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Clinical Guideline

Clinical Guidelines on the Management of Acute Bronchiolitis

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Disclaimer

These guidelines have been developed by the Hong Kong College of Paediatricians and the authors, according to the state of medical knowledge at the time of compilation. These guidelines are for **general guidance only** and are designed **to provide information to assist decision-making**. Paediatricians should use their up-to-date medical knowledge, clinical data of the patients and their own clinical judgement in applying the recommendations in this document to the management of individual patients.

Explanatory Notes on Level of Evidence and Grading System on Recommendation

The definition of types of evidence and grading recommendations originate from the US Agency for Health Care Policy and Research (AHCPR) and are also recommended and used by the Royal College of Paediatrics and Child Health.

Levels of evidence

Level	*Type of evidence (based on AHCPR 1992)*
Ia	Evidence obtained from meta-analysis of randomised controlled trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomisation
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grading of recommendations

Grade	*Type of recommendation (based on AHCPR 1994)*
A (Levels Ia, Ib)	Requires at least one randomised control trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation
B (Levels IIa, IIb, III)	Requires availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation
C (Level IV)	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality

Evidence is graded upon the methodological qualities. Guidelines normally contain many different recommendation based upon different levels of evidence. It is important that users are aware of the level of evidence on which each guideline recommendation is based. The link between guideline recommendation and the supporting evidence should be made explicit. Separating the strength of the recommendation from the level of evidence helps in situations where extrapolation is required to take the evidence of a methodologically strong study and apply it to the target population. Gradings of recommendation in addition to level of evidence allow more flexibility for future revision. However, it is important to emphasis that the grading does not relate to the importance of the recommendation.

Introduction

Acute bronchiolitis is one of the most common lower respiratory infections suffered by infants. Studies have shown the local epidemiology is very much similar to that of the rest of the world. The present guideline aims to summarise the current evidence on the diagnosis and treatment of the condition, resulting in recommendations that are practicable both in the office and the hospital.

Definition of Bronchiolitis for This Guideline[1]

A. Age of 24 months or less
B. Expiratory wheezing of acute onset
C. Signs of viral respiratory illness such as coryza, otitis media, or fever

A review of the case definitions and inclusion criteria used in epidemiological studies and clinical trials revealed that many studies simply stated that infants with signs and symptoms consistent with bronchiolitis were eligible for inclusion. In others with more details, 43 trials used tachypnoea in the case definition or inclusion criteria; 42 used wheezing; 37 used oxygen saturation; and 32 used retractions.[1] Notable differences of diagnostic criteria for bronchiolitis do exist among different studies. In America for example the term bronchiolitis seems to include a much wider range of illnesses. The North Carolina group whose epidemiological studies have been widely cited defined bronchiolitis as expiratory wheezing with or without tachypnoea, air trapping, and substernal retractions.[2] The Rochester group had more restrictive diagnostic criteria: 1) expiratory wheezing of acute onset, 2) an age of 24 months or less, 3) signs of viral respiratory illness such as coryza, otitis media, or fever, 4) the first such episode, and 5) the presence or absence of indications of respiratory distress, pneumonia, or atopy.[3] In U.K. or Australia the definition of bronchiolitis is generally even more restrictive. Studies of bronchiolitis have usually included only babies less than one year or 9 months.[4,5] Some included only babies who had fine crepitations on physical examination.[5]

It is important to note that eligibility criteria in the clinical trials varied, especially with respect to criteria such as age, duration of symptoms, co-morbidities (e.g. prematurity and chronic lung disease), history of previous wheezing, and severity of disease. Specific study objectives determined most of these variations (e.g. some studies included only infants with first episode of wheeze with proven RSV infection, others included children with recurrent wheezing associated with any respiratory infection). Special attention should be given to the differential diagnoses between asthma and acute bronchiolitis during the appraisal of therapeutic trials, especially in infants, as the two conditions may bear many similarities in their presentation.

