International Journal of Basic & Clinical Pharmacology
Ganapathy S et al. Int J Basic Clin Pharmacol. 2024 Nov;13(6):941-952
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20243049

Review Article

An expert consensus on managing cough in Indian pediatric practice: airway disease education and expertise 2.0 (2024)

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Received: 31 August 2024
Accepted: 02 October 2024

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ABSTRACT

Cough in children is one of the most frequent presenting symptoms in health care settings. Coughing can significantly affect a child's sleep and level of activity, which often causes parents' distress. Promptly addressing chronic cough may enhance the quality of life in children and reduce the considerable stress on parents. In 2017, airway disease education and expertise (ADEX) NEXT recommendations for diagnosis, management, and follow-up of persistent (chronic) cough were published. For the present work 27 modified Delphi consensus statements were prepared, and a survey was undertaken involving 30 expert pediatricians from across India. The opinions of the expert panel on the updates related to pediatric chronic cough awareness, diagnosis, and management were collected. Consensus was predetermined to be obtained if more than 75% of the participants agreed or remained neutral for the statement. All the statements were supported by the latest data from the literature search. All the statements reached consensus after an agreement of more than 75%. Consequently, all the opinions from experts were consolidated and expert recommendations were framed. Children presenting with cough should be treated in accordance with child-specific guidelines. The present expert recommendations can be utilized by pediatricians to make well-informed decisions when treating pediatric patients with cough. The management of cough in children should be determined by the underlying cause, where a prompt and efficient therapy can result in early resolution.

Keywords: Pediatric cough, ADEX 2.0, Expert consensus recommendations

INTRODUCTION

Cough is an inherent physiological reflex characterized by forceful exhalation that serves the dual purpose of clearing endogenous secretions and foreign substances, while also mitigating bronchospasm and safeguarding the integrity of the respiratory system. It is non-specific and frequently encountered across a range of medical conditions, with acute respiratory infections and allergic disorders, such as asthma, being among its predominant triggers.[1] Coughing may arise either spontaneously or be initiated voluntarily. It is considered chronic when it stays for more than four weeks in children or eight weeks in adults.[2,3] It is among the most frequent clinical presentations in children, prompting their visits to general practitioners or pediatricians[1]. In the worldwide COVID-19 epidemic, there was a noticeable rise in health-seeking activity among parents of children who had chronic cough.[4] Cough in pediatric age groups and an adult differs based on the symptoms, their duration, and etiology. Age exerts a significant impact on cough-specific physiology, respiratory functioning, as well as various other systems like the immune system. Children, particularly infants and young children, differ from adults due to maturation-

related alterations in airway structure, respiratory muscle development, chest wall composition, respiratory reflex responses, respiratory regulation, and characteristics related to sleep.[5,6] In children, it is affected by factors such as airway diameter and age. Potential causes of pediatric cough include conditions like asthma, tracheomalacia, protracted bacterial bronchitis, drug induced, habit-related cough, and many other systemic disorders.[2] Early recognition and treatment of the underlying cause may prevent further escalation and worsening, especially in pediatric cough cases. Moreover, promptly addressing cough may enhance the quality of life in children and reduce the considerable stress on parents. Apart from that, an early intervention minimizes the financial burden of recurrent medical consultations. A precise diagnostic approach significantly limits the utilization of unnecessary diagnostic tests and medications as well, thereby reducing the risk of severe adverse events.[7]

In 2016, a training module was developed known as airway diseases education and expertise (ADEX) in pediatrics to enhance knowledge and acceptance of United airway disease (with a specific focus on allergic rhinitis and asthma) amongst general practitioners in India. This was undertaken with the partnership of the Pediatric Allergy Association of India (PAAI) and the Indian Academy of Pediatrics (IAP) Allergy and Applied Immunology chapter.[8] Following the achievements of the ADEX module, ADEX NEXT was designed to develop recommendations for the clinical management of "persistent (chronic) cough" in both primary and secondary pediatric care. It addressed the knowledge gaps related to awareness, diagnosis, management, and referral of pediatric cases with chronic cough.

In 2017, this expert panel published the ADEX NEXT recommendations that was based on the assessment that had been conducted on the published articles between 1993 to 2017 period.

In the current manuscript, we conducted advisory board meetings with expert panel of 30 pediatricians from all over India to publish the 2024 ADEX 2.0 recommendations that is aimed to address the latest changes and concerns and provide latest consensus on the pediatric cough awareness, diagnosis, management, and referral guidelines.

METHODS

A total of 27 modified delphi statements were formulated regarding knowledge and management of pediatric cough following the literature survey from 2017 onwards. An expert group of 30 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 to be 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 a manuscript form and sent to panel members for final review.

