

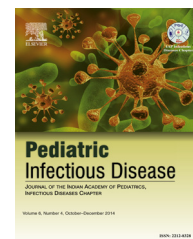


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Review Article

Bronchiolitis – Rationale for current recommendations for diagnosis and management

Sumitha Nayak*

Consultant Pediatrician, The Children's Clinic, Bangalore, India

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ABSTRACT

Bronchiolitis is a lower respiratory infection caused commonly by RSV in the initial 2 years of life. It is responsible for a large number of hospitalizations. Pulse oximetry plays an important role in monitoring the progression of disease. Supplemental oxygen administration is not recommended at saturation levels above 90%.

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1. Introduction

Bronchiolitis is a common pediatric ailment that occurs in children below the age of 2 years, often above 6 months of age. It is responsible for a large number of hospitalizations, that push up the resource utilization and medical costs considerably.¹ In 2006, the American Academy of Pediatrics had published a systematic review of the diagnosis and treatment of bronchiolitis, which was an attempt to standardize the diagnostic testing and medications that are used.² There has been a subsequent revision in the recommendations that have been published in 2014 by the American Academy of Pediatrics with a view to streamline the diagnosis and management and in turn reduce the economic burden due to this disease.

2. Etiopathogenesis

Bronchiolitis is a viral infection of the lower respiratory tract that is most often caused by the Respiratory Syncytial Virus (RSV) which accounts for 90% of the cases in the initial 2 years of life.³ Less commonly other viruses like human rhinovirus, human metapneumovirus, influenza, parainfluenza, adenovirus and coronavirus maybe responsible for the disease process.⁴ According to Denny et al., the most severe cases occurred below the age of 6 months and these were associated with a high morbidity and mortality.⁵ A large number of cases are presumed to be of unknown etiology, as there is no organism isolated. However, the data studies done by Denney et al. showed that these cases were referable to RSV infections.

* Tel.: +91 80 23416201.

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The viral infection is characterized by acute inflammation, edema and necrosis of the epithelial cells lining the small airways and associated with increased mucus production and bronchospasm.^{2,4} These changes are responsible for the symptoms and signs associated with bronchiolitis.

3. Economic burden of disease

The number of hospitalizations due to bronchiolitis is excessively high. Data collected from 1980 to 1996 from the National Hospital Discharge Survey had shown an increase in acute bronchiolitis hospitalizations rates of 152% among infants aged 1 year and 77% among those aged 4 years.⁶ According to Pelletier et al., bronchiolitis hospitalizations are responsible for a staggering expense of \$543 million annually. This is a huge burden on the existing healthcare resources. Leader and Kohlhasse have estimated that between 1997 and 2000 there were 718,008 ED visits by infants for lower respiratory infections that were subsequently diagnosed as bronchiolitis.⁷ Of these 29% of the cases were admitted and the total cost of hospitalization amounted to over \$2.6 billion.

4. Symptoms and signs

Bronchiolitis is recognized as a constellation of signs and symptoms which aid in the diagnosis of the disease. It usually begins as a viral upper respiratory infection which leads on to increased respiratory effort and wheezing in children below 2 years of age.^{2,4} The respiratory rate is high which is related to the infant's age. At 6 months the normal respiratory rate should be 40 min⁻¹ and reduce to 30 min⁻¹ by 12 months. This should be counted for 1 min before concluding the presence of distress.² According to the 2014 AAP guidelines, the respiratory rate above 70 min⁻¹ is considered to be suggestive of tachypnea.⁴ The absence of tachypnea rules out the risk of significant or severe viral or bacterial lower respiratory infection, but the presence of tachypnea does not help to distinguish between viral or bacterial infections.⁴ The current recommendations strongly suggest that bronchiolitis must be diagnosed by clinicians based on the history and physical examination of the patient.⁴

