

## Special Article - Bronchiolitis

# Diagnosis & Management of Bronchiolitis in Children: An Update

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**\*Corresponding author:** Sharma BS, Department of pediatrics, SMS Medical College, Jaipur, India**Received:** September 26, 2016; **Accepted:** February 08, 2017; **Published:** February 10, 2017**Abstract**

Bronchiolitis is the most common respiratory cause of hospitalization during infancy. It is caused by viral infections most commonly respiratory syncytial virus. It is characterized by acute inflammation, edema and necrosis of epithelial cell lining of small airways and increased mucus production. Signs and symptoms typically begin with nasal discharge & cough which may progress to tachypnea, wheezing, rales, use of accessory muscles, nasal flaring and feeding difficulty.

In most of patients disease is self limiting, typically lasting for 3 to 7 days. The management of Bronchiolitis in the outpatient as well as inpatient setting remains a challenge to the treating physician. There is widespread variation in management of patients with bronchiolitis. The effectiveness of various interventions used for treatment of bronchiolitis is still unclear. The objective of the present article is to review the available evidence and guidelines -

1. To reduce the use of unnecessary investigations and therapies by providing practical guidelines to the practitioners managing children with bronchiolitis.

2. To evaluate the evidence supporting the use of currently available treatment for infants with bronchiolitis.

3. To provide evidence based approach to the diagnosis and management of bronchiolitis.

**Conclusions:** The diagnosis of acute bronchiolitis is primarily clinical and laboratory investigations as well as chest radiograph are rarely required to make diagnosis. Pulse oximetry helps to guide the need for oxygen administration. The supportive care remains the cornerstone of therapy in bronchiolitis which comprises oxygenation & hydration. Many recent evidence based reviews have suggested that bronchodilators and corticosteroids should not be used routinely.

Number of other therapies like CPAP, hypertonic saline, surfactant, heliox and inhaled furosemide have been evaluated in clinical trials but has not proved to be of definite help consistently and hence not recommended for routine use.

**Keywords:** Bronchiolitis; Epinephrine; CPAP; Salbutamol; Humidified oxygen

## Introduction

Acute bronchiolitis is a leading cause of morbidity in infants and children. It is most common cause of hospitalization due to lower respiratory infection in the first year of life. The bronchiolitis is defined as "a acute inflammation, edema, necrosis of epithelial cells linings small airways, increased mucus production and bronchospasm" [1,2].

Another definition which has been used in many clinical studies is the first episode of wheezing in a child younger than one year to 2 year who has physical findings of acute viral respiratory infection and has no other explanation for wheezing. It usually presents initially with rhinitis and cough which may progress to tachypnea, wheezing, crackles, use of accessory muscles, and / or nasal flaring and often affects child ability to feed [3].

Approximately 1 in 3 infants will develop clinical bronchiolitis in first year of life. In most infants disease is self limiting, typically

lasting between 3 to 7 days. Most infants are managed at home, often with primary care support and 2 to 3 % of all infants require hospitalization [1].

## Etiology and Epidemiology

Acute bronchiolitis is typically caused by a viral infection. With improvement in diagnostic ability to identify viruses in respiratory secretions (nasopharyngeal aspirates) multiple viral agents have been identified as causative agents of acute bronchiolitis [4,5].

The most common etiology of bronchiolitis is Respiratory Syncytial Virus (RSV), accounting 50-90% cases. The highest incidence of infection occurring between December and March in North America, however regional variations occur. In Indian subcontinent the outbreaks of bronchiolitis occur from September to March. 90% of children are infected with RSV in first 2 years of life, and up to 40% will develop lower respiratory tract infection during

the initial infection [5-7].

Other viruses that cause bronchiolitis include, rhinovirus, human meta pneumo virus, influenza, adenovirus, corona virus and para influenza viruses [8,9].

In Indian studies, RSV infection was diagnosed in 30-70% of children with bronchiolitis [10].

Most of the studies implicate rhinovirus (which normally causes common cold) as the second most common cause of bronchiolitis. Molecular diagnostic techniques have also revealed a high frequency (15-25%) of mixed viral infections among children evaluated for bronchiolitis [11-13].

