REVIEW ARTICLE

CHALLENGES OF DIAGNOSIS AND MANAGEMENT OF PRESCHOOL ASTHMA: CURRENT KNOWLEDGE AND PRACTICE

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ABSTRACT

Preschool Asthma (PA) is among the commonest respiratory problems in children with a considerable diagnostic and therapeutic challenge for the pediatric provider. A number of challenges including the use of unclear and ambiguous diagnostic terms, provider and parental misconceptions, drug cost and availability, and common presence of other conditions with similar presentation but different treatment complicates the situation with delay in correct diagnosis and proper treatment. Preschool asthma should be approached systematically based on current symptom severity and frequency with exclusion of other causes of airflow obstruction. It is recommended to avoid the use of terms like "Reactive Airways Disease" in clinical practice and follow evidence based asthma guidelines to enhance the diagnosis and treatment of PA and facilitate communication between clinicians and parents.

Key words: *Preschool, Asthma, Wheeze, Reactive air ways disease*

INTRODUCTION

Asthma is a very common disease affecting more than 300 million people worldwide with most asthmatics having their first symptom during preschool age (1,2). Most of us as practicing pediatricians have seen preschoolers with recurrent episodes of wheeze, cough and dyspnea requiring frequent emergency visits and some with repeated admissions but not having "Asthma" as a diagnosis and thus not on controller therapy. It is the dogma of medicine to have a diagnosis before a definitive management is instituted that one will not treat a child with inhaled corticosteroids (ICS) unless preschool asthma (PA) is diagnosed. Thus, it is imperative that we appropriately diagnose PA for optimal care of many of these children in our day to day practice.

Wheezing is very common occurring in up to 50 % preschool children especially in the first 2 years. While viral infections including bronchiolitis are responsible for most of those conditions, 30-40 % of these children develop asthma in their life time (2). Despite the fact that asthma is such a common problem especially in preschool age, there is a wide heterogeneity of care even in western centers (3). PA is mostly underdiagnosed and undertreated in both low and high income countries contributing significantly to respiratory morbidity and possibly to mortality as well (4, 5). Many clinicians would rather put RAD as a diagnosis and most preschoolers are also treated with antibiotics for presumed bacterial pneumonia especially in developing countries (4). Some authors have used the previously bedside term "RAD" in literatures to mean asthma (6) or recurrent wheeze from asthma or lower respiratory infection (LRI) (5, 7-9), and others to mean all wheezing disorders (10). All these articles are very

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unclear on their use of the term RAD and gave it different meaning that it is confusing to readers, even in the field of respiratory medicine, compromising the standard of both research and clinical care. MedScape had a chapter on "Pediatric Reactive Airway Disease" but discussed pediatric asthma with no further mention of RAD and entails that asthma "cannot" be diagnosed before the age of 5 years (11). Others have condemned the use of RAD since its early inception (5, 8, 12, 13). Among them the earliest of these prominent authors have summarized their argument as: "At best the diagnostic label "reactive airways disease" is an annoyance to those of us who want to maintain diagnostic clarity in our discipline. At worst, the term represents a form of diagnostic laziness that may cause harm to patients."(12).

Looking at these literatures critically, we learn that RAD, though in common use in preschool age, is not the same as asthma and actually is a meaningless and confusing term that managed to sweep from the bedside to the literature recently (4-12). The only definition one can find for RAD is from Wikipedia read as "an informal label that physicians apply to patients with symptoms similar to those of asthma" (14). One can clearly see the growing confusion now more than ever as some authors expressed their fear years ago (12, 13). The future of asthma study and communication between researchers, clinicians and care receivers could get even more complicated if we fail to solve the problem once and for all; Abandon the use of nonspecific and unclear terms like recurrent wheeze, preschool wheeze and especially RAD as a diagnosis; and put PA in place. It is thus timely to clear this confusion, open a forum for discussion and knowledge sharing to refine our practice with the current evidences that lineup with better clinical outcome of the 21st century redefined asthma diagnosis and management goal with a zero tolerance to asthma exacerbation and death (15)! It is with this thought in mind that this review is undergone to hopefully contribute for a betterment of our preschool asthma care in Ethiopian children.

