

Management of bronchopulmonary dysplasia

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Abstract

Bronchopulmonary dysplasia (BPD) is a common and important complication of prematurity and is associated with significant mortality, morbidity and healthcare resource utilization. Despite advances in both perinatal and neonatal care the incidence of the condition continues to rise. The management of BPD and its related problems remains a major challenge to neonatologists and paediatricians. There is unlikely to be a single intervention which will dramatically alter the management of BPD and thus multiple interventions have been proposed to prevent and treat the disease. Many of these interventions are still not evidence based and some of those that have been shown to have unacceptable long-term effects. It is useful to conceptualize BPD in three stages, namely (i) prevention, (ii) treatment of evolving BPD and (iii) treatment of established BPD. In this review current and potential future management approaches to BPD and the relevant evidence for these are discussed within the framework of these three stages.

Keywords bronchopulmonary dysplasia; chronic lung disease of prematurity; corticosteroids; diuretics; macrolides; oxygen therapy

Introduction

Incidence

Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease that is a common and important complication of prematurity. It is associated with significant mortality, morbidity and resource utilization. Despite advances in both perinatal and neonatal care over the past few decades, the incidence of BPD continues to rise. This is likely to be related to improved survival at extremes of gestation and at very low birth-weights. Infants born at <1250 g account for 97% of cases of BPD. The reported incidence of BPD varies widely due to differing definitions used. The European MOSAIC cohort in 2003 reported incidences ranging from 10.2% in Italy to 24.8% in the UK.

Definition

The definition and classification of BPD have changed since its original description by Northway et al. in 1967. The National Institute of Child Health and Human Development (NICHD) defined BPD in a consensus statement in 2001. This definition

uses supplemental oxygen requirement for 28 days and then identifies 3 grades of severity, dependent on the respiratory support required at either 36 weeks postmenstrual age (PMA) or at discharge for those born at <32 weeks gestation or at 56 days of life or discharge for those born at >32 weeks gestation. This definition is validated and is thought to more accurately identify the risk of adverse outcomes than previous definitions.

Pathophysiology

The aetiology of BPD is multifactorial, complex and remains incompletely understood. Genetic predisposition, prematurity, infection, ventilator induced lung injury and oxygen toxicity are just a few of the risk factors that are associated with the development of BPD. These factors trigger an inflammatory cascade in the highly vulnerable premature lung (Figure 1). Inadequate or aberrant tissue growth and repair leads to impaired alveolarization and abnormal pulmonary vasculogenesis; the pathological hallmarks of “new” BPD.

Outcomes

BPD results in a significant burden not only to the preterm infant but also to their families. It has a major impact on daily life both during and beyond the neonatal period. It is associated with increased mortality and recurrent, often prolonged hospitalizations. These infants continue to have chronic respiratory difficulties and may experience reduced exercise tolerance as adolescents and impaired general and respiratory health as adults. Supplemental oxygen requirement and mechanical ventilation at 36 weeks postmenstrual age (PMA) is associated with an increased risk of cerebral palsy (CP) and BPD is independently associated with cognitive impairment and language delay.

Management

The management of BPD is challenging. Multiple interventions have been proposed to prevent and treat BPD but many are still not evidence based. Current treatments appear to have reduced the severity of BPD but have had little effect on its incidence. BPD is an evolving process of lung injury and its pathophysiology varies at different stages of the disease. Its future management therefore is unlikely to be in the form of a single intervention but rather a combined approach with different strategies used to target different points in the disease. For this reason, it is useful to conceptualize BPD in three stages when creating an overall management plan.¹ These are (i) prevention of BPD, (ii) treatment of evolving BPD and (iii) treatment of established BPD. In this review current and potential future management approaches within these three stages are discussed.

Prevention of bronchopulmonary dysplasia

Antenatal care

Continued improvements in antenatal care that aim to reduce preterm births would significantly impact on the incidence of BPD. Since the introduction of antenatal steroids there has been a dramatic reduction in the incidence of neonatal mortality and many morbidities, however antenatal steroids have not consistently been shown to have had an effect on the incidence of BPD itself.