### Diagnosis

A diagnosis of acute bronchiolitis should be considered in infants with nasal discharge and wheezy cough, in presence of fine inspiratory crackles and/or high pitch expiratory wheeze. Apnea may be presenting feature, especially in the very young and in premature or low birth weight infants. Most of the time diagnosis of bronchiolitis and assessment of severity of disease can be made only on basis of typical history and physical examination.

Routinely laboratory tests and chest X-ray are not required in making diagnosis of Bronchiolitis [14].

### Signs & symptoms of bronchiolitis

Most clinicians recognize bronchiolitis as a constellation of clinical sign and symptoms occurring in children younger than 2 years, including viral upper respiratory tract prodrome followed by increases respiratory efforts and wheezing [14].

Clinical sign and symptoms of bronchiolitis consist of rhinorrhea, cough, tachypnea, wheezing, crackles, and increased respiratory efforts as grunting, nasal flaring, and intercostals and/ or sub costal retraction and poor feeding.

The infant may show irritability, poor feeding, and vomiting. Though, in majority of cases, the disease remains mild and recovery starts in 3-5 days, some of these children may continue to worsen.

Assessment of child with bronchiolitis should consists detailed history including co- morbidities like prematurity, chronic lung disease, congenital heart disease, immunodeficiency, in utero smoke exposure, genetic abnormalities, atopy, conjunctivitis, otitis media, pharyngitis and thorough physical examination [15-17].

Pulse oximetry has been rapidly adopted into clinical assessment of children with bronchiolitis on the basis of data suggesting that it is reliably detects hypoxemia which is not suspected on physical examination.

Pulse oximetry helps us in deciding about the need for supplemental oxygen. The chest may appear hyper-expanded and may be hyper-resonant to percussion. Wheezes and fine crackles may be heard throughout the lungs. Severely affected patients have grunting, marked retractions. They may be cyanosed, and may have impaired perfusion. Apnea may occur in those born prematurely and in younger than two months of age [18,19].

### Course and severity of disease

The course of bronchiolitis is variable and dynamic, ranging from

transient events, such as apnea to progressive respiratory distress from lower airway obstruction.

Bronchiolitis usually is a self-limited disease. Although symptoms may persist for several weeks, majority of children who do not require hospital admission may continue to have low grade symptoms up to 4 weeks in previously healthy infants. The average length of hospitalization is three to four days. The course may be prolonged in younger infants and those with co-morbid conditions [20].

Various studies and treatment trials have also used clinical scores to predict the disease severity in children with bronchiolitis, but none of these scores have been validated for clinical predictive value in bronchiolitis. It should be emphasized that repeated observation over a period of time may provide a more valid overall assessment of the disease severity than a single examination [21].

#### Risk factors for mortality are following: [22-24]

- Younger age (<6 months)
- Prematurity
- Underlying chronic lung disease
- Cyanotic heart disease
- Immunodeficiency.

#### Clinical features of severe disease in bronchiolitis are as following: [24-26]

- Poor feeding (< 50% of usual fluid intake in preceding 24 hours)
- Lethargy
- History of apnea
- Respiratory rate > 70/ min.
- Presence of nasal flaring and/ or grunting
- Severe chest recession
- cyanosis

#### Criteria for hospitalization: [1]

- When assessing a child, admit them to hospital if they have any of following:
- Apnea
- Persistent oxygen saturation < 92% at room air
- Inadequate oral fluid intake (<50 % of usual volume)
- Persistent severe respiratory distress

### Investigations

Acute bronchiolitis is a clinical diagnosis. Clinicians assessing infants with bronchiolitis may perform investigation when diagnostic uncertainty exists. These investigations may include oxygen saturation recording, blood gas analysis, chest X- ray, virological or bacteriological testing, hematology and biochemistry.

### Oxygen saturation

Pulse oximetry should be performed in every child who attends

hospital with acute bronchiolitis [18,19].

- Infants with oxygen saturation <92% require hospitalization.
- Decision making around hospitalization of infants with oxygen saturation between 92% to 94% should be supported by detailed clinical assessment, consideration phase of illness and take account social and geographical factors.
- Infants with oxygen saturation >94% in room air may be considered for discharge.