Childhood asthma is a cause of significant morbidity and mortality (1, 4, 5, 16). Asthma, especially in preschoolers is significantly under diagnosed and undertreated all over the world despite limited evidence in our setting (1, 4, 5, 15, 16). A narrative review of recent literatures was done from PubMed, Google Scholar and Cochrane review pertinent to asthma in preschoolers in English language. Search terms used were RAD/ Preschool Asthma, diagnosis and management /treatment. Additionally Asthma guidelines and standard pediatric pulmonology references were included in the review as appropriate. A total of 30 studies including original articles, reviews and meta-analysis were included in the review.

The aim of this review is to highlight the importance of early recognition and treatment of preschool asthma and avoid diagnostic

jargons like RAD in PA to enhance therapeutic target. Additionally the review will hopefully raise discussion, communication and argument between the many practicing pediatricians in the country leading to a refined shared knowledge and possible collaboration and local future studies which will translate to improved clinical care.

Challenges in the care of Preschool Asthma

Caring for the PA patient is arguably one of the most challenging job for the pediatrician for a number of reasons (2, 4, 8, 15-17) (Table 1). It is important to address different misconceptions and their implications to the clinician so that better understanding and practice changes can follow. Some of these challenges include inadequate training and experience of clinicians in asthma care, diagnostic difficulty, inadequate parental knowledge, and misconception of practitioners (Table 1). Among these, the use of non-specific and unclear terms like RAD in the diagnostic challenge and providers' misconception deserve special mention to some detail (Tables 2 and 3).

Table 1 Challenges in the management of Preschool Asthma

- Use of non-specific and unclear diagnostic terms like RAD*
- Incompletely understood pathobiology
- Misconception in providers and public**
- Diagnostic difficulty
- Drug administration / inhalation difficulty
- Insurance(drug availability and cost)
- Presence of same pathology with different signs and different pathologies with same signs
- Difficulty measuring pulmonary function and inflammation
- Lack of expertise especially in health centers where IMNCI prioritize pneumonia
- Parental underestimation of preschool asthma symptoms
- Child too young to report symptoms

*see table 2 for detail. **see table 3 for detail.*

Use of unclear terms in clinical practice and research of Preschool Asthma

Though RAD had been discouraged by the scientific community since its undefined inception to a bedside use (12, 13), it even managed to continue to be in regular use especially in preschool children as a replacement or a bridge to the diagnosis of asthma. While no sound benefit is demonstrated, a list of potential and actual harms are related to the use of RAD as a diagnosis (12, 13) (Table 2). RAD and other similar terms still in use in the clinical arena in wheezing preschoolers had their historical origin in the 1990s (reviewed elsewhere nicely) (8), when there was limited knowledge on pathophysiology of the different obstructive airway diseases in children. It is unreasonable that we

continue to do the same ,actually worse to be precise, with our current advanced understanding that different pathologies that RAD collectively refers to are so imprecise (2,8).

Table 2 Problems of using nonspecific diagnostic terms like RAD in Preschool Asthma

a.	No ICD code for RAD , no formal report and documentation about RAD as a result (18)
b.	No mention of it in standard guidelines and books, no evidence based standard therapy can be practiced as a result (1,16)
c.	No clear clinical, laboratory or imaging feature to define or diagnose RAD, very different meaning for different clinicians; some might mean all wheezing disorders, others may mean asthma. (6-10).
d.	No clear treatment approach for a child with RAD
e.	Reactivity of air ways, while a feature of asthma, is neither mandatory for diagnosis of asthma nor exclude it when absent. While we are used to do no test of reactivity in clinical practice, a large Korean study showed increased inflammation and low lung function in preschool children with recurrent wheeze with no increase in airway reactivity contrary to the famous “REACTIVE” label (2, 19).
f.	No role for patient care, prognostication or research ; rather hinder proper diagnosis and treatment of children with asthma (13)
g.	Children with a ‘diagnosis of RAD’ are excluded from studies in the field of asthma for lack of any meaning in the scientific world.
h.	Lack of uniformity and difficulty in communication in the scientific world as this lumps bronchiolitis, bronchitis and asthma nonspecifically.
i.	Limit achievement of the new asthma therapeutic goals(15,20)
j.	Delay diagnosis and treatment of underlying disease other than asthma (12)

