and how to wean off therapy
• May have a role in children with high healthcare utilization even with h/o poor adherence
Conclusions

• Higher percentage of adolescents with:
  – Neutrophilic or mixed eosinophilic/neutrophilic airway inflammation
  – Vocal cord dysfunction
  – Obesity
  – Challenging to treat

• Still have need for community based interventions as a significant percentage do not come to clinic appointments
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