### Blood gas analysis

Blood gas analysis is not usually indicated in acute bronchiolitis. It may have role in assessment of infants with severe respiratory distress or who are tiring and may be entering respiratory failure [27].

### Chest radiograph

Chest X-ray should not be performed routinely in infants with typical acute bronchiolitis.

Chest X-ray should be considered in certain following conditions in infants with bronchiolitis:

- Diagnostic uncertainty
- Atypical disease course
- Co-morbidity like chronic lung disease or heart disease is suspected & immunodeficiency.
- No improvement with conventional therapy
- If the child is severely ill.

The radiographic abnormalities of bronchiolitis are variable and include hyperinflation and peribronchial thickening. Patchy atelectasis may result from airway narrowing and mucus plugging [1].

## Laboratory Tests

Laboratory tests are not routinely indicated in the evaluation of infants and young children with suspected bronchiolitis. Abnormalities in total and differential white blood cell counts do not predict serious bacterial infection in infants and young children hospitalized with lower respiratory tract infection due to RSV.

## Lactate Dehydrogenase

Measurement of Lactate Dehydrogenase (LDH) concentration in the nasal-wash fluid has been proposed as an objective indicator of bronchiolitis severity; increased values (suggestive of a robust antiviral response) have been shown to be associated with decreased risk of hospitalization. This observation needs further validation before nasal wash LDH measurement is used to make decisions regarding hospitalization for children with bronchiolitis [28].

## Virological Testing

Unless adequate isolation facilities are available, rapid testing of RSV is recommended in infants who require admission in hospital with acute bronchiolitis in order to guide cohort arrangements

Clinical course, treatment and outcome of acute bronchiolitis due to different viral infections are similar; therefore, identification of viral agents does not affect management in the majority of patients.

However, in the hospital setting, determining the responsible virus may help to avoid unnecessary antibiotic use and also prevent nosocomial transmission to other patients.

The available tools for etiologic diagnosis include Antigen detection, Immunofluorescence, Polymerase Chain Reaction (PCR), and culture of respiratory secretions obtained by nasal wash or nasal aspirate [29].

New techniques such as real-time Polymerase Chain Reaction (PCR), nested PCR, and multiplex PCR have improved the virologic diagnosis of Bronchiolitis immensely [29,30].

In a study to detect RSV in children <2 years with acute respiratory tract illness using three different techniques: viral culture, direct immunofluorescence, and nested PCR, it was found that PCR was the most sensitive technique (11.1% positivity), followed by direct Immunofluorescence (7.9% positivity) and viral culture (6.3% positivity) [31].

## Bacteriological Testing

Routine bacteriological testing is not indicated in infants with typical acute Bronchiolitis [32].

## Hematology

Full blood count is not indicated in infants with typical acute Bronchiolitis [33].

## Biochemistry

Measurement of urea and electrolytes is not indicated in routine assessment and management of infants with typical acute bronchiolitis but should be considered in those with severe disease [34].

## Treatment

Acute bronchiolitis is, in the majority of cases, a mild and self-limiting disease that can be managed on an ambulatory basis with supportive care alone. Management mainly consists of educating parents or caregivers about adequate feeding and to report any deterioration (such as increasing difficulty in breathing, chest in drawing or problems with feeding) to an appropriate health care facility.

## Supportive Care

Supportive care remains the cornerstone of treatment of children with bronchiolitis. It includes maintenance of adequate hydration, provision of respiratory support as necessary, and monitoring for disease progression.

## Nutrition and hydration

Clinicians should administer nasogastric or intravenous fluids for infants with diagnosis of bronchiolitis who cannot maintain hydration orally [1].

Children with bronchiolitis are at an increased risk of dehydration because of their increased needs (related to fever and tachypnea) and reduced oral acceptance. Clinicians should carefully assess hydration and ability to take fluids orally. Children having dehydration or difficulty in feeding safely because of respiratory distress should be given intravenous fluids [1].