RESULTS

All of the 27 statements reached consensus during the expert panel discussion and these statements along with the expert panel consensus percentages are given in Table 1.

Table 1: Delphi statements and expert panel responses.

Statement no.	Statement	Agree (%)	Disagree (%)	Neutral (%)	Consensus (agree + neutral) (%)
Statement 1	Acute cough, commonly caused by a viral upper respiratory tract infection (URTI), typically resolves spontaneously without treatment. Diagnosis in pediatric cases can usually be made through patient history and physical examination, typically without the need for further investigation. Parents may benefit from education and reassurance that the cough will naturally subside over time.	100	-	-	100
Statement 2	The most common causes of chronic pediatric cough are generally thought to be protracted bacterial bronchitis (PBB), asthma, and post-infectious cough.	96.7	-	3.3	100
Statement 3	After an initial assessment of medical history, diagnosing chronic cough in children typically involves performing a chest radiograph, CBC, and, when appropriate for age, spirometry. A chest X-ray is one crucial as a primary diagnostic tool to evaluate lung condition, ruling out conditions like pneumonia, lung cancer, or structural abnormalities leading to cough.	96.7	-	3.3	100
Statement 4	Assessing immunoglobulin E (IgE) levels is not reliable to diagnose or rule out allergic cough.	80	10	10	90

Continued.

Statement no.	Statement	Agree (%)	Disagree (%)	Neutral (%)	Consensus (agree + neutral) (%)
Statement 5	For pediatric patients who experience chronic cough, the management approach should be determined by the underlying cause of the cough.	100	-	-	100
Statement 6	In children with a persistent wet or productive cough lasting more than four weeks, not associated with an underlying disease and lacking specific indicators (e.g., coughing during feeding, digital clubbing), it is advisable to administer a course of antibiotics designed to combat common respiratory bacteria. If the cough persists even after 2 weeks of antibiotic treatment, then proper diagnosis should be made with the assistance of laboratory techniques and specialist's (e.g., allergists and pulmonologists) opinion.	80	10	10	90
Statement 7	In the case of children experiencing a persistent wet or productive cough not associated with an underlying disease but exhibiting specific cough indicators (e.g., coughing during feeding, digital clubbing), it is recommended to conduct additional investigations such as flexible bronchoscopy, chest CT, an assessment for aspiration and/or evaluation of immunologic competency should be undertaken to identify any potential underlying disease.	100	-	-	100
Statement 8	Antitussives are preferred drugs for dry cough affecting QoL.	90	3.3	6.7	96.7
Statement 9	Antitussives should not be used for productive coughs, where mucus or phlegm is being expelled, as these coughs serve the vital purpose of clearing the airways.	100	-	-	100
Statement 10	Codeine and its combinations is no longer a drug of choice for most coughs because of the potential for serious side effects including respiratory distress, decreases ciliary activity, increases bronchospasm, and causes dependence and constipation.	93.3	-	6.7	100
Statement 11	Bronchodilators are also preferred choice for wet bronchospastic cough in children as they facilitate improved air flow.	100	-	-	100
Statement 12	For young children having productive cough, levosalbutamol monotherapy can be preferred whereas for older children having productive cough, terbutaline monotherapy can be preferred.	76.7	10	13.3	90
Statement 13	Second generation antihistamines can be used in cases where allergy is suspected to be the cause of cough.	80	10	10	90
Statement 14	Mucoactive drugs such as acetylcysteine and guaifenesin are preferred drugs in productive cough and with excessive mucus production for clearing lung airways.	86.7	6.7	6.7	93.4
Statement 15	Antibiotics are not to be prescribed for uncomplicated coughs caused by viral infections, such as the common cold or flu.	100	-	-	100
Statement 16	Judicious use of antibiotics in management of productive cough due to bacterial illness is recommended.	100	-	-	100
Statement 17	Systemic steroids are generally not efficacious and are among the least well tolerated options in children, indicating a need for alternative.	86.7	6.7	6.7	93.4

Continued.

