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Review Article

An expert consensus on managing allergic cough in the pediatric set-up

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ABSTRACT

Allergic cough frequently serves as a symptom of more comprehensive allergic conditions and is associated with a range of environmental and genetic factors. The presence of chronic conditions such as asthma, rhinitis, and sinusitis play a substantial role in the development of allergic cough in children. Allergic rhinitis affects up to 40% child population worldwide. Modified Delphi statements were prepared, and an agreement/disagreement was taken by 12 expert paediatricians from India on these statements. The opinions of the expert panel were captured and documented. Consensus was predetermined to be obtained if more than 75% of the participants agreed (or remained neutral) on the statement. 12 pediatricians participated in the panel and provided opinions on 24 modified Delphi statements. All the statements were supported by the latest data from the literature search. 23 statements reached consensus after an agreement (agree + neutral) of more than 75%. In the event of non-agreement, 1 statement was amended as per the panel's recommendation and sent for another round of deliberation. In the final phase, all the opinions from experts were consolidated and recommendations were framed. The present manuscript provides consensus recommendations for the pediatricians while addressing the allergic cough and related complications in the children. The key outline is to diagnose the proper cause of the cough and follow the proper treatment approach to avoid complications and have better management.

Keywords: Allergic cough, Pediatric cough, Consensus statement

INTRODUCTION

Children frequently experience allergic cough, a prevalent form of chronic cough formerly identified as cough variant asthma. This condition is characterized by a persistent and repetitive dry cough, and a majority of afflicted children exhibit heightened sensitivity to cough triggers.¹ Paediatric cough is categorized into acute (lasting less than two weeks), subacute (lasting 2–4 weeks), and chronic (lasting over four weeks). Failure to identify and treat the root cause of acute cough may lead to its progression into subacute and chronic stages. Both primary care paediatrics

and allergists regularly encounter paediatric cough, emphasizing the importance of understanding its causes and proper management.^{2,3} Allergic cough in children is primarily caused by various environmental and genetic factors. Common triggers include house dust mites, pet dander, mold, smoke, outdoor dust, the winter season, exercise, and second-hand smoke from a parent or another person.⁴ Allergic cough frequently serves as a symptom of more comprehensive allergic conditions. The presence of chronic conditions such as asthma, rhinitis, and sinusitis play a substantial role in the development of allergic cough in children.⁵

Childhood respiratory diseases, including allergic rhinitis, affect a significant portion of the global paediatric population, with allergic rhinitis impacting up to 50% paediatric population worldwide.⁶ If left untreated and becoming chronic, allergic rhinitis can result in complications affecting both upper and lower airways. Cough, a crucial protective mechanism preventing the passage of foreign substances into the lower airways, is a symptom of various inflammatory respiratory tract diseases. It is commonly linked to upper respiratory tract disorders in children, with allergic rhinitis being the most prevalent allergic condition often associated with asthma.⁶ The Global Initiative for Asthma's 2022 guidelines defines asthma as a heterogeneous disease characterized by chronic airway inflammation and a history of respiratory symptoms, including wheeze, shortness of breath, chest tightness, and cough.⁷ Notably, cough frequently accompanies allergic rhinitis and asthma in children. Asthma stands out as one of the leading causes of chronic cough in pediatric population. While cough is a common symptom in asthmatic children, they are sometimes present with cough alone.

The prevalence of allergic asthma in children in India exhibits significant regional and demographic variations, reflecting a notable public health concern. Studies indicate an average prevalence ranging from 5.14% to 7.24%.⁸ Notably, in children aged 5-11 years, the prevalence of allergic asthma is found to be between 10% and 15%, particularly among those with allergic rhinosinusitis.⁹ A substantial overlap between allergic asthma and allergic rhinitis is evident, with about 50.84% of children with asthma also suffering from allergic rhinitis.¹⁰ This data underscores the varying burden of allergic asthma across different regions and demographics in India.