The course of the disease is dynamic and could vary from time to time. Hence the infant must be continuously monitored for improvement as well as sudden deterioration in the condition. Transient apnea may be found to occur periodically but may progress to respiratory distress due to the lower airway obstruction.⁴ Underlying morbidities and factors may cause the rapid progression and deterioration in the infant's condition. Prematurity, underlying cardiac and chronic pulmonary disease, immunodeficiency and previous episodes of wheezing may result in hemodynamic instability. Congenital cardiac anomalies, bronchopulmonary dysplasia, congenital anomalies and in utero exposure to smoke could all compromise the status and worsen the presentation of the condition. Genetic abnormalities are associated with more severe episodes of bronchiolitis.⁸ Prematurity is particularly associated with severe RSV infections, and the more premature infants have higher degree of risk of hospitalization

compared with the late preterms.⁹ The underlying anomalies must be assessed by the clinician while evaluating and managing a case of bronchiolitis. This recommendation by the AAP is of moderate strength and improves the ability to predict the course of illness, and possibly avoid unnecessary hospitalization.⁴

Hypoxemia may be associated with the tachypnea that develops in bronchiolitis. According to the study by Rajesh et al., tachypnea is a good predictor of hypoxia in infants under the age of 2 months.¹⁰ Pulse oximetry is a useful method of detecting the falling level of oxygen saturation which may be missed out during the physical assessments.⁴ A case control study was done by Al-Janabi et al. to identify the predictors of hypoxemia in acute lower respiratory tract infection in children.¹¹ They found a significant association between the presence of tachypnea and hypoxemia, and concluded that pulse oximetry is desirable for accurately identifying hypoxemia. However, some studies have not validated the effectiveness of pulse oximetry in predicting the clinical outcomes. The study on Gambian infants reported by Usen et al., reiterates that simple physical signs can be picked up with minimum expertise and can be used as a guide for oxygen therapy.¹² The current AAP guidelines provide a weak recommendation that clinicians need not use continuous pulse oximetry for infants and children with a diagnosis of bronchiolitis. While this recommendation may decrease the length of stay in hospital as well as reduce minor adverse effects like alarm fatigue, it will certainly reduce the hospitalization costs. However, the importance of pulse oximetry cannot be negated, as it is a convenient and relatively easy method to assess the percentage of hemoglobin bound to oxygen provided it is not considered a proxy for respiratory distress. The accuracy of pulse oximetry drops at ranges between 76% and 90%.⁴ But it is at these levels that a small increase in arterial pulse pressure is associated with a significant improvement in pulse oxygen saturation. However, no data exists regarding the improvement in patient symptoms, physiologic function or clinical outcomes associated with this increase in saturation. Hence the use of pulse oximetry for monitoring the children with bronchiolitis would be at the clinician's discretion.⁴ As has been mentioned by Al-Janabi et al., pulse oximetry is the best indicator of hypoxemia in children and although relatively expensive, its use may be cost effective in controlling the oxygen requirements.¹⁰

5. Investigations

The diagnosis of bronchiolitis is usually based on clinical symptoms and signs, wherein the infant has tachypnea with minimal or no signs on auscultation of the chest. The upper airway obstruction is predominantly responsible for the work of breathing.⁴ The current AAP guidelines, which is of moderate strength, does not support the need for chest radiography as a routine for all those suspected to be cases of bronchiolitis.⁴ Some studies have shown that those infants who had initial radiography would be more likely to receive antibiotics than others, yet did not demonstrate any significant difference in the outcomes.¹³ According to the guidelines, the initial radiography must be restricted to those cases where

in the tachypnea at presentation is severe enough to warrant admission directly into the ICU or where there is suspected to be the possibility of complications like pneumothorax that would require aggressive management.⁴

Testing for virus type that is responsible for the infection may be of significance in areas where there is routine seasonal anti-RSV prophylaxis being administered. Large studies have shown almost 60–75% positivity for RSV infections. Leader et al. did a retrospective analysis of data collected between 1997 and 2000 which showed that at least 22.8/1000 visits to the ED by infants for lower respiratory infection was attributable to RSV infections and RSV bronchiolitis was the leading cause of hospitalizations.⁷ Müller-Pebody et al. reviewed data of hospital admissions for lower respiratory tract infections between 1995 and 1998 and found that the annual incidence of hospital admissions attributable to RSV is 28.3/1000 children below 1 year and 1.3/1000 children between 1 and 4 years of age, while 76.8% of the cases had no specific organism isolated.¹⁴ Denny et al. suggest that a large number of cases where in no organism is isolated could be caused by RSV infections including all season infections caused by RSV which could further confound the diagnosis.⁵ The human rhinovirus causes bronchiolitis that is associated with a shorter course and could cause prolonged viral shedding.⁴ The accurate identification of the virus does not alter the course of treatment nor the outcomes, and hence routine viral testing is not recommended.⁴ In children receiving monthly palivizumab prophylaxis, in case a breakthrough RSV is confirmed, the recommendation is to discontinue the prophylaxis as the second RSV infection is highly unlikely during the same year.⁴