Statement no.	Statement	Agree (%)	Disagree (%)	Neutral (%)	Consensus (agree + neutral) (%)
Statement 18	For asthmatic cough, bronchodilators and anti-inflammatory medications are commonly prescribed to control airway inflammation and reduce coughing.	100	-	-	100
Statement 19	Fixed dose combinations tend to improve clinical effectiveness, reducing pill regimens, simplify packaging, improve patient adherence, and reduce administrative costs. However, caution is advised against irrational drug combinations, which can lead to unnecessary adverse effects and increased therapy costs. In managing pediatric cough, fixed-dose combinations can be preferred choice to manage paediatric cough. They are to be used as per treating physicians' discretion and judgment based on the clinical assessment of the patient. They are recommended for short term use only.	96.7	-	3.3	100
Statement 20	Bromhexine hydrochloride, combined with guaifenesin and terbutaline sulfate, is the preferred choice for symptomatic relief of bronchospasm in patients with bronchial asthma, chronic bronchitis, and related productive cough conditions.	80	6.7	13.3	93.3
Statement 21	Ambroxol hydrochloride + guaifenesin + levosalbutamol can be used to alleviate productive cough associated with bronchial asthma and chronic bronchitis.	80	10	10	90
Statement 22	Dextromethorphan hydrobromide + chlorpheniramine maleate is recommended specifically for temporary relief from dry cough caused by throat discomfort, sneezing, and a runny nose. Its application is restricted to dry coughs and should not be used for productive or infectious coughs. Similarly, levodropropizine + chlorpheniramine maleate fixed-dose combination is approved for treating non-productive dry cough and should not be administered for productive or infectious cough conditions.	90	6.7	3.3	93.3
Statement 23	Chlorpheniramine maleate +phenylephrine +paracetamol can be used as a SOS option in children to manage viral infection induced cold and coughs accompanied by fever	80	10	10	90
Statement 24	CPM and phenylephrine combination can be used in treating allergic cough for relief in symptoms on SOS basis	80	10	10	90
Statement 25	For the management of bronchiectasis, chest physiotherapy, postural drainage, and the use of bronchodilators and mucolytic agents is initially preferred.	100	-	-	100
Statement 26	Gastroesophageal reflux disease (GERD) is a more prevalent cause of chronic cough in adults as compared to children. Recommendations include the use of proton pump inhibitors (PPI), doneperidone, and H2-receptor antagonists.	66.6	16.7	16.7	83.3
Statement 27	Use of omega-3 fatty acids, probiotics, antioxidants, such as vitamins C and E is highly recommended in cough management. In children with chronic cough, oxidative stress from air pollution and infections induced airway inflammation can be reduced by the	60	16.7	23.3	83.3

Continued.

Statement no.	Statement	Agree (%)	Disagree (%)	Neutral (%)	Consensus (agree + neutral) (%)
	use of antioxidants and probiotics such as fruits and vegetables, butter, curds, fish, oils rich in omega 3 FA – (fish oil /flaxseed oil), and traditional food are recommended.				

DISCUSSION

Statement 1: Acute cough, commonly caused by a viral upper respiratory tract infection (URTI), typically resolves spontaneously without treatment. Diagnosis in pediatric cases can usually be made through patient history and physical examination, typically without the need for further investigation. Parents may benefit from education and reassurance that the cough will naturally subside over time.

Upper respiratory tract infection (URTI) or "the common cold" is a symptom complex usually caused by several families of virus; these are the rhinovirus, coronavirus, parainfluenza, respiratory syncytial virus (RSV), adenovirus, human metapneumovirus and influenza. Occasionally the enterovirus is implicated in summer.[8] Diagnosis involves physical examination accompanied by taking and reviewing detailed patient history.[9] Since, viral infections are generally responsible for acute cough and underlying URTIs; treatment should be avoided and parent education towards the cause and options should be emphasized. Improved parent education and awareness may reduce the usage of antibiotics and thus result in lower chances of developing antimicrobial resistance.[10]

Expert panel remarks

The most common cause for acute URTI associated cough is viral infection, that does not require further investigation unless it becomes chronic or other symptoms exacerbate. Management should involve symptomatic approach like giving paracetamol for fever.

The right course for every diagnosis starts with a proper patient history taking and physical examination. Parent's awareness and education can be the best way forward while managing pediatric cough.

Statement 2: The most common causes of chronic pediatric cough are generally thought to be protracted bacterial bronchitis (PBB), asthma, and post-infectious cough.

Potential causes of pediatric cough include conditions like asthma, tracheomalacia, protracted bacterial bronchitis, habit-related cough, and many other systemic disorders.[2] Out of these PBB, asthma and post-infection are most prevalent and account for majority of chronic pediatric cough instances.[2]

Expert panel remarks

There is a need to involve pediatric pulmonologists in the cases where PBB is suspected, i.e., in cases when wet cough is not responding to any treatment. Prolonged antibiotic treatment is recommended for combating PBB.

Statement 3: After an initial assessment of medical history, diagnosing chronic cough in children typically involves performing a chest radiograph, CBC, and, when appropriate for age, spirometry. A chest X-ray is one crucial as a primary diagnostic tool to evaluate lung condition, ruling out conditions like pneumonia, lung cancer, or structural abnormalities leading to cough.

Medical history plays the most important role in addressing pediatric cough problem, but in cases where the underlying cause is not apparent and/or some structural deformity or infection is suspected, the practitioner should employ techniques like chest X-rays, CBC or spirometry to uncover the underlying issues (Table 2).

