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Obstructive Airway Diseases –I: Bronchiolitis

Chugh K.*

Gupta N. D.**

BRONCHIOLITIS

Epidemiology and Etiology

Acute bronchiolitis is the most frequent and severe respiratory system syndrome involving children <2 years of age, with the peak incidence occurring at <12 months of age. Bronchiolitis is a seasonal disease with an epidemic pattern, with increase in prevalence during the fall and winter. It often coincides with the viral epidemics of respiratory infection.

The hallmark of the disease is bronchiolar inflammation and obstruction.

A wide range of agents (parainfluenza, adenovirus, influenza, Mycoplasma pneumoniae, rhinovirus, Chlamydia pneumoniae, human metapneumovirus, and coronavirus) may cause Bronchiolitis; however, RSV (with its A and B subtypes) is by far the most frequently involved agent.

Environmental and genetic factors contribute to disease severity. Passive tobacco exposure increases hospitalization risk in bronchiolitis .

Clinical profile

Typically, it begins with initial symptoms of an upper airway viral infection, such as fever and coryza. Children have abundant rhinorrhea and cough, along with poor food intake (4-6 days after symptoms start). The degree of fever in infants depends on the infecting organism. Children experiencing bronchiolitis caused by RSV are frequently febrile by the time of consultation (>38.5°C, in 50% of patients), and those with influenza or parainfluenza usually have a fever >39°C.

Within 4-6 days, the lower respiratory tract is involved, with clinical signs of cough, tachypnea, hyperinflation, chest retractions, widespread crackles, and wheezing. Children <6 months old are at increased risk for developing severe bronchiolitis disease. Physical examination may reveal audible wheezing, crackles, or rhonchi (apical ventilatory pattern), and a prolonged expiratory phase. Other common findings are conjunctivitis, acute otitis, and rhinitis. Many infants have a distended abdomen.

Wood and Downe had devised a scoring system for grading the severity of Bronchiolitis which is a useful tool to monitor disease course as well as therapy (See Table 1). [(1)]

The risk factors for clinical worsening of acute bronchiolitis include the following:

1. Initial presentation**:** Tachypnea (RR >60-80 bpm or retractions), Hypoxia (SaO_2 90%-95%),Feeding difficulty or dehydration
2. Age: <12 months (the younger the child, larger the risk).
3. Comorbidities: Bronchopulmonary dysplasia, Congenital heart disease

   Cystic fibrosis, Immunodeficiency.
4. Prematurity: Gestation age <36 weeks
5. Others: Malnutrition, Poverty, Overcrowding, Parents and/or family members who smoke ,Genetic RSV infection predisposition

LABORATORY INVESTIGATIONS

A mild leukocytosis with a normal differential is frequently found in infants

Auther's Affilation: *+**Centre for Child Health, Sir Gangaram Hospital, Rajendra Nagar, New Delhi.

Reprint's Request: Dr. Chugh K, Centre for Child Health, Sir Gangaram Hospital, Rajendra Nagar, New Delhi.

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experiencing bronchiolitis. Hypoxia is detected by pulse oximetry or arterial blood gases. CO_2 retention may be seen in severe cases.

Viruses may be detected from nasal samples by indirect fluorescence antibody detection, PCR, radioimmunoassay, or direct culture.

Chest x-rays often show nonspecific findings, including hyperinflation, gross infiltrates that are typically migratory and attributable to postobstructive atelectasis, and peribronchial filling. Bronchiolitis is not an alveolar space disease and, when a true alveolar infiltrate is seen, secondary bacterial pneumonia should be suspected.

Table 1: Wood-Downes Score: Used to evaluate and grade bronchiolitis severity

Score*	Wheezing	Retraction	RR	HR	Ventilation	Cyanosis
0	No	No	<30	<120	Good symmetrical	No
1	End expiratory	Subcostal/intercostals	31-45	>120	Regular symmetrical	Yes
2	All expiration	Supraclavicular+ nasal flaring	40-60		Very reduced	
3	Inspiration and expiration	+Intercostal+ suprasternal			Silent thorax	

*The highest scores from each column are summed to attain the total severity score: 1-3, mild; 4-7, moderate; 8-14, severe

TREATMENT

Clinical judgment remains the gold-standard criterion for hospital admission and cannot be replaced by objective criterion.