The distinctive feature of cough in asthma cases is a dry cough without sputum, often worsening at night or with physical activity, but could be productive of sputum also at times depending on triggers involved. Allergic cough encompasses a broader range of etiologies than asthma alone, including non-asthmatic eosinophilic bronchitis, allergic rhinitis, and adenoid hypertrophy with an allergic background.

While managing cough, it is crucial to focus on its underlying cause rather than the associated disease condition. The management of pediatric cough is particularly challenging due to scarcity of literature compared to adult cough.¹¹ For patients exhibiting chronic cough with features suggestive of asthma, identified through history, physical examination, or spirometry, treatment should align with national asthma guidelines.¹²

In cases of allergic cough during the pollen season, antihistamines and intranasal steroids prove beneficial for pediatric patients. It is important to tailor the treatment based on the severity and nature of symptoms, following established guidelines for optimal management.² Relevant allergen avoidance measures when practical must also be advised.

METHODS

A total of 24 modified Delphi statements were formulated about allergic cough in pediatric set-up following literature available in scientific reports and articles till the year 2023. An expert group of 12 pediatricians was formed to assess and provide consensus on these modified Delphi statements and an agreement of more than 75% (including agree and neutral responses) was used to reach such consensus. In the event of non-agreement, the Delphi statements were amended as per the panel's recommendation and sent for another round of deliberation. The final consensus statements and expert's recommendations were then compiled in the form of the manuscript and sent to panel members for final review.

RESULTS

Out of 24 statements compiled, 23 statements reached consensus during the expert panel discussion and the remaining 1 statement was amended as per the discussion. This statement was again sent for consensus agreement and a consensus was reached on all 24 Delphi statements. Table 1 compiles the statements and responses from round 1 of expert panel discussion.

Table 1: Modified Delphi statements and the consensus percentages after round 1 of expert panel discussion.

No.	Statement	Agree (%)	Disagree (%)	Neutral (%)	Consensus (agree + neutral) (%)
1	Most common allergic and non-allergic cough triggers among children include house dust mites, cockroach, pet dander, pollen, mold, outdoor dust, the winter season/cold air, exercise, and second-hand smoke from a parent or another person	100	-	-	100
2	Allergy skin testing is the gold standard test for diagnosing allergic triggers for pediatric cough	75	8.3	16.7	91.7
3	Specific IgE blood test is an alternative for evaluation of allergen sensitization for pediatric cough	83.3	16.7	-	83.3
4	Assessing total immunoglobulin E (IgE) levels may be considered a screening parameter for suspected allergic cough	66.7	25	8.3	75

Continued.