6. Treatment

Oxygen administration has been found to improve the saturation at levels below 90%. However, at levels above 90% it takes a very large elevation in arterial partial pressure to further increase the saturation.⁴ Hence a weak recommendation has been given out that clinicians may choose not to administer supplemental oxygen if the oxyhemoglobin saturation exceeds 90% in infants and children with bronchiolitis. The administration of high flow oxygen by nasal cannula is being increasingly recommended as the preferred mode of oxygen administration specifically for children with bronchiolitis of moderate to severe intensity.¹⁵ High flow nasal cannulas (HFNC) are designed in such a way as to deliver a mixture of air and oxygen that is heated and humidified, at a flow that is higher than the patient's inspiratory flow. Studies have shown that the HFNC is useful to overcome obstructive apnea, prevent pharyngeal collapse and provide inspiratory support, besides specific usage in bronchiolitis where it could decrease the electrical activity of the diaphragm, and decrease the esophageal pressure swings, all of which reduce the work of breathing.¹⁵ It decreases the work of breathing as has been shown by various studies.^{4,15} HFNC is feasible and well tolerated and has been shown to produce good results especially in cases of moderate intensity where there may be no room for CPAP/NIV treatment modalities.¹⁵ A large study performed in Australia has shown a significant decline in rates of intubation in infants diagnosed as bronchiolitis, with

reduction from 37% to 7% of cases.¹⁶ A randomized trial was conducted by Campaña et al. in two urban secondary pediatric hospitalization units to estimate the extent of benefit that could be derived in patients of bronchiolitis with the use of high frequency humidified nasal cannula oxygen therapy.¹⁷ The reports of this study did not show any beneficial value of using humidified oxygen by nasal cannula as compared to the use of hypertonic saline in terms of decreased severity or improved comfort levels. Despite this, HFNC continues to be popular therapy in infants with bronchiolitis and has been proven to be useful in reducing the requirement of intubation as well as being a well-tolerated non-invasive form of respiratory support.¹⁷

There has been a perception since a long time that bronchiolitis required the use of bronchodilators in order to improve the oxygen saturation and decrease the respiratory distress associated with the illness. According to the current guidelines, there is a strong recommendation that bronchodilators like salbutamol must not be administered to infants with bronchiolitis.⁴ This recommendation is based on the reports of several studies and reviews that did not show any benefits from the use of β -adrenergic agents in terms of improvement in disease resolution, need for hospitalization or the length of stay. Studies by Eber have also not shown any benefits, and the potential adverse effects in terms of tachypnea and the cost of these agents outweighs any possible benefit.¹⁸ Cochrane Database Systemic Reviews of trials that evaluated the role of bronchodilators in bronchiolitis have not shown any improvement in oxygen saturation or decreased the length of hospitalization.¹⁹

The AAP guideline provides a strong recommendation against the use of epinephrine in cases of bronchiolitis.⁴ Studies have been done to compare the effectiveness of epinephrine versus salbutamol in decreasing the inpatient outcomes and the length of hospitalization.²⁰ There has been no improvements found in either of these parameters. A randomized controlled trial has been reported by Wainwright et al. on the role of nebulized epinephrine in acute bronchiolitis.²¹ There was no reduction in the length of hospital stay or in the time till discharge in these infants. The only possible role of epinephrine could be as a rescue agent in cases of severe bronchiolitis, but in the absence of any formal study, there is no definite recommendation for its use.⁴ Another strong recommendation that has been placed is that systemic corticosteroids have no role in the management of acute viral bronchiolitis.⁴ This is based on the lack of beneficial effects and the possibility that the corticosteroid may increase the duration of viral shedding. Earlier studies had shown a role of steroids in accelerating the clinical recovery in children hospitalized for acute RSV bronchiolitis.²² Several further studies have evaluated the role of corticosteroids given via the nebulized route, orally and parenterally, but did not draw any conclusive evidence regarding the utility of corticosteroids during the acute phase or in the follow up of bronchiolitis infection.²³ A large study that was rigidly designed and executed by Cade et al. failed to show any benefits from the administration of nebulized budesonide, which could have been due to poor drug deposition in the lungs that occurred due to the tachypnea, gas trapping and increased secretions that are all associated with bronchiolitis.²³

