BRONCHIOLITIS: PRESENTATION, INVESTIGATION AND TREATMENT

A.J. Thompson, Senior Registrar, Paediatrics and M.D. Shields, Paediatric Respiratory Physician, Nuffield Department of Child Health, Queen's University of Belfast

INTRODUCTION

Acute bronchiolitis in infants and young children has come to represent a virally induced acute bronchiolar inflammation with signs of lower airway obstruction. Respiratory syncytial virus (RSV) (Figure 1) is the major viral pathogen responsible for the illness, although other viruses such as adenovirus, parainfluenza and influenza can all give a similar clinical picture. It is one of the major causes of hospital admissions in infants under the age of one year (peak rate of admission is between six weeks and six months), and RSV has been described as the single most important respiratory pathogen in children, causing an annual winter epidemic of respiratory infection.[1] In the course of such an epidemic, although a large proportion of the population develops RSV disease, the risk of infection is significantly greater in infancy.[2] Virtually all children have developed antibodies to RSV by the age of two years.[3] However, infection does not confer immunity and repeated infections with the virus are common.[4]

For the majority of infants infected with RSV the only manifestation is mild upper respiratory tract symptoms. However, about 10–20% of infants develop acute bronchiolitis, although only 1–2% of them will require hospitalisation.[2]

PRESENTATION

Early symptoms of the illness include rhinitis (inflammation of nasal mucosa) and coughing, with the development of lower respiratory tract symptoms one or two days later. Some children have a low grade pyrexia early in the illness but this is frequently absent when the infant eventually presents at hospital. This prodromal stage is then followed by the onset of tachypnoea, difficulty with breathing, chest retractions and audible expiratory wheezing with rhonchi and/or 'crackles' heard on auscultation. Agitation and poor feeding as a result of nasal obstruction and hypoxia are common, and the cough may cause vomiting with the risk of aspiration.[1, 2] Pre-term infants may present with an episode of apnoea.

Those at risk of severe disease include pre-term (with or without chronic lung disease) infants, children with congenital heart disease, cystic fibrosis and those with immunodeficiency. Respiratory syncytial virus bronchiolitis is a major hazard for these immunodeficient infants and has the potential to increase mortality.[1, 2]

INVESTIGATION

The diagnosis of acute viral bronchiolitis is based on the clinical findings, including the child's symptoms, age and

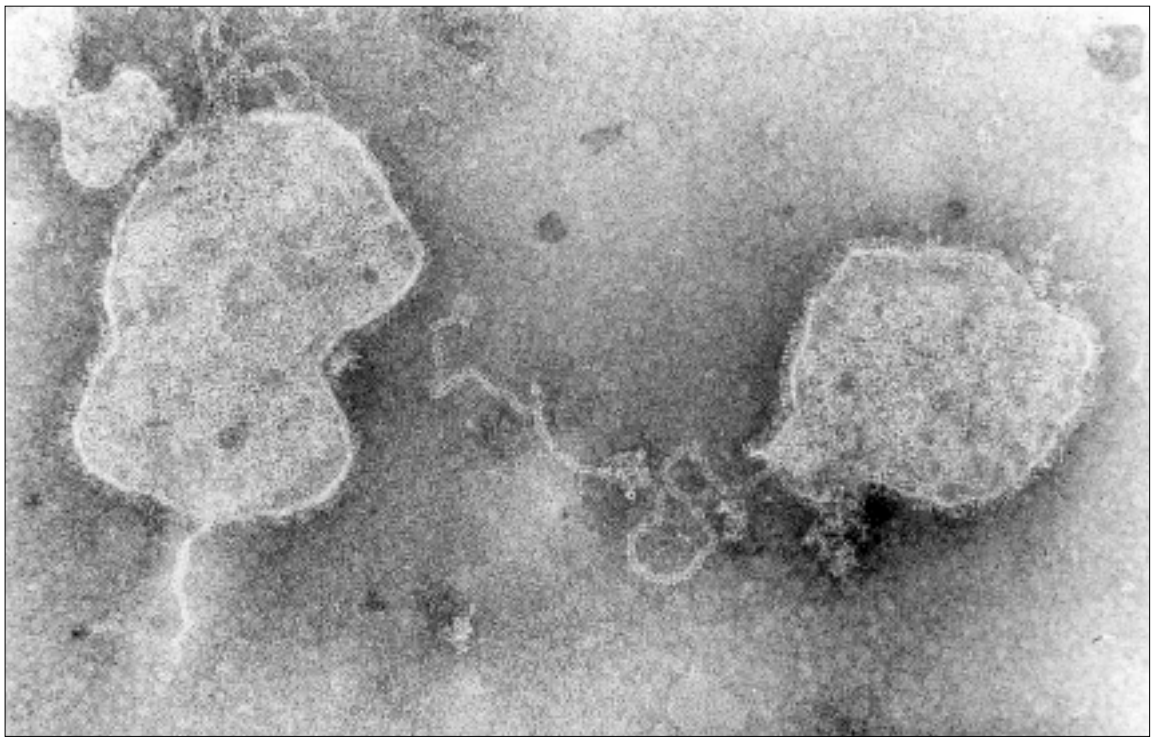

FIGURE 1
Electron microscopy of the respiratory syncytial virus.

the presence of an RSV epidemic in the community. This can easily be confirmed by the identification of the virus in nasopharyngeal aspirates using immunofluorescent antibody tests or enzyme-linked immunoabsorbant assays (ELISA).[5, 6] A negative test for RSV does not exclude the diagnosis. Confirmation of the causative virus may be helpful in the subsequent management of the child, e.g. in isolation/cohorting if the child requires admission.