No.	Statement	Agree (%)	Disagree (%)	Neutral (%)	Consensus (agree + neutral) (%)
5	Asthma is a heterogeneous disease characterized by chronic airway inflammation and a history of respiratory symptoms, including wheeze, shortness of breath, chest tightness, and cough	100	-	-	100
6	Asthma stands out as one of the leading causes of chronic cough in paediatric population	100	-	-	100
7	Cough variant asthma (CVA) can present with persistent cough, often occurring at night or early morning, and intensifies after exercise or exposure to cold air or specific smells	100	-	-	100
8	House dust mites have been found to cause coughing in up to 68% of patients with bronchial asthma and allergic rhinitis	91.7	8.3	-	91.7
9	Long-term exposure to allergens and air pollutants, including fine particulate matter (PM2.5) and various chemical irritants, can contribute to the development of chronic respiratory conditions, such as allergic rhinitis and asthma	100	-	-	100
10	Spirometry is most relevant test to identify air flow abnormalities	91.7	8.3	-	91.7
11	Fractional exhaled nitric oxide (FeNO) might help distinguish allergic/eosinophilic inflammation in chronic pediatric cough	75	8.3	16.7	91.7
12	For pediatric patients experiencing cough due to allergic rhinitis, second generation antihistamines and intranasal steroids are the recommended drugs of choice	100	-	-	100
13	Centrally acting non-opioid antitussive dextromethorphan is given to children above 4 years of age to alleviate symptoms of dry cough	83.3	16.7	-	83.3
14	Levocloperastine and levodropropizine can be adjuncts in the management of allergic cough	66.7	8.3	16.7	91.7
15	Bronchodilators are highly recommended for individuals having symptoms associated with asthma to alleviate symptoms such as cough, shortness of breath, wheezing, and chest tightness	100	-	-	100
16	Antihistamines are not a first-line treatment for asthma. but can help reduce allergy symptoms which can sometimes help manage allergic asthma	83.3	8.3	8.3	91.7
17	Antihistamines demonstrate mild bronchodilation and are effective in preventing allergen-induced non-specific airway hyper-responsiveness	58.3	33.3	8.3	66.6
18	CPM and phenylephrine combination can be used in treating allergic cough with increased secretions along with the recognised risk of sedation	50	25	25	75
19	Inhaled corticosteroids are particularly effective in reducing airway inflammation and hyper-reactivity, and are most important drugs in the management of allergic cough and asthma	100	-	-	100
20	Dextromethorphan hydrobromide + chlorpheniramine maleate might be recommended for the temporary relief from dry cough associated with throat discomfort, sneezing, and a runny nose. Its use is limited to dry cough and allergic cough where symptoms are not clearly defined	66.7	8.3	25	91.7
21	When allergic cough is associated with persistent asthma symptoms, incorporating a SABA such as Salbutamol administered at doses of 90 to 180 micrograms through inhalation every 4 to 6 hours for as needed quick relief as well as LABA such as formoterol or salmeterol administration via inhalation twice daily, always in conjunction with an ICS for	100	-	-	100

Continued.

No.	Statement	Agree (%)	Disagree (%)	Neutral (%)	Consensus (agree + neutral) (%)
	improved and prolonged asthma control is the recommended combination of choice				
22	The addition of leukotriene inhibitors or long-acting β 2-agonists (LABA) to inhaled corticosteroids in patients not controlled with ICS alone	83.3	8.3	8.3	91.7
23	The fixed-dose combination of montelukast and a histamine like bilastine, fexofenadine or cetirizine is more effective in treating perennial allergic rhinitis in patients with asthma compared with montelukast alone	91.7	8.3	-	91.7
24	Probiotics can play an important role as an adjunct therapy in managing allergy especially during the maintenance phase. They might help to reduce the severity of next bout of viral infection or allergy attack	83.3	-	16.7	100