For children who can tolerate enteral feeding, small frequent feedings or orogastric or nasogastric feedings may be used to prevent dehydration. Children with bronchiolitis are also at an increased risk of fluid retention (and subsequent pulmonary congestion) due to excessive antidiuretic hormone production, so urine output should be carefully monitored [1,35].

### Antiviral therapy

A Cochrane systemic review examined the effectiveness of nebulised ribavirin in infants and children with lower respiratory disease attribute to RSV infection.

Ribavirin, a synthetic nucleoside analog resembling guanosine, acts by inhibiting viral protein synthesis, and has a broad antiviral effect. It is delivered as a small-particle aerosol for 18 to 20 hours per day [1].

A systematic review of 10 RCTs has documented no improvement in clinical outcome of acute bronchiolitis after Ribavirin use [42].

Ribavirin may be considered in high risk infants (immune-compromised and/or hemodynamically significant cardiopulmonary disease) and in infants requiring mechanical ventilation [1,36].

Apart from ribavirin, no other antiviral is currently approved for use in bronchiolitis. Some other drugs currently under investigation are the small molecule fusion inhibitors (TMC353121, CL387626, RFI-641, JNJ-2408068 etc) that inhibit viral fusion by interacting with the RSV F protein (RSV F protein mediates the fusion of viral envelope with host cell membrane) [37].

Fusion inhibitors have also been shown to be effective against hMPV in experimental animals, and some researchers have suggested a possibility for use of these fusion inhibitors for early treatment in an epidemic context. However, more studies are needed to characterize the best delivery mode, dosage, and schedule of administration for this fusion inhibitors [38].

### Antibiotics

In children with bronchiolitis and fever, the risk of secondary bacterial infection is low, therefore, routine use of antibiotics is not recommended [1].

It is recommended that antibiotics should be used only in children having specific indications of coexistence of a bacterial infection. Presence of infiltrates or atelectasis on chest X-ray film may not indicate bacterial infection. Clinical setting, with consolidation on X-ray film may indicate a possibility of bacterial pneumonia in infants with Bronchiolitis [39].

A systematic review including five studies did not find significant benefits for use of antibiotics in acute bronchiolitis. However, the review indicated a need for research to identify a subgroup of patients who may benefit from antibiotics [40].

### Inhaled bronchodilators

**Beta 2 agonists & epinephrine:** In a meta-analysis of 30 trials comparing bronchodilators other than epinephrine (included salbutamol, terbutaline, ipratropium) with placebo, there were no significant differences in improvement in oxygenation, hospitalization rate, or duration of hospitalization [41].

On the basis of current evidence it is not easy to decide about bronchodilator uses. It is also difficult to distinguish bronchiolitis from viral infection associated wheezing or multi-trigger wheeze. In the latter condition, bronchodilators may improve clinical outcome but not recommended in acute bronchiolitis. Therefore, we consider a trial of bronchodilator with careful monitoring. Choice of bronchodilator may be based on personal or family history of atopy or asthma; if present, salbutamol inhalation may be given [42].

**Anticholinergic:** Two studies have shown that there was no benefit of the use of nebulised ipratropium in infants with bronchiolitis. Nebulised ipratropium is not recommended for treatment of acute bronchiolitis in infants [43].

### Hypertonic saline

Hypertonic saline may reverse some pathophysiological abnormalities in acute bronchiolitis by decreasing epithelial edema, improving elasticity and viscosity of mucus and thus improving airway clearance [44].

A recent randomized controlled trial reported that high volume normal saline was as effective as 3% saline in children with mild bronchiolitis. It may be inferred that improved clearance of mucus in airway may be function of total mass of NaCl rather than concentration of NaCl. Hypertonic saline inhalation may be considered as potential treatment for bronchiolitis. The potential side effects, principally acute bronchospasm, remain a concern with nebulized hypertonic saline [45].

However, there are still issues related to its use including optimal volume, concentration of saline, frequency of administration and effective device. The use 3% saline is not recommended till all these are addressed by further studies [46].

### Inhaled furosemide

Use of furosemide as inhalation in acute bronchiolitis has been proposed as hypothesis that it may improve outcome by acting on airway smooth muscle, airway vessels, electrolytes and fluid transport across respiratory mucosa, and reducing airway inflammation.