Arterial O_2 saturation (SaO_2) is the most consistent clinical predictor of a worsening clinical condition (the cut-off point ranging from 90% to 95%).

Most severe disease are found in patients with SaO_2 <95%, prematurity (<34 weeks of gestational age), congenital heart disease, neurologic disease, RR >70 bpm, pulmonary atelectasis, sick or toxic appearance, and age <3 months.

The single best predictor of a more severe total disease course is arterial saturation of <95% on pulse oximetry[1].Generally, the predictors of the need for intensive care are RR>80 bpm and hypoxia with SaO_2 <85%[2].

HYDRATION AND OXYGENATION

Adequate hydration and oxygenation are the backbone of bronchiolitis treatment. IV fluids and O_2 support is essential, when feeding is not tolerated. Supplemental O_2, is the single most useful therapy. SaO_2 should be kept over 92%[3]. Careful monitoring, mainly among the more sick and high-risk children, is important, as more aggressive ventilatory support may be required (mask, nasopharyngeal continuous positive airway pressure ventilation, or even endotracheal ventilation), and the timely introduction of ventilatory support is important to prevent further complications

BETA-2 AGONISTS

Still has no scientifically defined recommendation. If clinical improvement does not immediately occur or if worsening is observed after 60 mins of inhalation, beta-2 agonists should be discontinued. As beta-2 agonists help to relieve bronchoconstriction, the degree of their effectiveness can be expected to be directly related to the contribution of bronchoconstriction to wheezing (i.e., the greater the contribution, the more effective the agonists). Bronchodilator treatment is more effective when administered early.[4]

RACEMIC EPINEPHRINE

Racemic epinephrine 2.25% and L-epinephrine 0.1% are used at 0.1 mg/kg and 0.05 mg/kg, respectively, every 4 hrs. This treatment should only be used in the hospital setting with clinical, heart rate, and electrocardiographic monitoring. As a rebound effect may occur, the child should be observed for at least 1-2 hrs following cessation of treatment and a decision to discharge prematurely should be avoided.

In a study conducted in centre for child health, SGRH, New Delhi 14 were admitted in the salbutamol group as against 10 in the adrenaline group, study showed good efficacy with adrenaline being better than salbutamol in preventing hospital admission rates.(unpublished data)

INHALED AND SYSTEMIC STEROIDS

The use of inhaled and systemic steroids is also a controversial therapy, as these agents may produce little or no response at all.[5]

AEROSOLIZED RECOMBINANT HUMAN DNASE

Mucus in patients with cystic fibrosis, bronchiectasias, and RSV bronchiolitis was shown to contain significant extracellular DNA from degenerated leukocytes and epithelial debris (6). DNA increased pulmonary secretion viscosity and adhesiveness, hence DNAse has been tried in bronchiolitis and results have not been very encouraging. DNAse may also be effective in infections complicated by atelectasis, bronchial secretions, and mucous plugs that have high DNA concentration.

RIBAVIRIN

Ribavirin is an antiviral drug that inhibits the structural protein synthesis of the virus, reducing viral replication and immunoglobulin (Ig) E response. Following the initial excitement regarding this drug, problematic issues arose related to its high cost, logistic issues, has to be given as continous aerosol over several hours, possible teratogenesis, and low clinical efficacy. It has to be given as continous aerosol over several hours. A Cochrane review found no conclusive evidence that ribavirin use is beneficial for bronchiolitis due to RSV[7].

ANTIBIOTICS

Antibiotics have no benefit in treating RSV but are important in treating secondary bacterial infection, such as Streptococcus and Staphylococcus, which can occur following initial RSV infection.[5]

OTHER MEASURES

Heliox

The helium-oxygen mixture (heliox) reduces the work of breathing and expiratory wheezing in children with obstructive disease . It is recommended that its use should be restricted to the intensive care setting. However it has not been found to be clinically beneficial.