Table 3 Misconceptions on Preschool Asthma and their practice implications

Misconception	Practice implication	Current knowledge
1. Asthma cannot be diagnosed before 5 years of age.	Use of RAD instead of PA, overtreatment of pneumonia	Asthma can be diagnosed at any age including infancy (1, 16, 20, 21).
2. We cannot call it sthma if we are not sure that it is a life-long disease	RAD replace PA ,PA under treatment	Asthma is a heterogeneous disease and can be asymptomatic for many years. Accurate prediction of persistence is not possible in early life when the clinical decision has to be made individually (2, 16, 21).
3. Asthma treatment is based on chance of persistence after preschool	Under diagnosis and treatment of PA	Asthma treatment should be based on current symptoms and future risk of exacerbation, not on chance of persistence (1, 2, 16, 21).
4. Preschool asthma is a benign condition outgrown in later childhood without need of treatment.	Underestimate burden and complication of asthma	Recurrent attacks of preschool asthma can affect lung growth, lead to fixed airway obstruction and pathologic features that persist beyond adolescence (2, 10).
5. Airway remodeling in asthma occurs with long lasting inflammation of airways.	Undermine long term effects of PA	Recurrent and severe attacks are associated with increased risk of fixed air way obstruction and remodeling early in asthma progression (8, 16, 22- 24).
6. Inhalation medications are unsafe and had unacceptable side effects and may also lead to dependence /persistence	Frequent systemic use, decreased use of inhalation drugs, non-adherence to treatment	Inhalations drugs are safer than their systemic counterparts , no dependence/role on persistence, better suited at targeted airway delivery that are superior in all aspects except for administration challenge(1,16,20,21).

Diagnosis of Preschool Asthma

While the diagnosis of preschool asthma is a difficult and clearly challenging, a systematic approach can balance the under and over diagnosis and treatment plan (1, 16, 25-27). Table 4 summarizes diagnostic steps in a systematic and simplified approach for practical purpose.

Table 4 Practical steps in the diagnosis and care of preschool asthma

1.	**Detailed History* : The typical child**
a.	Episodic / recurrent wheeze (> 2 episodes) (typically with symptom variability)
b.	Dry cough (significant wet cough is atypical for asthma)
c.	First degree family history of asthma /allergy
d.	Self-history of atopic dermatitis (AD)
e.	Exercise ,laugh and cry trigger symptoms
f.	Repeated or prolonged colds with normal periods in between
g.	Worsens with sleep/worse at night and upon awakening
2.	**Physical Examination :**
a.	Confirm presence of airflow limitation objectively (never diagnose asthma from parental history of wheeze alone, different sounds like stridor and snoring can be reported as wheeze)
b.	Bilateral polyphonic wheeze/prolonged expiration
c.	Hyperinflation/bulged chest
d.	Document reversibility of airway obstruction by:
	i) Bronchodilation test: Use optimal dose of BD and reevaluate in 15-20 minutes to document reversibility OR
	ii) Spirometry as appropriate (even some 3-4 years kids may perform well with proper coaching and can aid diagnosis and treatment selectively)
e.	Look for other systemic causes of respiratory symptoms
f.	Skin allergy : look for evidences of AD
g.	Remember that physical exam could also be normal apart from exacerbation
3.	**Exclude masqueraders and comorbidities (especially in atypical wheeze ***)**
a.	CXR , make sure at least one x-ray is documented
b.	Echo, only if cardiac problems suspected clinically
c.	Assess and treat comorbidities : AR and GERD
4.	**Laboratory : Determine for all preschool asthmatics the following if possible**
a.	Blood eosinophil (> 300 is supportive of allergic asthma with good response to ICS) , beware of parasitic infection in eosinophilia
b.	SPT : specific evidence for allergic asthma
5.	**If the above 4 steps didn't settle the diagnosis, go to one of the following as indicated**
a.	Therapeutic trial**+
b.	Referral to a respiratory physician
c.	Regular follow up@+