Table 2: Laboratory tests and their implications.

Laboratory tests		Implications
Complete blood count (CBC)		
Leukocytes	High	Pneumonia
ESR	High	
CRP	High	
Leukocytes	High	
Eosinophils	High	Allergic cough, asthma
Leukocytes, neutrophils	Very high	COVID-19
	Low	
Neutrophils	Low	
	High	Lung cancer
TLC, lymphocytes	High	Pertussis

Continued.

Laboratory tests	Implications
Chest X-ray/radiograph	Regularly advised for a persistent cough. Used to identify various lung-related conditions, including nodules (lung cancer), tuberculosis, pneumothorax, pneumonia, atelectasis, cardiomegaly, consolidation, emphysema, fibrosis, and COVID-19. If a clear anomaly is detected in standard X-rays, further examination is chosen depending on the nature of the lesion.
CT	To assist and further investigate the findings of chest X-ray. With and without contrast, virtual air bronchography.
Sputum microscopy culture	To investigate and diagnose lower respiratory tract infections like bronchitis, pneumonia, bronchiolitis, and tuberculosis.
PET	Specifically for the diagnosis of lung cancer, employing a specialized tracer that identifies and labels cancerous cells.
Other tests	
Pulmonary function tests	Comprises pulmonary ventilation assessments, spirometry, and the bronchial provocation test. These tests are used to diagnose conditions like asthma, ILD, and other respiratory disorders.
Cough provocation test	Identifying positive results in the cough provocation test plays a significant role in diagnosing CVA. An average daily peak expiratory flow variation exceeding 10% indicates the likelihood of CVA.
CRP	A low CRP test result can be useful in ruling out the need for antibiotics or postponing antibiotic prescriptions.
PCT	Can be used as a marker of bacterial infection
lgE	This test is crucial for assessing cough related to suspected allergies.

COPD: Chronic obstructive pulmonary disease; COVID: coronavirus disease 2019; CRP: C-reactive protein; CT: chest computed tomography; CVA: cough variant asthma; ESR: erythrocyte sedimentation rate; IgE: immunoglobulin E; NT-proBNP: N-terminal pro-brain natriuretic peptide; PCT: procalcitonin; PET: positron emission tomography

Chest X-ray is regularly advised for a persistent cough if an underlying cause is suspected that could be diagnosed using a radiograph like nodules (lung cancer), tuberculosis, pneumothorax, pneumonia, atelectasis, cardiomegaly, consolidation, emphysema, fibrosis, and COVID-19. If a clear anomaly is detected in standard X-rays, further examination is chosen depending on the nature of the lesion.[11]

Expert panel remarks

Spirometry could only be done in children above at least 4 years of age. Laboratory techniques can assist in cases where diagnosis is not apparent, or chances of differential diagnosis are more.

Cough is an airway disorder, not a parenchymal one, so X-ray should only be done when the practitioner suspects a plausible cause. The use of lateral X-ray might reveal more details in specific cases where retrosternal and retrocardiac spaces are of relevance and have clinical significance.

Statement 4: Assessing immunoglobulin E (IgE) levels is not reliable to diagnose or rule out allergic cough.

Serum IgE levels increase in the cases involving IgE mediated allergic reactions, but the non-specific nature of total IgE testing does not provide a true representation of the allergy status as many factors may contribute to increased and decreased total IgE levels. Pollution is one such factor which increases the total IgE levels in children, even though there might not be any allergic reaction present in such cases. Similarly, long term use of corticosteroid may suppress the total IgE levels and may be deluding in cases involving allergy.

Expert panel remarks

IgE levels may not reveal all the instances of allergy and might be misleading.

Statement 5: For pediatric patients who experience chronic cough, the management approach should be determined by the underlying cause of the cough.

Expert panel remarks

The approach to manage the chronic cough should always be to address the underlying cause rather than giving symptomatic treatments. It becomes even more relevant in cases of wet cough where the cause could be more severe and threatening if not treated properly, like prescribing anti-tussive for wet cough.

Statement 6: In children with a persistent wet or productive cough lasting more than four weeks, not associated with an underlying disease and lacking specific indicators (e.g., coughing during feeding, digital clubbing), it is advisable to administer a course of antibiotics designed to combat common respiratory bacteria. If the cough persists even after 2 weeks of antibiotic treatment, then proper diagnosis should be made

with the assistance of laboratory techniques and specialist's (e.g., allergists and pulmonologists) opinion.

Antibiotics are prescribed in cases where the cause for wet cough is suspected to be of bacterial origin, and in such cases, there should be an improvement in the condition and alleviation in the associated cough after 2 weeks of antibiotic treatment. But in cases where wet cough persists even after 2 weeks of continued antibiotic treatment, special care should be taken, and involvement of specialists should be sought to address the case in question.

