Using Biomarkers and Genomics to Personalize Therapeutics for Allergies and Asthma

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Evolving Patterns in Asthma Management

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<thead>
<tr>
<th>Period</th>
<th>Goal of Management</th>
<th>Medications</th>
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<tr>
<td>1960s</td>
<td>Relieve bronchospasm</td>
<td>Short-acting β-agonists</td>
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<tr>
<td>1970s</td>
<td>Prevent bronchospasm</td>
<td>Albuterol, theophylline</td>
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<td>1980s</td>
<td>Prevent allergen-induced bronchospasm</td>
<td>Cromolyn</td>
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<tr>
<td>1990s</td>
<td>Prevent and resolve inflammation</td>
<td>Inhaled glucocorticoids, leukotriene modifiers, long-acting β-agonists, combination therapy</td>
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<td>2000s</td>
<td>Asthma control</td>
<td>Anti-lgE</td>
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<td>2010s</td>
<td>Personalized medicine: Early intervention</td>
<td>Prevention</td>
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Areas of Need for Asthma Management in Children

- Prevention of exacerbations
- Prevention of progression
- Personalized or individualized approach to improve asthma control
- Primary prevention of disease onset

Developing New Approaches to “Personalize” Asthma Management

- Biomarkers – Which ones? What application?
- Combination therapy – How soon? What type?
- Genetics/epigenetics – Can we move discovery to application?
- Immunomodulators – Benefit-risk? Do we have the right ones? Is there an age difference in response? Cost effective?

Conclusions

How does the asthma-related phenotype influence the choice of medication selected to improve pulmonary function?

- Children with lower pulmonary function or higher levels of markers associated with allergic inflammation should receive ICS therapy.
- Children without these indicators could receive a therapeutic trial of either ICS or LTRA.


Follow-up Study

Can we predict who would have a better response to montelukast over ICS?

- LTE4/FEV1 ratios were associated with a greater response to montelukast than FP for FEV1, and for asthma control days.
- Children with high LTE4/FEV1 ratios were likely to be younger and female and exhibit lower levels of atopic markers and methacholine reactivity.

Ref: Rabkovich N and the CARE Network.
Hospitalizations for Asthma in Children: Canada

20 - 25% of all hospitalizations in Canada for childhood asthma exacerbations occur in September

ICATA Study

Omalizumab reduced fall exacerbations

Ref, Busse and NIAID ICAC, NEJM 2011

Potential New Treatments

- Tiotropium
- Anti-IgE in children less than 12 years
- Anti-IL-5
- Anti-IL-13
- Anti-IL4/13
- Re-evaluation of allergen immunotherapy

Other Biomarkers

- Serum periostin
- Blood eosinophils
- Sputum eosinophils
- Urinary leukotrienes
- Exhaled breath condensates

Future Directions for Pediatric Asthma

- Prevention – exacerbations, progression and onset of disease.
- Communication – patients, families, providers and schools.
- Utilization of large data bases to guide clinicians to individualize treatment strategies.