Hx is more important than PE for making the Dx. ** In unclear cases a therapeutic trial with ICS for 2-3 months followed by discontinuation to see for reappearance of symptoms after which asthma can be diagnosed. This should not be done in the presence of an alternate clinical condition that explain the condition or in the presence of strongly suspected masquerader/atypical wheeze. @ Follow up and reevaluation also help to modify treatment plan and sometimes may be all that is required especially for a parental anxiety as the main concern. + Beware of the time period effect as well where the remission of symptoms may be the natural resolution than by your treatment. * Atypical wheeze is associated with one or more of: onset in early infancy (birth), lack of variability/persistent wheeze, localized wheezing, feeding related wheeze, associated with FTT, coexistence of stridor, clubbing and fine crackles. Causes of atypical wheeze to consider includes airway/lung malformations, Tracheobronchomalacia, protracted bacterial bronchitis (PBB), foreign body aspiration,*

Key: Hx-History, PE- physical exam, FTT-Failure to thrive, AR-Allergic rhinitis, GERD-Gastroesophageal reflux, ICS-Inhaled corticosteroid, SPT - skin prick test

When to refer to a pediatric pulmonologist?

While most asthmatic preschoolers can be managed by the general pediatrician adequately, few children may require /benefit from a visit to the respiratory pediatrician (16, 23, 26,27). (Table 5). Such children especially with atypical presentation may require one or more of Echocardiogram, chest CT +/- angiography, bronchoscopy, swallow and sleep study, sweat chloride test, evaluation of immunodeficiency etc.

Table 5. Reasons to refer a preschool child with wheezing to a pediatric pulmonologist

Diagnostic difficulty
No treatment response
Parental anxiety/ request
Severe exacerbation requiring ICU admission
Physician not sure how to proceed with the future treatment plan
PA not well controlled with GINA step 3 management
Others: including requirement of bronchoscopy or other procedures for diagnostic/ therapeutic purpose

Management of Preschool Asthma

Goals and principles of Preschool Asthma care

The goals of asthma therapy are considerably revised in the recent few years as compared to previous standards. The goals are similar in preschool children as well and are summarized below (1, 15, 16, 20, 26, 27).

- Minimal or no chronic symptoms day or night
- Minimal to no asthma attack; early intervention and investigate every attacks thoroughly
- No limitation of activities; have physically active lives
- No missed school due to asthma
- Normal pulmonary function
- Minimal use of inhaled short-acting β2-agonist
- Minimal or no adverse effects from medications

Treatment of preschool asthma should be based on the frequency and severity of symptoms rather than the unreliable prediction of persistence in later childhood. There is no evidence of any clinical alteration of the course of illness with treatment that treatment focusing on possibility of persistence or not is not reasonable (1, 2, 16, 21).

The known principles of asthma management still holds true for PA and all the four of them should be addressed properly (1, 2, 16, 26, 27).

Child and family/parent education

i. What PA is , goals and treatment options ,aerosol therapy techniques
ii. Management of exacerbations
iii. Written asthma plan

Environmental and comorbidity control
Avoid smoking
AR and GERD
Allergen and other trigger avoidance when possible

Pharmacotherapy (see below)

Monitoring and follow up (See below)

What to tell for parents about their Childs' Preschool Asthma?

Discussion with parents is one of the most important part of the care and the most difficult as well. The information to parents should be genuine with our inability to accurately predict if their child is going to be a lifelong asthmatic or will outgrow his symptoms of PA (2, 15, 16). Clinicians discussing outcome with parents should make clear that (2, 16):

1. Wheezing is very common in the first few years of life
2. Most resolve by school age with a minority persisting
3. Increased chance of persistence if > 3 year and in the presence of atopy
4. Treatment depends on current symptom, not persistence possibility

Pharmacotherapy of Preschool Asthma

Relievers: SABA (Salbutamol) pMDI with spacers

Controllers: based on preference in order

1. Daily ICS (with spacers)
2. LRIs
3. Intermittent high dose ICS (with spacers)

The general treatment should follow recommendation by GINA with inhalational corticosteroids (ICS) as first line controllers (1). Stepping up and down can be done on follow up, the duration of controller treatment should be individualized to the severity, frequency and risk of exacerbation with a minimum of 3-6 months of well controlled asthma maintained before stopping controllers (*(1, 2, 15, 16, 26-32).*

Parental education on the nature of the disease, inhalation technique, environmental control and the uncertainty of persistence or remission and the 'difference from what they know as adult asthma" is the center of the preschool asthma care to have optimal asthma control with no symptom or exercise limitation and normal growth of the "lung" with the child *(1, 2, 15, 16, 26-32).*

Aerosol therapy in preschoolers

There are limited and incomplete data in our setting on the use of inhalation devices and techniques but a significant limitation is expected as is seen worldwide (1, 16, 32, 33).