Expert panel remarks

Antibiotic therapy should be discontinued after two weeks of non-responsiveness and specialists should be involved to assess the case and recommend further use of appropriate antibiotics if needed.

Statement 7: In the case of children experiencing a persistent wet or productive cough not associated with an underlying disease but exhibiting specific cough indicators (e.g., coughing during feeding, digital clubbing), it is recommended to conduct additional investigations such as flexible bronchoscopy, chest CT, an assessment for aspiration and/or evaluation of immunologic competency should be undertaken to identify any potential underlying disease.

In cases where wet or productive cough is not resolved by antibiotic treatment of two weeks, and specific cough indicator like digital clubbing are present, additional investigations like flexible bronchoscopy, chest CT and immunity testing can identify the underlying cause and may assist in the diagnosis.[12]

Expert panel remarks

Referral to pediatric pulmonologist/ specialist should be considered in cases where wet cough is not resolved by prolonged antibiotic treatment of more than 2 weeks, to diagnose and manage the underlying disease.

Statement 8: Antitussives are preferred drugs for dry cough affecting QoL.

In cases involving dry cough, when the cause is unclear and cough reflex is increased, antitussives play an excellent role.[13,14] They suppress the cough reflex and can be especially beneficial in nocturnal incidences so that sleep disturbances don't affect the quality of life.

Expert panel remarks

Anti-tussive play an excellent role as a rescue medication while addressing the dry cough. In cases where sleep is affected by night-time cough and daily activities are affected by persistent day time cough, antitussives could be the medicine of choice.

Statement 9: Antitussives should not be used for productive coughs, where mucus or phlegm is being expelled, as these coughs serve the vital purpose of clearing the airways.

Expert panel remarks

In cases where cough is productive and mucus or phlegm is getting expelled, anti-tussive might be counter intuitive as they stop the cough, and this might lead to accumulation of mucus in the airways. This mucus accumulation results in decreased pulmonary function and may worsen the situation.

Statement 10: Codeine and its combinations are no longer a drug of choice for most coughs because of the potential for serious side effects including respiratory depression, decreases ciliary activity, increases bronchospasm, and causes dependence and constipation.

Codeine and its combinations have serious side effects including but not limited to respiratory distress, decreased ciliary activity, increased bronchospasm and constipation, and hence they far exceed the potential benefit of cough suppression in children.[15]

Expert panel remarks

The risks associated with codeine and its preparations far outweigh the potential benefits in the pediatric population.

Statement 11: Bronchodilators are also preferred choice for wet bronchospastic cough in children as they facilitate improved air flow.

Bronchospasm involves the constriction of the smooth muscle layers of the small airways. Hence the role of bronchodilators become prominent in cases where cough is accompanied by bronchospasm so as to relieve them and improve the air flow in small airways.

Expert panel remarks

Bronchodilators alleviate the cough in cases of asthma and ILDs where bronchospasm is present.

Statement 12: For young children having productive cough, levosalbutamol monotherapy can be preferred whereas for older children having productive cough, terbutaline monotherapy can be preferred.

In a double-blind, randomized study, levosalbutamol was found to be safe and effective in children with asthma aged 2-5 years.[16,17] Terbutaline is shown to be effective with mild and transient adverse effects in children with bronchial asthma aged 6 to 13 years[18] and chronic asthma aged 7 to 14 years.[19] Terbutaline has shown to be better when prescribed in cases involving ineffectiveness of levosalbutamol because of the downregulation of beta-2 adrenergic receptor.[16]

Expert panel remarks

Contra-indications should be considered while prescribing brochodilators

Statement 13: Second generation antihistamines can be used in cases where allergy is suspected to be the cause of cough.

Antihistamines may be considered for managing cough in certain cases where cough is associated with allergies or postnasal drip.[20] In patients with allergic rhinitis and associated cough is present, use of antihistamines can be beneficial and may improve the outcome.

Expert panel remarks

Due to the dryness produced by antihistamines monotherapy, they should only be considered in special circumstances and should never be used in case of dry cough.

Statement 14: Mucoactive drugs such as acetylcysteine and guaifenesin are preferred drugs in productive cough and with excessive mucus production for clearing lung airways.

Mucolytics are mucoactive agents, that exert their effect on the mucus layer lining of the respiratory tract and increase mucus clearance rate. In conditions like asthma, chronic irritation of the airways leads to mucus hypersecretion. Mucociliary mechanism gets overwhelmed and there is deposition of mucus in the airways. This in turn leads to the formation of mucus plugs, which further decrease the clearance like a vicious circle. Mucoactive drugs help clean this mucus and improves the outcome.[21]

Expert panel remarks

Mucolytic drugs being GI irritant, should only be given with food. An age reference should also be considered while prescribing mucolytic drugs.