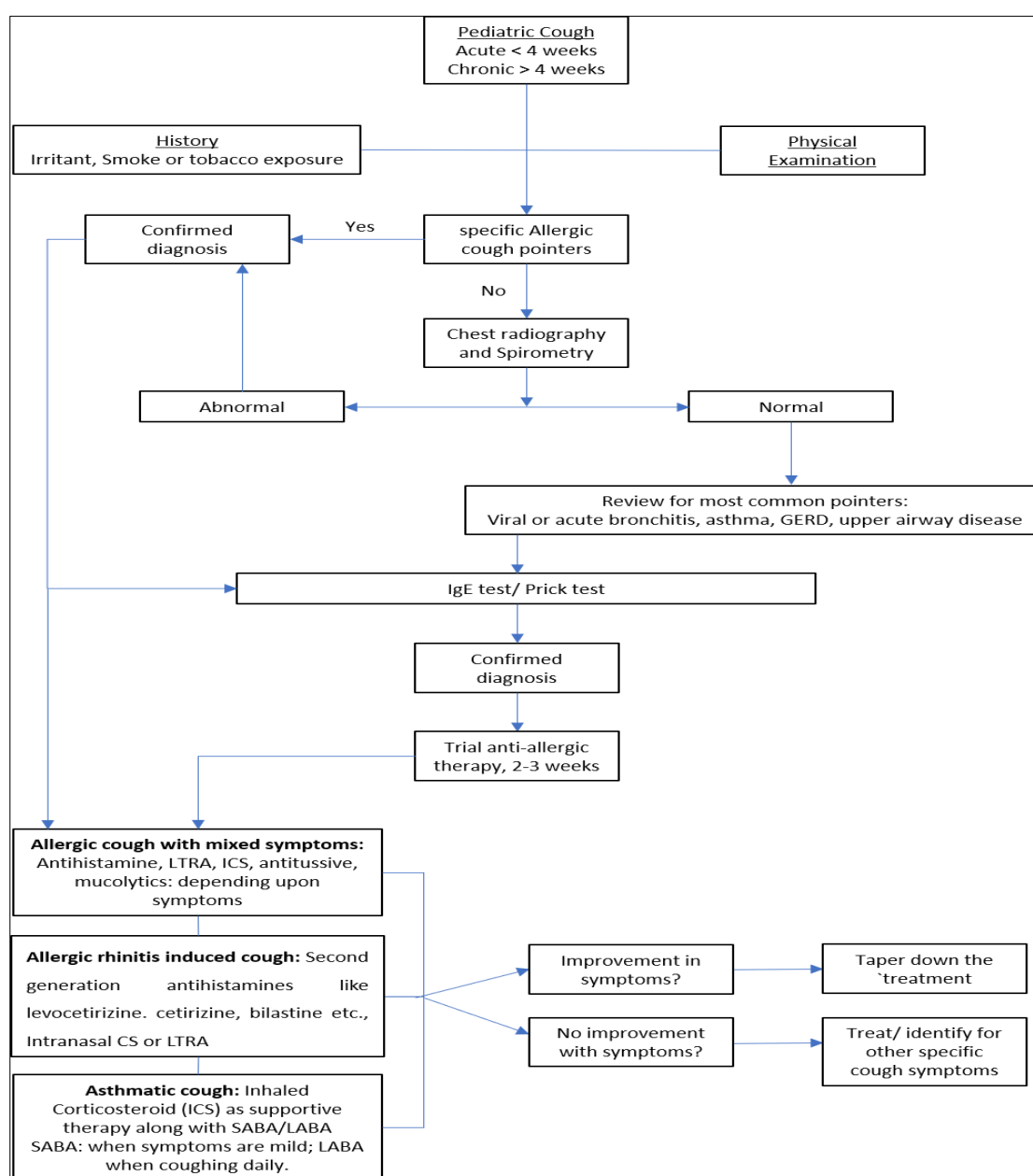


Figure 1: Paediatric allergic cough management algorithm.

DISCUSSION

Statement 1: Most common allergic and non-allergic cough triggers among children include house dust mites, cockroach, pet dander, pollen, mold, outdoor dust, the winter season/cold air, exercise, and second-hand smoke from a parent or another person.

Common allergens that have the potential to trigger symptoms of allergic rhinitis, including coughing, encompass a diverse range of substances. Fungi, such as mold spores found both indoors and outdoors, can also contribute to allergic rhinitis symptoms, including persistent coughing.¹³ Epithelial animal tissues, particularly proteins found in pet dander (skin flakes), saliva, and urine, are notorious triggers, leading to coughing, congestion, and other respiratory issues in those allergic to them.¹⁴ Additionally, house dust mites, tiny arthropods that thrive in mattresses, pillows, carpets, soft toys etc., and release allergenic proteins that can induce coughing and other allergic rhinitis symptoms when inhaled by house dust mite allergic individuals.¹⁵

Expert panel remarks

A 100% consensus was reached for this statement.

Statement 2: Allergy skin testing is the gold standard test for diagnosing allergic triggers for pediatric cough.

Skin prick test is used for the diagnosis of IgE-mediated allergic disorders. The development of cutaneous reaction on the application of an allergen is used as a surrogate marker in determining “sensitization” to a particular allergen.¹⁶ This reaction along with clinical presentation can be used in conjunction for diagnosing allergic triggers for pediatric cough.

Expert panel remarks

Relevance of positive skin test with clinical correlation is higher than other approaches.

Statement 3: Specific IgE blood test is an alternative for evaluation of allergen sensitization for pediatric cough.

In such cases where skin prick test (SPT) is not possible or available, specific IgE blood test can be done to detect the potential sensitizations which when correlated with clinical history can point to allergen triggers of pediatric cough.