The role of nebulized hypertonic saline is slightly controversial, as the guidelines suggest a moderately strong recommendation against its use in the ER, while a weak recommendation has been given for its use in hospitalized patients.⁴ A study was done by Mandelberg et al. to determine the usefulness of nebulized hypertonic saline in children admitted for viral bronchiolitis.²⁴ This study has reported benefits of using nebulized 3% saline in hospitalized patients, which decreased the symptoms as well as length of hospitalization. A 2 year follow up of this study was reported by Tal et al. which pooled and analyzed the 2 year data and reported that 3% hypertonic saline is an active drug in viral bronchiolitis and is an effective therapeutic modality.²⁵ In combination with 1.5 mg epinephrine nebulizations, these authors found good results in hospitalized as well as ambulatory patients. Cochrane database studies have favored the use of nebulized hypertonic saline as compared to normal saline in the treatment of acute bronchiolitis, with reduction of hospitalization duration as well as improved severity score.²⁶ There is a strong recommendation against the use of antibacterial agents in patients diagnosed to have viral bronchiolitis, unless there is evidence of a concomitant bacterial infection.⁴

Chest physiotherapy is used as a modality of treatment in several chronic respiratory diseases, wherein there is increased airway hypersecretions. A randomized controlled study was performed in seven pediatric departments by Gajdos et al. which included infants ranging from 15 days to 24 months who were admitted for the first episode of wheezing that was diagnosed as acute bronchiolitis.²⁷ It was found that there was no difference in the recovery between the group that received physiotherapy and the control group that had only nasal suction performed. Another study by Postiaux et al. reported a new technique of performing chest physiotherapy that consists of 15 prolonged slow expirations followed by 5 provoked cough manoeuvres.²⁸ The results were encouraging and there was some short term benefits found to some of the respiratory symptoms. These maneuvers possibly aid the mucus drainage which assists in improvements in symptoms. Cochrane database reviews report several studies that have compared physiotherapy with no intervention.²⁹ The results are negative for chest physiotherapy that included vibration and percussion techniques as well as passive expiratory techniques. Another report by Bohé et al. has evaluated the outcome of conventional chest physiotherapy and not found any significant benefits in the treatment of acute bronchiolitis.³⁰ The current guidelines from AAP is a moderately strong one that does not recommend the use of chest physiotherapy in infants diagnosed with bronchiolitis.⁴

While concentrating on symptom reduction and making the patient comfortable and disease free at the earliest, it is essential to ensure that the hydration and nutritional requirements are adequately addressed. The need for intravenous or nasogastric fluids in those unable to maintain adequate hydration is strongly recommended. According to Verma et al., the supportive care remains the cornerstone of management of infants with bronchiolitis.³¹ Conventionally IV fluids are recommended for use, as the chances of aspiration are lower and there is no interference with breathing.³² However, with prolonged usage, there may be a negative catabolic state due to calorie denial, and hence many countries

prefer to use nasogastric feeds for better nutritional status. The NG feeds may be administered continuously in cases of major respiratory distress or as bolus therapy and recent randomized studies have not shown any differences in the outcomes.³² IV fluids may be preferred when there is moderate to severe respiratory difficulty with marked tachypnea, apnea episodes or marked tiring out during feeding.³³ Another suggested indication for the use of IV fluids is if the patient vomits or is unable to accept the oral feeds, then sufficient fluids must be administered to prevent dehydration.³⁴ The role of palivizumab has been recommended for the first year of life for high risk infants with significant heart disease or chronic lung disease of prematurity who are below 32 weeks 0 days gestation and require >21% oxygen for the first 28 days of life.⁴ It is not recommended for administration to otherwise healthy infants who are over 29 weeks 0 days gestational age.

Conflicts of interest

The author has none to declare.

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