

YUNIBESITHI YA PRETORIA

Faculty of Health Sciences

Fakulteit Gesondheidswetenskappe Lefapha la Disaense tša Maphelo

Preschool Wheeze

AC Jeevarathnum

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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



Bush A, Grigg J, Saglari S. Clinical review: managing wheeze in preschool children. BMJ 2014;348:1136.

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 – Differential Diagnosis

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







The correlation



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





The Fundamental Question



Phenotypes of preschool wheeze

1995 Martinez et al

2008 ERS task force



Tucson Group – a time based classification



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

Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ et al. Asthma and wheezing in the first six years of life. NEJM 1995;333(3):133-138.

ERS 2008 – A symptom based classification



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



Controller Therapy

The Acute Episode

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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Castro-Rodriguez JA, Rodrigo G. Efficacy of inhaled corticosteroids in infants and preschoolers with recurrent wheezing and asthma: a systematic review with meta-analysis.. Pediatrics. 2009;123(3):e52—e525.

Value of ICS as controller therapy

	ICS		Placebo		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	
Baker et al ³⁰	89	386	37	95	15.1%	0.59 [0.43, 0.81]		
Bisgaard et al ³¹	36	156	30	81	10.0%	0.62 [0.42, 0.93]		
Connett et al 25	3	20	8	20	2.0%	0.38 [0.12, 1.21]	13	
de Blic et al ²⁷	8	20	15	18	4.0%	0.48 [0.27, 0.85]		
Gleeson et al ²⁰	1	39	4	39	1.0%	0.25 [0.03, 2.14]		
Guilbert et al ⁹	57	132	89	130	22.8%	0.63 [0.50, 0.79]	•	
Kraemer et al ²⁸	1	9	8	14	1.6%	0.19 [0.03, 1.30]	· · · · · · · · · · · · · · · · · · ·	
Carlsen et al 41	5	79	10	81	2.5%	0.51 [0.18, 1.43]	10 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
Murray et al ¹⁰	16	101	14	99	3.6%	1.12 [0.58, 2.17]		
Nielsen et al ³⁴	9	19	14	19	3.6%	0.64 [0.37, 1.11]		
Noble et al ²⁴	0	24	2	24	0.6%	0.20 [0.01, 3.96]	3 0 - 30 - 1 5	
Qaqundah et al ⁴³	12	239	15	120	5.1%	0.40 [0.19, 0.83]		
Roorda et al ³⁶	38	152	54	153	13.7%	0.71 [0.50, 1.00]		
Shapiro et al ²⁹	12	134	16	44	6.1%	0.25 [0.13, 0.48]		
Teper et al ⁴²	2	14	4	12	1.1%	0.43 [0.09, 1.94]		
Wasserman et al ⁴⁴	25	219	21	113	7.0%	0.61 [0.36, 1.05]	2 	
Total (95% CI)		1743		1062	100.0%	0.59 [0.52, 0.67]	•	
Total events	314		341					
Heterogeneity: Chi ² =	16.63, df=	= 15 (P	= 0.34); [= 109	6		to the terms	
Test for overall effect:	Z = 8.15 (P < 0.0	0001)		5		0.01 0.1 1 10 100	

Castro-Rodriguez JA, Rodrigo G. Efficacy of inhaled corticosteroids in infants and preschoolers with recurrent wheezing and asthma: a systematic review with meta-analysis.. Pediatrics. 2009;123(3):e52—e525.

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

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²Research Centre, CHU Sainte-Justine and the Department of Pediatrics, University of Montreal, Montreal, Canada

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Kumar 2007	0/30	0//0			Not estimable
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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.

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



Szefler SJ, Baker JW, Uryniak T, et al. Comparative study of budesonide inhalation suspension and montelukast in young children with mild persistent asthma. J Allergy Clin Immunol 2007; 120: 1043–1050.

Value of steroids during the acute attack



Panickar J, Lakhanpaul M, Lambert PC, et al. Oral prednisolone for preschool children with acute virus-induced wheezing. N Engl J Med 2009; 360: 329–338.

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 ilness
 - 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)

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Stepwise approach – pharmacotherapy (children ≤5 years)





'Low dose' inhaled corticosteroids (mcg/day) for children ≤5 years

Inhaled corticosteroid	Low daily dose (mcg)
Beclometasone dipropionate (HFA)	100
Budesonide (pMDI + spacer)	200
Budesonide (nebulizer)	500
Fluticasone propionate (HFA)	100
Ciclesonide	160
Mometasone furoate	Not studied below age 4 years
Triamcinolone acetonide	Not studied in this age group

Lets 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

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- Dr. Katya de Campos
- Dr Adele Roux
- Ms Odette Coetzee