Expert panel remarks

In the event when allergy skin testing is not available or plausible, specific IgE blood test could provide insights to the allergen cause. With the advent of in-vitro molecular allergy testing, we have optional tools for diagnosing allergic triggers at our disposal which could help in making

therapy decisions as well. The economic viability and availability of newer component resolved diagnostic testing tools keeps them out of routine usage currently. Clinical correlation with symptoms is a must for any positive blood test for allergy.

Statement 4: Assessing total immunoglobulin E (IgE) levels may be considered a screening parameter for suspected allergic cough.

Total IgE levels may be considered as a screening parameter for suspected allergic cough and these patients can then be subjected to either specific IgE blood test or SPT. In a study conducted by Satwani et al in 2009, they found out that approximately 64% patients between the age of 6-14 with allergic asthma had raised total IgE levels, indicating the importance of total IgE levels as screening parameter.¹⁷

Expert panel remarks

The clinical presentation and observation should be given utmost importance while analyzing the results of IgE blood test as low IgE might not mean absence of allergic response and vice versa. Prolonged use of oral corticosteroids might drive down serum IgE levels.

Statement 5: Asthma is a heterogeneous disease characterized by chronic airway inflammation and a history of respiratory symptoms, including wheeze, shortness of breath, chest tightness, and cough.

The global initiative for asthma's latest guidelines defines asthma as a heterogeneous disease characterized by chronic airway inflammation and a history of respiratory symptoms, including wheeze, shortness of breath, chest tightness, and cough.¹⁸

Expert panel remarks

It should be noted that not all patients have all the above symptoms, and some might have cough as the only manifestation of asthma.

Statement 6: Asthma stands out as one of the leading causes of chronic cough in pediatric population.

Cough is a persistent symptom in children with asthma. In asthmatic children cough is usually associated with wheeze and dyspnoea and they can be used for distinguishing features.¹⁹

Statement 7: Cough variant asthma (CVA) can present with persistent cough, often occurring at night or early morning, and intensifies after exercise or exposure to cold air or specific smells.

Cough variant asthma presents as persistent cough that worsens after physical exercise or vigorous playing or other physical activity tasks and usually occurs at night or

early morning. It can be diagnosed by methacholine challenge test and contributes to majority of allergic chronic cough cases.²⁰

Statement 8: House dust mites have been found to cause coughing in up to 68% of patients with bronchial asthma and allergic rhinitis.

House dust mites have been known to cause allergy, with various identified allergens present on them. They are the leading cause of indoor allergy development particularly in children below 4 years of age. The prevalence of house dust mite allergy is as high as 68% in children with bronchial asthma and allergic rhinitis.¹⁵

Statement 9: Long-term exposure to allergens and air pollutants, including fine particulate matter (PM_{2.5}) and various chemical irritants, can contribute to the development of chronic respiratory conditions, such as allergic rhinitis and asthma.

Air pollutants including environmental tobacco smoke and other indoor as well as outdoor air pollutants are a challenging set of irritants that are ubiquitous nowadays and could play a crucial role in development of or perpetuation of asthma and other allergic complications in children.²¹

Statement 10: Spirometry is the most relevant test to identify air flow abnormalities.

Spirometry is used to assess the pulmonary function and hence the air flow abnormalities in patients. In children above 4-5 years of age, spirometry can be the best tool available to differentiate the airflow limitation associated with airways inflammation and bronchospasms.

Expert panel remarks

Impulse oscillometry studies (IOS) and forced oscillometry testing (FOT) could also be used as and when required and is available since it can be done even down to 3-year-old children sometimes.

Statement 11: Fractional exhaled nitric oxide (FeNO) might help distinguish allergic/eosinophilic inflammation in chronic pediatric cough.

Fractional exhaled nitric oxide (FeNO) provides a distinguishing objective measure for presence of eosinophilic airways inflammation.²² It becomes especially useful when chronic cough is thought to be allergic asthma induced and is not responding to conventional approaches.

