Bronchopulmonary dysplasia: the outcome

Since 1980 when the last annotation on bronchopulmonary dysplasia appeared in the Archives there have been few advances in the understanding or prevention of this condition. In spite of considerable improvements in ventilatory care it is certainly no less a problem; there is a growing population of children who are surviving improved neonatal care and who develop varying degrees of respiratory difficulty. Evidence suggests that many of these infants will require long term follow up, not only for the audit of neonatal intensive care units, but also because of their increased morbidity and mortality from respiratory problems throughout life.

Definition

Northway et al first described the series of changes that occurred in groups of infants with respiratory distress syndrome during prolonged ventilation. This sequence included the acute and resolving stages of idiopathic respiratory distress syndrome. Now, most paediatricians would consider the criteria of Bancalari et al as being the most useful for follow up: intermittent positive pressure ventilation during the first week of life and for at least three days; clinical signs of chronic respiratory disease for more than 28 days; supplemental oxygen for more than 28 days to maintain a PaO₂ of 6-7 kPa (50 mmHg); and chest x-ray pictures showing persistent strands of radio density and areas of increased lucency that may coalesce into large bullae.

There are many infants who do not fulfil the clinical criteria for bronchopulmonary dysplasia but who have persistently abnormal lung function. Either prematurity or neonatal ventilation may be the precursor of long term airway abnormalities. Thus infants fulfilling the clinical criteria may form just the tip of the iceberg as far as long term problems are concerned. The problem of definition makes the assessment of incidence difficult; it has been reported as being between 2-5 and 40% depending on the series and the range of birth weights studied.

Optimal management of idiopathic respiratory distress syndrome includes careful control of ventilation and inspired oxygen, treatment of patent ductus arteriosus, and of intercurrent infection. Recently other therapeutic options have been suggested including high frequency ventilation, the use of exogenous surfactant, systemic or inhaled steroids, and even inositol which may reduce the impact of bronchopulmonary dysplasia.

Outcome

The oldest survivors are still less than 20 years of age, but there are increasing numbers of studies being reported concerning the long term follow up of survivors of bronchopulmonary dysplasia. Even recent studies report a mortality of 11 to 20% after discharge, and if the infant requires oxygen after 5 months of age there is a particularly poor prognosis. It may take some years before we have a complete picture of the long term outcome of the condition and a lifetime before its full impact on adult respiratory disease is known.

Follow up studies have included clinical observation, lung function tests, tests of pulmonary haemodynamics, and of bronchial hyper-reactivity. It has been shown that in the first year of life infants may have relative hypoxaemia, carbon dioxide retention, reduced lung compliance together with raised airway resistance, increased thoracic gas volume, right ventricular hypertrophy, and increased pulmonary vascular resistance. Oddly, many of these measurements may not have been abnormal before discharge from the neonatal unit and they are of limited value in predicting later lower respiratory tract illness.

Subsequently these abnormalities may resolve slowly after 1 to 2 years. During the first 2 years of life infants with bronchopulmonary dysplasia have an increased incidence of lower respiratory tract infections and a high risk of respiratory failure during such illnesses. It was shown in one study that more than 95% of survivors had abnormal growth, development, and x-ray appearances at 2 years of age, while another showed a 78% incidence of abnormal x-ray appearances at 2 years. There does not seem to be a strong correlation between radiographic resolution and symptoms among survivors.

Electrocardiographic abnormalities have also been documented. More recently cardiac catheterisation has allowed measurements of pulmonary artery pressure and pulmonary vascular resistance and their response to treatment with oxygen. In one study the degree of pulmonary hypertension did not correlate well with results of pulmonary function...
tests.\textsuperscript{19} As in adults, PaO\textsubscript{2} correlated better with other measurements of pulmonary haemodynamics than routine spirometry. Continuous oxygen treatment may lead to a gradual reduction in pulmonary vascular resistance, but this requires careful supervision with frequent 24 hour tape recordings of oxygen saturation.

Spirometry has shown airways obstruction in children aged 7 to 10 years, and metacholine challenge tests were positive in 43–45\%, indicating bronchial hyper-reactivity.\textsuperscript{5} The increased bronchial reactivity may be a non-specific response similar to that found in children after repair of tracheoesophageal fistulas, children with cystic fibrosis, and adults with chronic suppurative lung disease. The suggestion that a genetic predisposition to hyper-reactivity may underlie the development or the progression of bronchopulmonary dysplasia is not borne out by an association with atopy.

Problems in adult life

The hypothesis that lower respiratory tract illness is a predictive factor of chronic airflow limitation in adult life has been much debated.\textsuperscript{21–23} Adults with chronic obstructive lung disease and bronchial hyper-reactivity have a more rapid deterioration in lung function.\textsuperscript{24} Much of the data have been generated from retrospective studies which rely on preferential recall of symptoms in early childhood. Thus the association of chronic obstructive airways disease in relation to early respiratory problems will only be established by long term prospective studies. Follow up of large numbers of survivors of bronchopulmonary dysplasia into adult life will show whether they are particularly at risk of chronic obstructive airways disease. Many other factors are likely to interact including respiratory infection, atopy, parental smoking, air pollution, and socio-economic circumstances.

Implications

If bronchopulmonary dysplasia and clinically undetectable abnormalities of lung function are not to be precursors of long term respiratory morbidity in infants surviving prematurity and neonatal ventilation then certain preventive strategies and therapeutic regimens need to be introduced. Firstly, maintaining adequate oxygenation to reduce pulmonary hypertension is a priority. The oxygen treatment may be needed for several months or even years and even now long term home ventilation services are being established in some parts of the world.

Secondly, the prevention of further respiratory morbidity during childhood will be required. This will necessitate an increase in the use of the standard vaccinations and the use of a wider range of vaccines among preterm survivors. Prompt treatment of respiratory infections, with parents being taught physiotherapy and the provision of broad spectrum antibiotics, will also reduce further airways damage. If atopy is associated with increased bronchial hyper-reactivity this should be treated with appropriate antiasthma drugs. Hopefully intervention will reduce morbidity secondary to parental smoking, but as these infants grow into adolescence they must be advised against smoking themselves.

Finally there is a need for centres to establish a service for long term follow up of infants who survive with bronchopulmonary dysplasia to allow collection of data and help in ensuring optimum management.

References


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