Aetiology and Epidemiology

As in Western countries, respiratory syncytial virus (RSV) is the commonest cause of acute bronchiolitis in Hong Kong. Other aetiological agents include parainfluenza and influenza viruses, adenoviruses, and mycoplasma pneumoniae. There are seasonal variations of incidence with a peak in the summer months, contrasting with winter outbreaks in Western countries.[6]

Clinical Features and Diagnosis[3,7-10] *(Level of evidence IV)*

Diagnosis is based on clinical features:

A. Symptoms
   1) Affected infants are aged up to 24 months, with the majority less than 12 months
   2) Fever is usually present, may be up to 41°C
   3) Symptoms of viral infection: rhinorrhoea and cough followed by onset of rapid respiration, chest retraction and wheezing in next few days
   4) Feeding difficulties due to dyspnoea may be present
   5) Central cyanosis or apnoea may occur in more severe cases

B. Physical findings
   1) Tachycardia
   2) Tachypnoea
   3) Respiratory distress: Subcostal, intercostal, suprasternal and supraclavicular insucking
   4) Prolonged expiration
   5) Fine inspiratory crackles
   6) High pitch expiratory wheeze in all lung fields
   7) Mild conjunctivitis, otitis media, or pharyngitis may be present

Investigations

A. Chest radiograph is indicated in: ***(Level of evidence III)***
   1) patient for whom intensive care is contemplated
   2) patient with unexpected clinical deterioration
   3) patient with underlying respiratory or cardiac disease

   Chest radiographs may be useful in predicting which patients are likely to have more severe disease.[11]

B. Haematological and biochemical investigations are not routinely indicated.[12] It may be useful for the assessment of the general status of the patient. ***(Level of evidence III)***

C. Pulse oximetry is useful in assessing the severity.[13] ***(Level of evidence IV)***

D. Blood gas analysis should be performed if the patient has.[13] ***(Level of evidence IV)***
   1) severe respiratory distress
   2) signs of exhaustion
   3) hypoxia

Factors Associated with Severe Disease[14-23] *(Level of evidence III)*

A. Premature infants (birth at gestation age less than 36 weeks)
B. Patients with broncho-pulmonary dysplasia, congenital heart disease, immunodeficiency, recurrent aspiration pneumonia, tracheoesophageal fistula, cystic fibrosis, neurological and genetic disorders
C. Infants aged less than 6 weeks at presentation
D. Infants exposed to high levels of particulate air pollution
E. Infants having environmental tobacco smoke exposure

Indications for Hospital Admission[13] *(Level of evidence IV)*

A. Clinical signs of significant respiratory distress or exhaustion
B. Apnoea
C. Inability to feed
D. Special social circumstances
E. Hypoxaemia
F. Patients with underlying medical conditions

Indications for Admission to Paediatric Intensive Care Unit (PICU) [24] *(Level of evidence IV)*

A. Worsening respiratory distress
B. Increasing oxygen requirement
C. Apnoea
D. Poor perfusion
E. Bradycardia
F. Disturbed conscious level

Management

A. Supportive measures
   1) Monitoring[10] ***(Level of evidence IV)***
      Cardio-respiratory monitoring for inpatients
      Pulse oximetry may be indicated for inpatients
   2) Oxygen ***(Level of evidence IV)***
      Give warmed, humidified oxygen to correct or prevent hypoxaemia.[10,25]
   3) Fluid management
      Care must be taken to prevent fluid overload.[26,27] ***(Level of evidence IV)***
      Intravenous fluid may also be required in infants with severe respiratory distress to avoid vomiting and aspiration.[28] ***(Level of evidence IV)***

B. Bronchodilators
   1) Salbutamol
      There is currently no evidence to support the routine use of salbutamol but a trial followed by assessment of the effect may be considered since there is conflicting evidence on its efficacy (Grade A).

      Conclusions from four recent meta-analyses on the use of bronchodilators in bronchiolitis are not completely consistent, as each evaluated a somewhat different group of studies. Two of the meta-analyses concluded that bronchodilators are safe and efficacious in a subset of RSV patients; however, no known criteria exist to prospectively identify that subset.[29,30] Two other meta-analyses concluded that there is no compelling evidence to use broncho-dilators at all in the treatment of RSV infections.[31,32]

   2) Ipratropium
      The use of ipratropium is not recommended (Grade A).

      There is currently no evidence to document the efficacy of this medication.

3) Adrenaline

There is insufficient evidence to support the use of adrenaline for the treatment of bronchiolitis among inpatients. There is some evidence to suggest that adrenaline may be favourable to salbutamol and placebo among outpatients but only short-term effects were studied. Therefore routine use of nebulised adrenaline is not currently recommended. But a trial followed by assessment may be considered in the outpatient setting. (Grade A)

Nebulised adrenaline has been suggested in a meta-analysis that consists mainly of small-scale studies to improve clinical status and airway resistance in acute bronchiolitis.[29] Two studies also showed lower hospital admission and earlier discharge with adrenaline.[30] Subsequent to this meta-analysis, three further studies have been published and did not support the positive effects seen with adrenaline.[33-35] The study by Wainwright et al.[35] in particular, adopting a randomised, double-blinded, placebo-controlled design with meticulous methodology demonstrated that nobulised adrenaline had no significant advantage over placebo in terms of clinical status and hospital stay. In 4 inpatient studies comparing adrenaline with salbutamol,[33,36-38] only one of the seven outcomes was statistically significant: respiratory rate at 30 minutes favoured adrenaline.