Respiratory Physiotherapy

In a systematic review, the recommended techniques for children with bronchiolitis are based on positioning therapy, alveolar

recruitment and expiratory airflow increase using hand vibration[8]. Due to copious airway secretions in RSV, airway suctioning is an effective measure for tracheobronchial hygiene. Approximately 60% of respiratory resistance is in the upper airways, and as infants predominantly breathe through the nose, the clearance of these secretions may have a positive impact on work of breathing and relieve symptoms.

Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation (ECMO) is an option for severely ill children who cannot be supported by conventional mechanical ventilation due to their ventilation and cardiocirculatory condition. While use of ECMO for RSV is infrequent, good survival has been obtained, even with prolonged durations of this support while the patient is awaiting lung recovery[9].

Inhaled Nitric Oxide

Nitric oxide used in the treatment of children severely infected with RSV improved oxygenation and respiratory system resistance.[10] The use of this therapy should be reserved for patients with severe hypoxemia, refractory to ventilatory support.

Exogenous Surfactant

Children with bronchiolitis infected by RSV have surfactant deficiency. The use of exogenous surfactant as potential treatment for bronchiolitis patients was evaluated, and the results suggest that surfactant has an important role on small-airway patency as well as on pulmonary compliance; however, its use is restricted to patients in the ICU.[11]

Conventional Mechanical Pulmonary Ventilation

Conventional mechanical ventilation, using pressure-control ventilation mode, is indicated in those children with either obstructive or restrictive hypoxemic disease; however, a mixed mode (pressure regulated, volume controlled) can also be chosen. Due to the possibility of intrinsic positive end-expiratory pressure (PEEP), efforts should be focused on maintaining a low RR (20 bpm) and an inspiratory:expiratory ratio of 1:3. Additionally, the initial PEEP should be ~5 cm H_2O, with adjustments being made according to the degree of alveolar recruitment and clinical response.

High-frequency Oscillation Ventilation

High-frequency oscillation ventilation is indicated for those patients whose condition continues to worsen despite conventional mechanical ventilation or for those with significant air leak (pneumothorax, interstitial emphysema, pneumopericardium). It is also indicated for patients with restrictive disease, with an oxygenation index >13 at some centers. The main advantage of this therapy is the possibility of optimizing ventilation and oxygenation with a lower risk of pulmonary injury induced by mechanical ventilation.

Noninvasive Positive-pressure Ventilation

Noninvasive positive-pressure ventilation use in bronchiolitis children keeps airways open, improves respiratory flow, maintains functional residual capacity, improves pulmonary compliance, facilitates secretion mobilization, reduces work of breathing, improves gas exchange, and preserves surfactant synthesis and release. This therapy is indicated as first-choice ventilatory support in children who are experiencing apnea episodes and for preventing the use of invasive mechanical ventilation. This noninvasive support can be performed using continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) ventilatory mode. New modes of high-flow nasal cannula therapy with devices such as Vapotherm may also be advantageous in some patients. When CPAP is chosen, it is recommended to start with 4-6 cm H_2O; if BiPAP is chosen, it is recommended to begin with an inspiratory pressure of 8 cm H_2O and expiratory positive airway pressure of 4 cm H_2O. Noninvasive positive-pressure ventilation parameter changes should be titrated to the child's clinical response.

PROPHYLAXIS

Preventing RSV infection in young infants, mostly in those at high risk, is clearly the best

strategy. Two measures are availble for preventing RSV infection: use of vaccines (active immunization) and parenteral immunoglobulins. Efforts to obtain an effective vaccine have not yet yielded positive results. Passive immunization against RSV may be made with monoclonal antibodies (palivizumab, approved by the US Food and Drug Administration in 1998). Once per month during the epidemic months, an intramuscular dose of 15 mg/kg should be administered. Premature infants with chronic pulmonary disease benefit more from palivizumab, its use is indicated in children with congenital heart disease and significant hemodynamic impairment[12].

PROGNOSIS

Most children with bronchiolitis, regardless of severity, recover without sequelae. The natural course of the disease usually ranges from 7 to 10 days; however, some children remain ill for weeks. More than half of bronchiolitis patients have recurring episodes of wheezing till 7-11 years of age ref. Children predisposed to asthma may wheeze more when infected by RSV or another allergic stimulus.

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