All children with PA should be treated with pMDI drugs of both relievers and controllers (1, 16, 27, 32). DPIs are not convenient for under 6 years (16, 27) and nebulizers are unavailable and expensive in our setting. While increasing local effectiveness in the respiratory system, aerosol therapy will also decrease systemic side effects (16). Children less than 4 years should use pMDI with spacer and facemask but those ≥ 4 years of age should be trained to use spacers with mouth

pieces. Commercial spacers with valve are preferred if available and affordable (Figure 1), locally prepared plastic spacers can be used for both < 4 years and > 4 years with little modifications (Figure 2).

Figure 1. Examples of commercially available spacers with face mask used in < 4 years (A) and with mouthpiece for > 4 years of age (B)

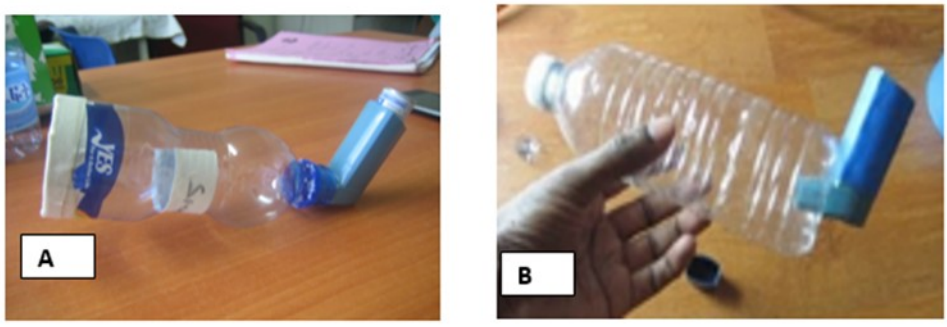

Figure 2. Locally made plastic spacers for infants and toddlers replacing facemask (A) and for children ≥ 4 years with a mouth piece (B). When preparing the plastic spacers, use 500-600 ml volume plastic bottles preferably with the final volume of 300-500 ml based on child age and length of 10-13 cm. too short (< 10 cm) and too large (> 700 ml) will decrease deposition in the lung with wastage of most of the drugs in the spacer, face, nasopharynx and to the environment if not tightly fit during inhalation. (26, 27, 32).

Follow up and related practice tips

Regular follow up is key for asthma care irrespective of symptoms (1, 2, 16, 25-27).

If we don't want to see the child sick, we should see him while he is healthy and happy.

a. See the treatment response if on regular medications and how child is doing without treatment
b. Check if inhalation technique is correct at each visit
c. Evaluate at each visit if:
    i. Symptoms are well controlled
    ii. No need for more treatment
    iii. No adverse effects
    iv. The child does indeed have atopic or non-atopic wheezing and other diagnoses have been excluded.

v. Nothing will inform you better about the child asthma status than reevaluation in the coming few weeks to months

D. Always prefer objective means of evaluation than overreliance on subjective perceptions of the child or parents

E. Avoid use of antibiotics in the absence of evidence for bacterial infection

F. Communicate clearly with parents and agree on No quick fix

G. Don't stick to a previous label (diagnosis) as a standard, be ready to change, challenge the situation based on new evidences and advance your care as the evidences get better.

H. Remember that many adult chronic respiratory conditions including chronic obstructive pulmonary disease (COPD) set their ground up in early childhood in those with low lung function (34-36).

Conclusion

The review tried to show that PA is a special entity of childhood asthma with inadequate diagnosis and therapy requiring special approach in the arena of pediatric clinical practice. Being more precise in our diagnostic label, (includes replacing RAD with PA), following systematic diagnostic approach, and symptom frequency and severity based management will all facilitate early diagnosis and management of PA. Such an approach should enable us prevent debilitation in those children with PA and prevent long term poor lung function that traces to adulthood especially in those with severe and repeated asthma attacks setting the stage to COPD as an adult before celebrating their 6th birthday

Conflict of interest

The author has no conflict of interest to declare

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