One RCT studied the effect of inhaled furosemide in hospitalized infants with bronchiolitis, and recorded no significant clinical effects in these infants. Therefore, inhaled furosemide is not recommended in management of acute bronchiolitis [47].

### Steam inhalation

Steam inhalation has been proposed to improve airway clearance of mucus and outcome of acute bronchiolitis. Being less expensive and easily available, steam was considered to be a suitable intervention in low income countries.

A systematic review could identify only one RCT that compared role of nebulised salbutamol, nebulised saline and mist in a tent in children with acute bronchiolitis.

In view of limited experience with mist/ steam inhalation, more studies are required to prove or disprove role of steam inhalation in acute bronchiolitis [48].

### Anti-inflammatories

**Inhaled corticosteroids:** Two RCTs in infants with bronchiolitis

have demonstrated that inhaled corticosteroids have no effect on length of hospital stay, time to becoming asymptomatic or rate of respiratory readmission to hospital within 12 months [49].

A systematic review of 5 studies did not demonstrate an effect of ICS, given during the acute phase of bronchiolitis, in the prevention of recurrent wheezing following bronchiolitis [50].

An additional RCT involving 240 infants with RSV-related LRTI did not find any effect of inhaled corticosteroids on recurrent wheezing.

Therefore, inhaled corticosteroids are not recommended for treatment of acute bronchiolitis infants [50].

**Systemic corticosteroids:** Cochrane systematic review concluded that oral systemic corticosteroids did not reduce length of hospital stay in previously well infants less than 12 months of age with acute bronchiolitis [51].

A meta-analysis evaluating the use of systemic glucocorticoids (oral, intramuscular, or intravenous) and inhaled glucocorticoids for acute bronchiolitis in children (0 to 24 months of age) included 17 trials with 2596 patients. In pooled analyses, no significant differences were found in hospital admission rate, length of stay, clinical score after 12 hours, or hospital readmission rate. Hence, systemic corticosteroids in healthy infants and young children with a first episode of bronchiolitis are not recommended [52].

### Hospital based respiratory supportive care

**Supplemental oxygen:** The airway obstruction with poor distribution of ventilation and perfusion in bronchiolitis leads to hypoxemia. Humidified oxygen should be administered to hypoxemic infants with acute bronchiolitis. Humidified oxygen is mainstay of treatment for infants and children with bronchiolitis who have hypoxia [1,53].

Pulse oximetry is the most commonly used tool to decide about oxygen supplementation. Pulse oximetry is convenient method to assess the percentage of hemoglobin bound to oxygen in children [54].

The Supplemental oxygen is indicated if SpO<sub>2</sub> falls persistently below 90% in previously healthy infants. Oxygen may be discontinued if SpO<sub>2</sub> is at or above 90% and the infant is feeding well and has minimal respiratory distress [1]. Supplemental oxygen provided for infants not requiring additional respiratory supports is best initiated with nasal prongs, although exact measurement of fraction of inspired oxygen is unreliable with this method [55].

Use of humidified, heated, high flow nasal cannula to deliver air oxygen mixture provides assistance to infants with bronchiolitis through multiple proposed mechanisms [56]. There is evidence that high flow nasal cannula improves physiologic measures of respiratory effort and can generate continuous positive airway pressure in bronchiolitis [56].

As the child's clinical course improves, continuous measurement of SpO<sub>2</sub> is not routinely needed because it leads to unnecessarily prolonged oxygen supplementation and hospital stay [57,58].

**Cpap (continuous positive airway pressure):** The early intervention in form of continuous positive airway pressure in acute

severe bronchiolitis has been used to prevent mechanical ventilation.

Airway resistance in terminal airways is reduced with CPAP by recruitment of collapsed alveoli by opening terminal bronchioles and also there is decreased air trapping, hyperinflation and work of breathing [59].

Systematic review in 2011 on use of CPAP in acute bronchiolitis has shown that the evidence supporting the use of CPAP to reduce PCO<sub>2</sub> and respiratory distress in bronchiolitis, however that was of low methodological quality, and there was no conclusive evidence that CPAP reduced the need for intubation [60].