Expert panel remarks

FeNO is one of the most useful tools to not only help support the diagnosis of allergic asthma but also to help

monitor the effectiveness of the therapy with inhaled corticosteroids.

Statement 12: For pediatric patients experiencing cough due to allergic rhinitis, second generation antihistamines and intranasal steroids are the recommended drugs of choice.

The second-generation antihistamines effectively reduce all the symptoms associated with allergic rhinitis including cough. They along with intranasal corticosteroid constitute the first line of therapy against allergic rhinitis. Intranasal corticosteroids (INS), when used properly, effectively reduce nasal inflammation and help with managing flare ups as well.²³

Statement 13: Centrally acting non-opioid antitussive dextromethorphan is given to children above 4 years of age to alleviate symptoms of dry cough.

Multiple studies show that dextromethorphan improved dry cough clinical outcomes when given at therapeutic dosage in children. At high dosage, the metabolites of dextromethorphan may cause euphoria and hallucination by blocking NMDA receptors. There exists a potential for abuse at high dosage, so monitoring of dosing is a must while prescribing dextromethorphan.²⁴

Expert panel remarks

Dextromethorphan should be used with caution, and it should be given for a limited duration and dosing should not increase from recommended values.

Statement 14: Levoclorperastine and levodropropizine can be adjuncts in the management of allergic cough.

Levodropropizine is an effective antitussive drug in children and adults, with statistically significant better overall efficacy outcomes versus central antitussive drugs (codeine, cloperastine,) in terms of reducing cough intensity and frequency, and nocturnal awakenings.²⁵

Expert panel remarks

Both levoclorperastine and levodropropizine may be prescribed adjunctly in the instances of allergic dry cough with anti-allergic therapy and that too in patient population of age 4 and above, if the practitioner finds it suitable in their opinion.

Statement 15: Bronchodilators are highly recommended for individuals having symptoms associated with asthma to alleviate symptoms such as cough, shortness of breath, wheezing, and chest tightness.

Bronchodilators (such as salbutamol), open the air passages and relieve symptoms and reduces the risk of severe asthma attacks.²⁷ If repeated or frequent use of bronchodilators are noted, then inhaled corticosteroids

and/ or long-acting bronchodilators might be necessary based on available asthma guidelines.²⁸

Statement 16: Antihistamines are not a first-line treatment for asthma. But can help reduce allergy symptoms which can sometimes help manage allergic asthma.

Antihistamines are not a first-line treatment for asthma. However, they are used for the treatment option in allergic asthma because they can reduce allergen triggered asthmatic episodes and can help control allergic rhinitis which contributes to asthma control and hence might support in its management.²⁹

Expert panel remarks

Only second-generation antihistamines should be used in such instances.

Statement 17: Second-generation antihistamines can help in symptom relief in cases where allergen-induced non-specific airway hyper-responsiveness is observed.

Second generation antihistamines have been used successfully against allergen induced early and late asthmatic response in studies and have been used in clinical practice for symptomatic relief against allergen induced airway hyper-responsiveness.^{30,31}

Expert panel remarks

Antihistamines have small degrees of protection against early asthmatic response and late asthmatic response following allergen challenges in clinical research.

Statement 18: Chlorpheniramine and phenylephrine combination can be used in treating allergic cough with increased secretions along with the recognized risk of sedation.

Chlorpheniramine maleate is a competitive histamine H1 receptor antagonist and has mild sedative effects due to its anti-cholinergic action.³² Despite the known risk of sedation, in cases where intranasal corticosteroids are contraindicated, this combination can be used as rescue option.

Expert panel remarks

This combination can be used as a rescue option and could be given in the SOS situations but should not be used in general practice as the potential side-effects outweigh the potential benefits. Phenylephrine side effects should be monitored, and parents counseled to administer within age-appropriate doses only.

Statement 19: Inhaled corticosteroids are particularly effective in reducing airway inflammation and hyperreactivity and are most important drugs in the management of allergic cough and asthma.