Any infant admitted with a diagnosis of RSV bronchiolitis should have oxygen saturation monitoring to detect hypoxaemia.

A chest X-ray (CXR) is not routinely indicated but should be considered if the diagnosis is in doubt or if there is a suspicion of secondary bacterial infection (deterioration in clinical condition; high, prolonged fever; neutrophilia; or evidence of septicaemia). In uncomplicated bronchiolitis, the CXR demonstrates hyperinflation, areas of peribronchial thickening, patchy atelectasis or consolidation, typically in the right upper lobe.[1, 2] The white cell count may be normal or raised. Blood electrolyte estimation should be performed in severe cases where infants have been unable to feed because of severe respiratory distress. For the majority of infants, blood tests are not helpful.

Hyponatraemia, suggesting inappropriate release of antidiuretic hormone (ADH) and fluid overload, will require further fluid restriction on the recommended intake of 80% of maintainance.[7, 8]

TREATMENT

Supportive and symptomatic

Bronchiolitis is a self-limiting illness; the majority of cases are mild and do not warrant admission to hospital. For those infants who are admitted to hospital, the mainstay of treatment is supportive and includes the administration of oxygen and appropriate fluid management with careful monitoring of the infant for hypoxia, apnoea and exhaustion. Less than 2% of infants and children hospitalised in developed countries will progress to require assisted ventilation, usually because of persistent apnoea or progressive respiratory failure.[3, 9-11] Some infants greatly improve after intubation because this has facilitated the removal of the copious tracheal mucus. Other infants have severe small airway obstruction and can be difficult to ventilate. For a very small number of infants who are impossible to ventilate adequately, the option of extra corporeal membrane oxygenation (ECMO) should be considered.

Humidified oxygen can be delivered via a nasal cannula or, in smaller infants, by means of a headbox. In small infants there is often obstruction of the nasal passages and regular gentle suction helps to relieve this distress and facilitate feeding. Infants presenting late to hospital may have a mild metabolic acidosis or show features of dehydration because of poor oral intake. We have preferred to use intravenous fluids rather than nasogastric feeding in this situation so as not to block a nostril. Care is needed with fluid replacement to prevent overloading the circulation as bronchiolitis is associated with ADH secretion.[7, 8]

Secondary bacterial chest infection is unusual, and the routine use of antibiotics has not been shown to favourably influence the course of bronchiolitis.[12, 13] However, in infants with severe respiratory distress requiring a high percentage of additional oxygen, the use of intravenous antibiotics can be justified when there is the possibility of concomitant bacterial infection. The extensive handling associated with physiotherapy can be detrimental and its routine use is not recommended.[14, 15]

Bronchodilators

The role of bronchodilators in bronchiolitis is controversial, despite many controlled studies looking at their efficacy.[16] In one meta-analysis, inhaled salbutamol has been shown to provide a moderate short-term improvement in mild to moderate illness, but it did not avert the need for hospitalisation.[17] In another, no benefit was established in the short-term use of beta2-agonists on clinical outcome measures or hospital stay.[18] Sympathomimetic agents such as adrenaline have been shown to be more effective than salbutamol in improving oxygen saturation and clinical scores,[19-21] and in decreasing the need for admission in babies with this illness.[22] It seems reasonable to try a bronchodilator (such as nebulised adrenaline) in severe cases, but only to continue this therapy if benefit is shown. Other bronchodilators have been tried.[23]

Despite a lack of consensus on the use of bronchodilators, many experienced paediatricians would use them in the treatment of bronchiolitis.[3] Clearly, for the majority of infants with RSV bronchiolitis, bronchodilators are, at most, marginally beneficial.