However, a recent RCT, comparing nasal CPAP and oxygen inhalation concluded that CPAP resulted in rapid reduction in work of breathing and improvement in the respiratory distress score at 6 hours. The improvement was proportional to the initial severity, suggesting that, early use of CPAP in severe forms of the disease may be beneficial [61].

Current evidence is inconclusive regarding routine use of CPAP in children with acute bronchiolitis and more studies with adequate numbers and better quality are required.

### Mechanical ventilation

The major indications for intubation and mechanical ventilation are as following: [62]

- Clinical deterioration (worsening respiratory distress, listlessness, and poor peripheral perfusion).
- Apnea
- Bradycardia
- Hypercarbia.

In a prospective cohort study done in children admitted with RSV LRTI, approximately 9% of patients required mechanical ventilation. The median duration of mechanical ventilation is relatively short, about 5 days, but protracted courses of ventilation may be required [62].

### Chest physiotherapy

Chest physiotherapy clears the excessive respiratory secretions, and thus helps to reduce airway resistance, the work of breathing, and enhances gas exchange.

A systematic review of nine randomized trials concluded that chest physiotherapy using vibration and percussion or passive expiratory techniques did not improve respiratory parameters, reduce supplemental oxygen requirement, or reduce length of hospital stay.

The use of chest physiotherapy is not recommended in children with bronchiolitis, because it may increase the distress and irritability of ill infants [63-65].

### Nasal suction

Saline nose drops and cleaning of nostrils by gentle suction may help to relieve nasal block. Instilling saline drops and cleaning nostrils by gentle suction before feeding may be helpful. Parents should be educated about instilling saline drops and cleaning secretions from nose before discharge from hospital.

Nasal suction should be used to clear secretions in infants hospitalized with bronchiolitis who exhibit respiratory distress due to nasal blockage [66].

### Surfactant

There may be secondary surfactant insufficiency in severe bronchiolitis that suggesting possible role of administration of exogenous surfactant [67]. A meta-analysis (included three RCTs with total 79 participants) evaluated the effect of exogenous surfactant in infants and children with bronchiolitis requiring mechanical ventilation [68].

The duration of mechanical ventilation and duration of ICU stay were significantly lower in the surfactant group compared to the control group. Use of surfactant had favorable effects on oxygenation and CO<sub>2</sub> elimination.

No adverse effects and no complications were observed. Current evidence suggests that surfactant therapy may have potential use in acute severe bronchiolitis requiring mechanical ventilation [68].

However, in view of few studies including small numbers of participants, reliable estimates of the effects of surfactant cannot be made.

There is a need for larger trials with adequate power and to establish beneficial role of administration of surfactant in infants with severe bronchiolitis.

### Heliox

Heliox (mixture of helium and oxygen) may improve alveolar ventilation as it flows through airways with less turbulence and resistance. This may reduce work of breathing and improve oxygenation in respiratory illness with moderate to severe airway obstruction including acute bronchiolitis.

A meta-analysis of four clinical trials, using heliox demonstrated that improved respiratory distress scores in first hour in children with moderate to severe acute bronchiolitis.

However, heliox inhalation did not affect need for intubation and mechanical ventilation and length of stay in pediatric intensive care unit. There was significant heterogeneity in the included studies. It is concluded that evidence for beneficial role of Heliox in acute bronchiolitis are inadequate and more experience is required [69].

### Conclusions

Acute bronchiolitis is one of the leading causes of lower respiratory tract infection in infancy.

The commonest etiological agent of acute bronchiolitis is respiratory syncytial virus.

The diagnosis of acute bronchiolitis is clinical and laboratory investigations a well as chest skiagram have a limited role in diagnosis and management.

The current main stay of management primarily consists of supportive care, including hydration, humidified supplemental oxygen, and mechanical ventilation when required.

Till now, there is no specific treatment for bronchiolitis is recommended. It may be appropriate to administer nebulized

salbutamol or epinephrine in a given child and continue these if found beneficial and discontinue if there is no effect.

Corticosteroids are ineffective and not recommended in management of acute bronchiolitis.

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