Statement 15: Antibiotics are not to be prescribed for uncomplicated coughs caused by viral infections, such as the common cold or flu.

In several studies and reviews, it has been concluded that antibiotics play no role in the treatment of common colds. Antibiotics should only be considered as a treatment option if a bacterial infection has developed concurrently with the cold.[22]

Expert panel remarks

Antibiotics should always be used judicially as there is a precarious situation arising from advent of MDR and XDR strains of bacteria developing due to misuse of antibiotics.

Statement 16: Judicious use of antibiotics in management of productive cough due to bacterial illness is recommended.

There are evidence present that outline the effectiveness of antibiotics in managing chronic wet cough.[22] However, antibiotics have adverse effects and should be used with proper care and attention to clinical parameters so that it does not compromise the overall wellbeing of the child.

Expert panel remarks

Clinical parameters like liver function and kidney function should be monitored cautiously while prescribing antibiotics and follow ups.

Statement 17: Systemic steroids are generally not efficacious and are among the least well tolerated options in children, indicating a need for alternative.

Because of the inflammatory mechanisms of most chronic upper airway diseases such as rhinitis and chronic rhinosinusitis, systemic steroids have been used for their treatment for decades. However, it has been very well documented that potentially severe side-effects can occur with the accumulation of systemic steroid courses over the years. These side effects become even more pronounced in the children and hence there is a need for alternatives for systemic steroids.[23]

Expert panel remarks

There is a need for prescribing alternatives instead of systemic steroids in the pediatric population.

Statement 18: For asthmatic cough, bronchodilators and anti-inflammatory medications are commonly prescribed to control airway inflammation and reduce coughing.

In cases involving asthmatic coughing and airway inflammation, bronchodilators play an excellent role. They are also used to prevent exercise-induced asthma. They work by stimulating beta-adrenergic receptors to widen (dilate) the airways and relieve the asthmatic symptoms.[24] Anti-inflammatory medicines also help relieving the inflammation of the airways and thus improve air flow and reduce the cough reflex in children with asthmatic cough.

Expert panel remarks

Bronchodilators and anti-inflammatory medication combination is the right choice for management of asthmatic cough.

Statement 19: Fixed dose combinations tend to improve clinical effectiveness, reducing pill regimens, simplify packaging, improve patient adherence, and reduce administrative costs. However, caution is advised against irrational drug combinations, which can lead to unnecessary adverse effects and increased therapy costs.

In managing pediatric cough, Fixed-dose combinations can be preferred choice to manage paediatric cough. They are to be used as per treating physicians' discretion and judgment based on the clinical assessment of the patient. They are recommended for short term use only.

Fixed-dose combination decreases the risk of medication non-compliance and should be considered in children for improving medication compliance which can translate into better clinical outcomes.

Expert panel remarks

FDCs lead to better compliance rate, though there is a need to check for proper dosage of all components while prescribing FDCs and not just the common ones like paracetamol. Proper dosage and proportions of all components should be checked before prescribing FDCs, that too for a limited duration use.

Statement 20: Bromhexine hydrochloride, combined with guaifenesin and terbutaline sulfate, is the preferred choice for symptomatic relief of bronchospasm in patients with bronchial asthma, chronic bronchitis, and related productive cough conditions.

Guaifenesin, terbutaline, and bromhexine combination relieves productive cough associated with bronchitis, and bronchial asthma. Guaifenesin is an expectorant that promotes effective cough by increasing mucus volume while decreasing its viscosity, hence making it easier to expel out.[25] Terbutaline is a bronchodilator, which works by relaxing the muscles in the airways and thus widens the airways to improve the air flow. Bromhexine is a mucolytic agent that loosens mucus, making it easier to cough out.[26] Together, they make breathing easier and clear out the mucus from the airways, thus relieving cough.

Expert panel remarks

Age reference should be considered while prescribing this combination as this combination can be prescribed in children above the age of 2 years only. This combination is recommended for short-term use to alleviate symptoms in individuals experiencing productive cough.

Statement 21: Ambroxol hydrochloride + guaifenesin + levosalbutamol can be used to alleviate productive cough associated with bronchial asthma and chronic bronchitis.

Ambroxol is a mucolytic agent that decreases the amount of mucus from the airways, guaifenesin being an expectorant makes it easy to remove the mucus, whereas levosalbutamol dilates the airways for making the breathing easier. A clinical trial conducted by Kiran et al showed the effectiveness of this combination in alleviating the symptoms associated with productive cough in children with bronchial asthma and chronic bronchitis. The study showed that this combination reduced the severity of cough by up to 85% on day 5.[27]

Expert panel remarks

Ambroxol can be preferred in cases where noisy breathing is observed. This combination is recommended for short-term use to alleviate symptoms in individuals experiencing productive cough.