Corticosteroids

Like bronchodilators, conflicting evidence surrounds the use of corticosteroids in infants and children with bronchiolitis.[24-27] A recent randomised placebo controlled trial of nebulised corticosteroids (budesonide) concluded that there were no short-term clinical benefits in the acute phase of RSV bronchiolitis.[28] Despite this, their use is widespread in North America and a recent meta-analysis in the US showed that systemic corticosteroids actually improved the clinical course, shortened the duration of symptoms and reduced the length of stay in hospital.[29]

Ribavirin

Initial optimism about ribavirin as a breakthrough in RSV treatment has not been realised in the clinical setting, although it may have a role in the treatment of selected patient groups. Ribavirin is a synthetic nucleoside, not dissimilar to guanosine, with antiviral properties, delivered by small particle aerosol for 12 to 20 hours a day. Initial studies showed improvement in clinical condition and oxygenation with its use.[30-32] However, a meta-analysis of several conflicting studies looking at the use of ribavirin in RSV-positive bronchiolitis concluded that there was no significant benefit or reduction in overall mortality with its use.[33] Problems of administration, high cost and concerns about long-term teratogenicity have restricted its use to high-risk patients such as those with congenital heart disease, premature infants (particularly those with chronic lung disease), children with cystic fibrosis or the immunocompromised.[34, 35]

Prevention

It is hoped that a vaccine for RSV disease will reduce or eradicate the morbidity and mortality associated with this disease. However, the ability to produce a vaccine which gives immunity in the first few months of life (and indeed

can afford protection in immunologically immature and premature babies) when infants are most susceptible to serious illness has proven difficult. Early attempts with live attenuated RSV vaccines, administered intranasally, have been unsuccessful. In the late 1960s a formalin-inactivated RSV vaccine caused enhanced disease on subsequent exposure to the virus. More recently, problems with infection, protection against natural disease, the potential to infect other individuals and sensitivity to extremes in temperature have slowed progress in the development of a live attenuated vaccine.[3, 36]

Genetically engineered live vaccines, where the vector virus can be manipulated, have the advantage of combining several immunogenic strains of RSV whilst inactivating potentially harmful genes.[37] Such vaccines may soon become available.

Monthly infusions of intravenous RSV hyperimmune globulin (RSVIG) prior to the RSV 'season' have been shown to reduce the viral load in nasopharyngeal secretions[38, 39] and protect against serious RSV disease, although not against acquiring the illness.[40, 41] The time, expense and difficulty in administration, and potential side-effects (fluid overload potential, urticaria, abnormal liver function tests and fever), may limit its usefulness to high-risk groups only.

Humanised RSV monoclonal antibody (palivizumab) can be administered once a month as an intramuscular injection for the duration of the RSV season. This has also been shown to be safe and effective in the prevention of RSV bronchiolitis. An international multi-centre trial showed a significant reduction in hospitalisation and oxygen requirements with minimal adverse reactions.[42] The American Academy of Pediatrics has recommended the use of palivizumab or RSVIG in the treatment of infants and children under two years of age with chronic lung disease, but financial constraints and limited experience has restricted the use of palivizumab to high-risk patients only.[43]

Immunisation of the mother with high levels of RSV antibody has the advantage of protecting the baby at birth when the potential for severe disease is greatest.[37] It also gives the mother immunity and therefore limits disease transmission to her child. Vertically acquired antibody would also offer protection to premature infants. However, a large scale immunisation programme would seem a long way off, since safety concerns would need to be addressed in both mother and unborn child.

Prevention of nosocomial acquired infection is a continual source of anxiety for any health care professional involved in the treatment of RSV bronchiolitis. Respiratory syncytial virus is spread primarily by droplet inhalation from coughing and sneezing, and this makes cohort nursing important. In addition, deposition and inoculation of the RSV onto the hands of medical staff and transmission to other infants can be prevented by careful hand washing between patients.[44, 45] Some units would advocate more stringent policies, such as the use of gowns, gloves, facemasks and goggles. However, one randomised controlled trial showed no significant benefit in nosocomial infection rate when staff used gowns, masks and hand washing.[46]

SUMMARY

Bronchiolitis is a major viral pathogen causing a seasonal epidemic affecting children, particularly infants. For most infants the disease is a self-limiting upper respiratory tract infection, but in premature or immunocompromised infants the illness may be life threatening. Classically, infants present with tachypnoea, indrawing, audible wheeze and fine 'crackles' on chest auscultation. Apart from isolation of the virus from secretions, blood and radiological investigations have a limited role in diagnosis. The mainstay of management is supportive, with oxygen, suction and appropriate fluids. Despite the widespread use of bronchodilators in RSV disease there are few evidence-based studies showing efficacy.

Corticosteroids are not routinely used in RSV disease. Selected infant groups with severe disease may benefit from ribavirin therapy. Passive immunisation, and particularly monoclonal antibody administration to selected patient groups, may protect against severe disease. Nosocomial acquired infection can be prevented by isolation or cohort nursing and hand washing. The treatment of RSV in the future lies in the development of a safe and effective vaccine.

LEARNING POINTS

- Bronchiolitis is a seasonally acquired viral illness
- Bronchiolitis is usually due to respiratory syncytial virus
- Infants are most at risk, and particularly those who are immunocompromised
- Most infants require supportive treatment with oxygen and respiratory suction
- Bronchodilators, corticosteroids and ribavirin have limited roles in management
- Protection of high-risk groups with passive immunisation may prevent severe disease
- A safe and effective vaccine is needed and offers the best hope for the future

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