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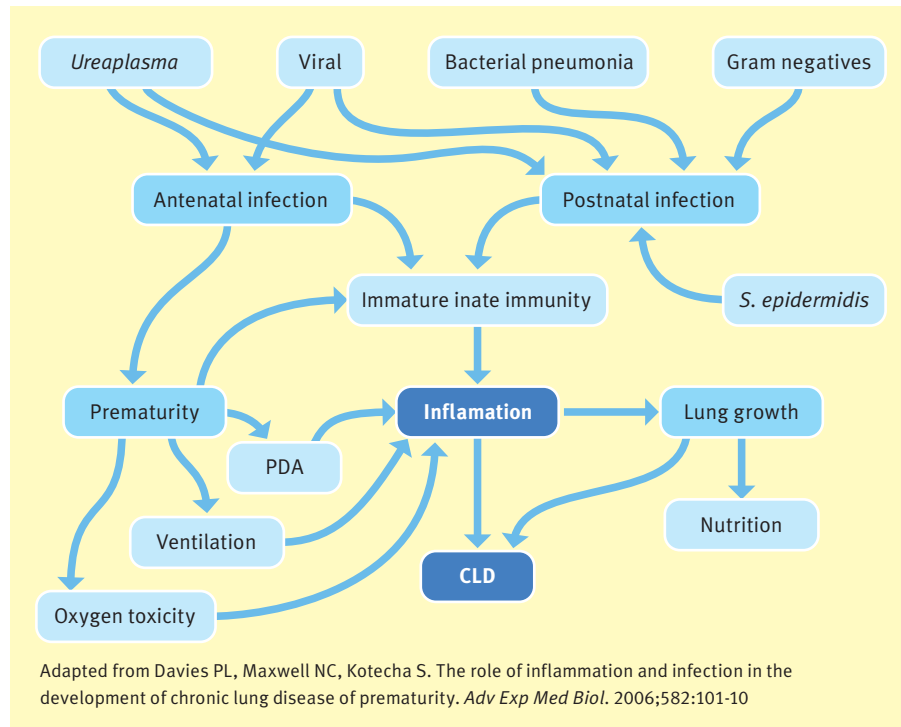


Figure 1 The Pathogenesis of BPD.

Preterm infants born to mothers with chorioamnionitis seem to be at greater risk of developing BPD. Antenatal interventions to treat chorioamnionitis have not influenced BPD rates and there remains debate surrounding a causal link between the two. A recent systematic review by Hartling et al. concluded that chorioamnionitis could not definitely be considered a risk factor for BPD although this was more likely when combined with postnatal infection. Early recognition and treatment of antenatal and postnatal infection still remains paramount.

Neonatal resuscitation

The management of BPD for neonatologists begins as soon as the infant is born. The preterm lung is highly susceptible to injury and a protective respiratory support strategy from birth is imperative. Current recommendations include good airway management, initial mask ventilation with lowest possible inflation pressures and the use of pressure limited devices. Pre-ductal pulse oximetry allows changes in heart rate and peripheral oxygenation to guide intensity of medical intervention. As yet no ideal oxygen concentration has been defined for preterm neonatal resuscitation. Although a study by Vento et al. demonstrated that in infants <32 weeks gestational age a starting FiO₂ of 0.3 was usually sufficient to meet target oxygen saturations. Neonatal resuscitation techniques will continue to evolve in attempts to reduce the incidence and severity of BPD.

Surfactant treatment

Despite evidence that the introduction of surfactant has not reduced the incidence of BPD, it has reduced the combined outcome of death or BPD and had a positive effect on its severity. For every 100 infants treated with animal derived surfactant

there were nine fewer cases of BPD or death. Original studies surrounding surfactant suggested that prophylactic therapy was better than selective rescue therapy, but these were undertaken in an era with limited antenatal steroids and little CPAP use. More recent trials have shown improved outcomes with early stabilization on CPAP and rescue surfactant only when progressive signs of respiratory distress develop. It is important that once surfactant is clinically indicated, early rescue therapy at a lower FiO₂ (via the INSURE technique) rather than late rescue therapy is used. Currently under evaluation are different methods of surfactant delivery designed to avoid intubation and mechanical ventilation altogether. These may further reduce the development of BPD.

Initial respiratory support

Even a few large volume breaths given to a surfactant deficient lung are enough to create persistent inflammatory changes. Non-invasive ventilation can avoid the harmful effects of positive pressure ventilation and may reduce the risk of developing BPD. Several recent randomized control trials have evaluated whether early stabilization in the delivery room with non-invasive ventilation has advantages over immediate intubation and ventilation in infants born <28 weeks gestation. The COIN, SUPPORT and CURPAP trials all address the issues surrounding the immediate management of the preterm infant. When considering the results of these trials together a policy of early stabilization with CPAP will result in similar if not better short-term outcomes than a policy of immediate intubation and ventilation in the spontaneously breathing infant. However a reduction in BPD has not consistently been shown. When using non-invasive ventilation it is important to have strict failure criteria to allow infants that require surfactant to receive it early.

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