Statement 22: Dextromethorphan hydrobromide + chlorpheniramine maleate is recommended specifically for temporary relief from dry cough caused by throat discomfort, sneezing, and a runny nose. Its application is restricted to dry coughs and should not be used for productive or infectious coughs. Similarly, levodropropizine + chlorpheniramine maleate fixed-dose combination is approved for treating non-productive dry cough and should not be administered for productive or infectious cough conditions.

Chlorpheniramine maleate (CPM) is an antiallergic that binds to H1 receptors and blocks the activity of endogenous histamines, thereby leading to a short-term relief to allergic symptoms.[28] Whereas dextromethorphan hydrobromide belongs to the class of cough suppressants that block the transmission of nerve signals from the cough centre in the brain to the muscles that produce cough.[29] Combination of chlorpheniramine maleate and dextromethorphan hydrobromide helps to relieve cough, cold and allergic symptoms.

Levodropropizine is a cough suppressant which relieves cough by blocking the production of neuropeptides from C-fibres.[17] In combination with CPM, this could be used for alleviating symptoms of dry allergic cough. Whereas in cases with productive cough, the activity of these drugs is counter intuitive as it will stop the clearance of airways and hence may complicate the breathing.

Expert panel remarks

The treating pediatrician should use their discretion on individual case basis while prescribing it. These combinations can be used for the management of dry cough only, while being vigilant regarding the side effects associated with CPM.

Statement 23: Chlorpheniramine maleate + phenylephrine + paracetamol can be used as a SOS option in children to manage viral infection induced cold and coughs accompanied by fever.

Chlorpheniramine maleate has shown potential antiviral activity against a number of viruses including various strains of Influenza virus and SARS CoV2.[30,31] Its combination with phenylephrine and paracetamol can be used to treat children with fever, cough, and cold induced by virus infections.