Intranasal corticosteroids effectively reduce airway inflammation and reduce mucus production leading to much lesser instances of asthma flare ups and cough. This also helps in reducing the usage of short acting beta agonists (SABA) based rescue inhalers.³³

Statement 20: Dextromethorphan hydrobromide + chlorpheniramine maleate might be recommended for the temporary relief from dry cough associated with throat discomfort, sneezing, and a runny nose. Its use is limited to dry cough and allergic cough where symptoms are not clearly defined.

This combination is particularly effective in relieving cough when runny nose is presented as another symptom indicating histamine activity and thus the recommendation of antihistamine.³² Dextromethorphan suppresses the cough while CPM counters the histamine release, thus reducing runny nose as well as relieving cough. Postnasal drip contributing to cough might also be countered by the antihistamine in the combination.

Statement 21: When allergic cough is associated with persistent asthma symptoms, incorporating a SABA such as Salbutamol administered at doses of 90 to 180 micrograms through inhalation every 4 to 6 hours for as needed quick relief as well as LABA such as formoterol or salmeterol administration via inhalation twice daily, always in conjunction with an ICS for improved and prolonged asthma control is the recommended combination of choice.

Short acting beta-agonists (SABA) are the rescue option in cases with sudden asthma flare up, while long-acting beta-agonists (LABA) combined with inhaled corticosteroids are used for the long-term management of asthma. LABA must be given along with low- or medium- dose inhaled corticosteroids for better and prolonged asthma control.^{34,35}

The combination of ICS and LABA is the first-choice long term management option for asthma in most cases and is generally available as fixed dose combination (FDC) inhalers. LABA primarily has bronchodilatory action but also has some mast cell stabilisation effects and reduces plasma exudation, while ICS reduces multiple aspects of airway inflammation. Thus, these two work in tandem to complement each other while addressing asthma that has multifaceted pathology.³³

Expert panel remarks

Newer guidelines suggest combining this with inhaled corticosteroids for optimal control of airway inflammation and relief of symptoms.

Statement 22: The addition of leukotriene inhibitors or long-acting β_2 -agonists (LABA) added to inhaled corticosteroids in patients not controlled with ICS alone.

In patients with asthma that is inadequately controlled by low-dose ICS with significant bronchodilator reversibility, the addition of LABA or LTRA to ICS can reduce the episodes of oral corticosteroid-treated exacerbations.³⁶

Statement 23: The fixed-dose combination of montelukast and an antihistamine like bilastine, fexofenadine or cetirizine is more effective in treating perennial allergic rhinitis in patients with asthma compared with montelukast alone.

In individuals with allergic rhinitis, the synergistic combination of bilastine and montelukast treatment has a twofold influence on early- and late-phase allergic responses. Combining bilastine and montelukast to treat a specific patient population, particularly those with hyperreactive airway diseases like asthma, is an appealing choice because improved outcomes require both medication classes.³⁷

Expert panel remarks

Despite some level of anti-cholinergic activity of antihistamines, they are better in conjunction with montelukast for treatment of perennial allergic rhinitis. All children and adolescents must be counseled about monitoring the rare behavioral side effects associated with montelukast use.

Statement 24: Probiotics can play an important role as an adjunct therapy in managing allergy especially during the maintenance phase. They might help to reduce the severity of the next bout of viral infection or allergy attack.

Probiotics, like LP-33 (*Lactobacillus paracasei*), are effective in supportive treatment of perennial allergic rhinitis in children.³⁸

Expert panel remarks

Need for more evidence-based research to further support this statement as well as further guide regarding the choice of probiotic strains, doses and duration of such therapy.

CONCLUSION

The present manuscript provides an expert consensus on the management and treatment options available for pediatric allergic cough in Indian scenario. Allergic cough management is a crucial endeavour and should involve proper care while addressing it. Taking detailed medical history and applying sound clinical acumen with appropriate testing are mandatory to diagnose and effectively distinguish allergic cough from non-allergic cough. The present set of statements is aimed at providing such clinical assistance to the practitioners.

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