A recently published Cochrane systemic review has shown improvement in some of the short term clinical outcomes favouring use of adrenaline in outpatient settings.[39] Among these outpatient studies, change in oxygen saturation at 60 minutes, heart rate at 90 minutes, respiratory rate at 60 minutes post-treatment and "improvement" (OR 4.51; 1.93, 10.53) favoured adrenaline. Admission rates were not significantly different.

C. Steroid

Results from various studies on the use of systemic steroid in bronchiolitis are controversial. The evidence of its use in different clinical settings are as follows:

1) Outpatient

Use of systemic steroid in patients with acute bronchiolitis may be considered but total course should not be given for more than 5 days. (Grade A)

Three recent RCTs which were carried out in the emergency department have shown that systemic steroid was beneficial in the treatment of acute bronchiolitis by reducing severity of clinical signs, duration of clinical symptoms and hospitalisation rate.[40-42] ***(Level Ib)*** However, more studies should be done to clarify the dosage, safety and efficacy.

2) Inpatient

Systemic steroid should not be routinely prescribed for inpatients with bronchiolitis in view of the conflicting results from the scientific studies. (Grade A)

A meta-analysis and 3 other RCTs not included in the meta-analysis were performed on hospitalised patients. Improvement in the clinical outcomes including severity and duration of symptoms, length of hospital stay, need for additional asthma medications after the use of steroid was found in the meta-analysis[43] and one RCT.[44] ***(Level of evidence Ia and Ib)*** But the two RCTs failed to document any benefit.[45,46] ***(Level of evidence Ib)***

3) Intensive care patient

Systemic steroid may be considered in managing severe bronchiolitis. (Grade A)

Two RCTs showed that systemic steroid reduced duration of mechanical ventilation, supplemental oxygen and hospital stay in their subgroup analyses.[47,48] ***(Level of evidence Ia)*** However, another RCT did not detect any difference in the clinical outcomes after administration of steroid.[49] More studies are required to elucidate the issue further.

4) Inhaled steroid (Budesonide and Fluticasone)

These is little evidence that inhaled steroid is efficacious in treating bronchiolitis. Its routine use is not recommended. (Grade A)

D. Ribavirin

There is no evidence to recommend use of ribavirin in treating bronchiolitis. (Grade A)

In one recently published meta-analysis, the authors found that the trials of ribavirin for RSV lacked sufficient power to provide reliable estimates of the

effects. The cumulative results of three small trials showed that ribavirin reduced length of mechanical ventilator support and might reduce days of hospitalisation.[50] The authors of another systemic review concluded that there was no evidence that ribavirin use led to consistent or more than transient improvements in clinical outcomes.[51] A large randomised controlled trial of ribavirin for ventilated and other high risk patients is indicated.

E. Other medications
   1) ***There is no evidence to support use of antibiotics in uncomplicated bronchiolitis.[52,53] (Level of evidence: Ib, IIb) (Grade A)***

   2) ***Interferon and vitamin A have not been shown to be useful.[54-56] (Level of evidence: Ib) (Grade A)***

   3) ***The use of exogenous surfactant may be considered in severe cases of acute bronchiolitis with respiratory failure. (Grade A)***

      One recent study showed that infants with respiratory failure from bronchiolitis experienced a more rapid improvement in both oxygenation and ventilation indices after receiving exogenous surfactant and had a slightly shorter length of stay in the intensive care unit.[57] ***(Level of evidence: Ib)*** Further studies are indicated.

   4) **Chinese medicine**. One RCT showed benefit of a mixture of Chinese herbs (Shuang Huang Lian).[58] ***(Level of evidence: Ib)*** The role of Chinese medicine in management of acute bronchiolitis warrants further investigation.

F. Respiratory care therapy
   1) ***Chest Physiotherapy is not recommended. (Grade B)[59,60] (Level of evidence IIa)***
   2) ***Cool mist therapy is not recommended. (Grade C)[59,61] (Level of evidence IV)***
   3) ***Supervised cough and suction is not recommended. (Grade B)[59,60] (Level of evidence IV)***

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