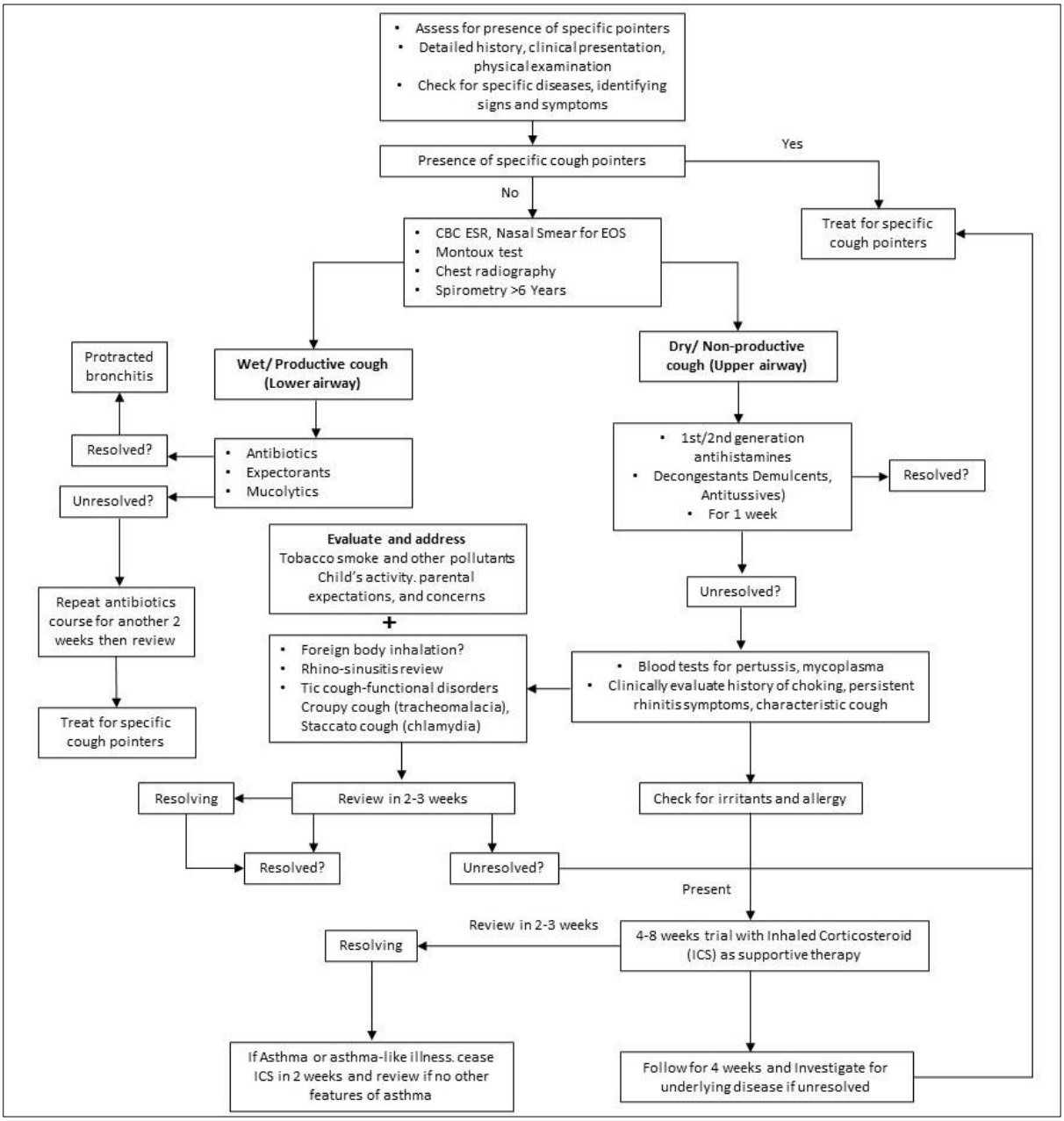

Figure 1: Algorithm for paediatric cough-diagnosis and management.

Expert panel remarks

Combinations with CPM should be used cautiously and risk to benefit assessment should be carried out while prescribing it in the pediatric set-ups.

Statement 24: CPM and phenylephrine combination can be used in treating allergic cough for relief in symptoms on SOS basis.

Expert panel remarks

CPM should be used cautiously in the pediatric set-up and a thorough risk to benefit assessment should be carried out on a case-to-case basis.

Statement 25: For the management of bronchiectasis, chest physiotherapy, postural drainage, and the use of bronchodilators and mucolytic agents is initially preferred.

Bronchiectasis is a chronic respiratory disease characterised by cough, sputum production and bronchial infection, and can be radiologically diagnosed by abnormal and permanent dilatation of the bronchi. The goals of bronchiectasis treatment are to halt the disease from progressing, lessen symptoms, enhance quality of life, and avoid exacerbations. The most common symptoms are coughing and sputum production, although other common ones include rhinosinusitis, tiredness, haemoptysis, and thoracic pain. In addition to bronchodilators, the use of mucolytic medicines reduces

dyspnoea and increases expectoration to open the airways.[32]

Expert panel remarks

Use of mucolytic agents and bronchodilators can be the first-choice option for the management of bronchiectasis.

Statement 26: Gastroesophageal reflux disease (GERD) is a more prevalent cause of chronic cough in adults as compared to children. Recommendations include the use of proton pump inhibitors (PPI), domperidone, and H2-receptor antagonists.

GERD is more common in adult population and hence, refractory chronic cough due to GERD is also more prevalent in adults. This does not respond well to the classical acid reflux therapy and may require adding H2-receptor antagonists with the PPIs to successfully manage.[33]

Expert panel remarks

PPI and H2 receptor antagonists should be included in the treatment regimen for chronic cough where GERD is diagnosed as the cause.

Statement 27: Use of omega-3 fatty acids, probiotics, antioxidants, such as vitamins C and E is highly recommended in cough management. In children with chronic cough, oxidative stress from air pollution and infections induced airway inflammation can be reduced by the use of antioxidants and probiotics such as fruits and vegetables, butter, curds, fish, oils rich in omega 3 FA – (fish oil /flaxseed oil), and traditional food are recommended.

A randomized controlled trial on 192 asthmatic schoolchildren aged 10-12 showed that the use of fruit plus vegetable concentrate, fish oil and probiotics reduced the medication use and improved pulmonary function.[34]

Expert panel remarks

There is a need for further research and more evidence regarding cough management by nutraceuticals.

CONCLUSION

The expert recommendations gathered in this manuscript can be utilized by pediatricians to efficiently make informed decisions when treating patients with chronic and acute cough and associated complications. The expert group strongly felt that pediatric cough is a challenge as not only it may be a symptom of underlying ailment, but it also affects the quality of life and hence growth of the child. An algorithm outlining the diagnosis and management of pediatric cough is given in Figure 1.

ACKNOWLEDGEMENTS

Authors would like to thank NeoCrest Life Sciences Consulting Private Limited for providing medical writing assistance for this manuscript. The authors would also like to thank the panel for sharing their expertise, insights, and valuable time to develop the expert consensus statements and recommendations.

Funding: The study was funded by scientific grant from Dr. Reddy's Laboratories Pvt. Ltd
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Ganapathy S, Mathur A, Chakarvarty A, Joshi DK, Gala M, Muchhala SS, et al. An expert consensus on managing cough in Indian pediatric practice: airway disease education and expertise 2.0 (2024). Int J Basic Clin Pharmacol 2024;13:941-52.