Preschool Wheeze

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Overview

• Introduction
• Phenotypes of preschool wheeze
• Who/how to treat
• GINA guidelines
• Conclusion and way forward
Introduction

• Wheeze is common
• 1/3rd of children have had a wheezy illness by the 3rd birthday
• Mostly caused by viral triggers
• First episode of wheeze especially if less than 1 year of age is secondary to bronchiolitis
• In patients diagnosed with asthma – symptoms start in the preschool years in 80% of cases

What is wheeze?

• Wheeze is a high pitched musical sound usually on expiration

Asthma

DEFINITION OF ASTHMA

• Asthma is a heterogeneous disease usually characterised by chronic airway inflammation.

• It is defined by history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that may vary over the time and in intensity together with variable expiratory airflow limitation. [GINA2015]
The correlation

Wheeze

==

Asthma
Wheeze – Differential Diagnosis

- Foreign body aspiration
- BPD
- Tracheomalacia/Bronchomalacia
- Congenital abnormalities
- TB
- Vascular Rings
- CF
- PCD
- GORD
- PBB
The correlation

Wheeze ≠ Asthma
How is the diagnosis of asthma made
Asthma in children > 6 years of age

• Diagnosis
  • Typical history and examination
  • Demonstration of reversibility
    • FeV1 increase > 12% with bronchodilator
    • FeV1 decline > 15% during an exercise challenge
    • +ve metacholine challenge test
    • Role of FeNO is controversial
Recurrent wheeze in children < 6 years of age

- Clinical bronchodilator response
- Diagnostic challenge
- Organic pathology
- Is this the same disease at all?
The Evolution

• From wheezing to screaming
• Many children become symptom free by 3-8 years of age
• Half of children will stop wheezing by school age no matter what the phenotype

Hossny E. Treatment of asthma in children 5 years and under, based on different global guidelines. Www.worldallergy.org
The Fundamental Question

Preschool Wheeze

Asthma
Phenotypes of preschool wheeze

1995 Martinez et al

2008 ERS task force
Tucson Group – a time based classification

- Transient early wheezers
- Non-atopic wheezers
- IgE-associated wheeze/asthma

- Great for population studies
- No clinical correlation
- Does not assist with treatment

ERS 2008 – A symptom based classification

Episodic Viral Wheeze

Multiple Trigger Wheeze
Episodic Viral Wheeze

- Wheezing during discrete episodes
- Usually associated with a viral trigger
- No symptoms in between

Outcome:
- Declines by the age of 6
- Continues into childhood
- Becomes MTW

Multiple Trigger Wheeze

- Wheeze during discrete episodes
- Also symptoms in between episodes
- URTI usually the trigger
- But wheeze in response to other triggers:
  - Exercise
  - Inhaled allergens
  - Environmental tobacco smoke
- ?Evolution to asthma but poor evidence to support this
2008 Guidelines – who to treat?

• MTW – Inhaled corticosteroids
• EVW – Monteluklast

Problems with the classification 2014 update

- No tests/markers to differentiate between EVW/MTW
- EVW/MTW may represent extremes of a disease- in actual fact patients lie between
- Problems with history differentiating between the two
- Patients may change their phenotype
- This phenotypic classification does not take severity into account
- Inter current illness between viral colds may be under reported

Who to treat - 2014

- Multiple Trigger Wheeze
- Episodic viral wheeze
How to treat

- ICS
- Montelukast
- Black box warning on the use of LABA in < 4 year olds
Efficacy of ICS as controller therapy

REVIEW ARTICLE

Efficacy of Inhaled Corticosteroids in Infants and Preschoolers With Recurrent Wheezing and Asthma: A Systematic Review With Meta-analysis

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Financial Disclosure: Dr Castro-Rodriguez has received lecturing and consultancy fees from Merck Sharp & Dohme, GlaxoSmithKline, and Grünenthal; Dr Rodrigo has participated as a lecturer and speaker in scientific meetings and courses under the sponsorship of Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Dr Esteve SA, and Merck Sharp & Dome, and he also received honoraria as a consultant for Cydex Inc and Discovery Laboratories.
Value of ICS as controller therapy

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ICS Events</th>
<th>ICS Total</th>
<th>Placebo Events</th>
<th>Placebo Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
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<tbody>
<tr>
<td>Baker et al</td>
<td>89</td>
<td>386</td>
<td>37</td>
<td>95</td>
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<td>0.59 [0.43, 0.81]</td>
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<td>Bisgaard et al</td>
<td>36</td>
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<td>0.38 [0.12, 1.21]</td>
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<td>de Blic et al</td>
<td>8</td>
<td>20</td>
<td>15</td>
<td>18</td>
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<td>Guilbert et al</td>
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<td>Carlsen et al</td>
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<td>10</td>
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<td>Murray et al</td>
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<td>101</td>
<td>14</td>
<td>99</td>
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<td>1.12 [0.58, 2.17]</td>
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<td>Nielsen et al</td>
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<td>19</td>
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<td>3.6%</td>
<td>0.64 [0.37, 1.11]</td>
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<td>Noble et al</td>
<td>0</td>
<td>24</td>
<td>2</td>
<td>24</td>
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<td>Qaquadah et al</td>
<td>12</td>
<td>239</td>
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<td>120</td>
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<td>Roorda et al</td>
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<td>54</td>
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<td>Shapiro et al</td>
<td>12</td>
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<td>16</td>
<td>44</td>
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<td>Teper et al</td>
<td>2</td>
<td>14</td>
<td>4</td>
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<td>1.1%</td>
<td>0.43 [0.09, 1.94]</td>
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<tr>
<td>Wasserman et al</td>
<td>25</td>
<td>219</td>
<td>21</td>
<td>113</td>
<td>7.0%</td>
<td>0.61 [0.36, 1.05]</td>
</tr>
</tbody>
</table>

Total (95% CI) 1743    1062  100.0%  0.59 [0.52, 0.67]

Total events 314 341
Heterogeneity: Chi² = 16.63, df = 15 (P = 0.34); I² = 10%
Test for overall effect: Z = 8.15 (P = 0.000001)

ICS vs Montelukast

Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children

Bhupendrasinh F Chauhan¹ and Francine M Ducharme²
¹Clinical Research Unit of Childhood Asthma, Chu Sainte-Justine hospital Research Centre, Montreal, Canada.
²Research Centre, CHU Sainte-Justine and the Department of Pediatrics, University of Montreal, Montreal, Canada

Chauhan BF, Ducharme FM. Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. Cochrane Database Syst Rev 2012; 5: CD002314.
ICS vs Montelukast

Chauhan BF, Ducharme FM. Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. Cochrane Database Syst Rev 2012; 5: CD002314.
ICS vs Montelukast

Comparative study of budesonide inhalation suspension and montelukast in young children with mild persistent asthma

Stanley J. Szefler, MD, a James W. Baker, MD, b Tom Uryniak, MS, c Mitchell Goldman, MD, PhD, c and Philip E. Silkoff, MD c
Denver, Colo,
Portland, Ore, and Wilmington, Del

ICS vs Montelukast

Value of steroids during the acute attack

GINA - 2015

• Agreement that asthma in the preschool child is a difficult diagnosis to make

• Differentiation into phenotype shouldn’t be the aim - as the clinical significance of this is uncertain

• Asthma is more likely if:
  • Wheeze on exercise or illness in between viral illness
  • History of other allergic disorders – allergic rhinitis or eczema
  • Family history of asthma
  • Response to controller therapy and worsening on cessation
Probability of asthma diagnosis or response to asthma treatment in children ≤5 years

GINA 2014, Box 6-1 (1/2)
Stepwise approach – pharmacotherapy (children ≤5 years)

**Step 1**
- Daily low dose ICS
- Leukotriene receptor antagonist (LTRA)
- Intermittent ICS
- As-needed short-acting beta₂-agonist (all children)

**Step 2**
- Double ‘low dose’ ICS
- Low dose ICS + LTRA

**Step 3**
- Continue controller & refer for specialist assessment
- Add LTRA inc. ICS frequency
- Add intermittent ICS

**Consider this step for children with:**
- Infrequent viral wheezing and no or few interval symptoms:
  - Symptom pattern consistent with asthma and asthma symptoms not well-controlled, or ≥3 exacerbations per year
  - Symptom pattern not consistent with asthma but wheezing episodes occur frequently, e.g. every 6–8 weeks.
  - Give diagnostic trial for 3 months.

- Asthma diagnosis, and not well-controlled on low dose ICS
- First check diagnosis, inhaler skills, adherence, exposures

- Not well-controlled on double ICS
‘Low dose’ inhaled corticosteroids (mcg/day) for children ≤5 years

<table>
<thead>
<tr>
<th>Inhaled corticosteroid</th>
<th>Low daily dose (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclometasone dipropionate (HFA)</td>
<td>100</td>
</tr>
<tr>
<td>Budesonide (pMDI + spacer)</td>
<td>200</td>
</tr>
<tr>
<td>Budesonide (nebulizer)</td>
<td>500</td>
</tr>
<tr>
<td>Fluticasone propionate (HFA)</td>
<td>100</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>160</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Not studied below age 4 years</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Not studied in this age group</td>
</tr>
</tbody>
</table>
Let's Conclude

- Distinction into Phenotypes
- Daily controller therapy
- Treatment of the acute episode
Distinction of phenotypes

- Preschool wheeze is defined as recurrent wheeze before the age of 6
- The younger the patient the more likely there is an organic cause
- First establish if there is actually a wheeze
- The first episode especially if younger than 1 year of age is most likely to be secondary to bronchiolitis
- The overall outcome is poorly understood
- Differentiation between EVW/MTW is a poor phenotypic classification and the differentiation is not clear
- Rather use frequency/severity of illness – as markers to treat
Daily controller therapy

• MTW – ICS – first line therapy
• EVW – Either ICS/Montelukast
  • Treat if:
    • Attacks are severe – requiring hospital admission
    • Attacks are frequent
    • Interval symptoms are being under-reported

• Any controller therapy should be viewed as a trial of treatment and discontinued if there is no response
• Taper down to lowest possible dose
Treatment of the acute episode

• First line – use of B2 agonists
• Not all exacerbations require steroids
• Steroids should be reserved for those admitted to hospital
Thank you

• Professor Robin Green
• Professor Andre van Niekerk
• Professor Refiloe Masekela
• Dr. Denise Parris
• Dr. Xandre Dearden
• Dr. Wim Wijnant
• Dr. Katya de Campos
• Dr. Adele Roux
• Ms Odette Coetzee