Hypoxic Episodes in Bronchopulmonary Dysplasia

Richard J. Martin, MD[a,*], Juliann M. Di Fiore, BSEE[b], Michele C. Walsh, MD, MSEpi[a]

KEYWORDS

- Neonatal respiratory control • Apnea of prematurity
- Desaturation episodes in preterm infants

KEY POINTS

- Intermittent hypoxic episodes frequently accompany bronchopulmonary dysplasia (BPD).
- Immature respiratory control superimposed on abnormal pulmonary function is a major contributor to intermittent hypoxia in BPD.
- Pulmonary hypertension may aggravate predisposition to intermittent hypoxia.

INTRODUCTION

Hypoxic episodes remain a major source of frustration for care providers of preterm infants in the neonatal intensive care unit. Although optimizing oxygen saturation remains a challenge, the newest generation of pulse oximeters has enabled us to document the incidence of episodic desaturation in this population. These episodes persist beyond the first weeks and even months of postnatal life and, therefore, are temporally related to the development of bronchopulmonary dysplasia (BPD) in a high proportion of extremely low birth weight infants. Unfortunately, there are limited data on how development of BPD modifies respiratory control, airway function, and the pulmonary vascular contribution to hypoxic episodes during postnatal maturation. Although the primary etiology of intermittent hypoxic episodes in preterm infants is immature respiratory control,[1] abnormal lung function present in developing BPD clearly aggravates vulnerability to desaturation.

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[a] Division of Neonatology, Department of Pediatrics, Rainbow Babies & Children's Hospital, Case Western Reserve University School of Medicine, 11100 Euclid Avenue, Suite RBC 3100, Cleveland, OH 44106-6010, USA; [b] Division of Neonatology, Department of Pediatrics, Rainbow Babies & Children's Hospital, Case Western Reserve University, 11100 Euclid Avenue, Suite RBC 3100, Cleveland, OH 44106-6010, USA
* Corresponding author.
E-mail address: rxm6@case.edu

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ROLE OF IMMATURE RESPIRATORY CONTROL IN BRONCHOPULMONARY DYSPLASIA

The multiple contributors to apnea of prematurity and resultant desaturation are summarized in Fig. 1. They comprise upregulation of brainstem-mediated inhibitory pathways, altered peripheral chemosensitivity, decreased central chemosensitivity, enhanced inhibition from upper airway afferents, and an unstable upper airway.[2] Apnea is clearly more likely to elicit desaturation with the low functional residual capacity (and other abnormalities of lung function) that characterizes BPD (see Fig. 1).

Data from Animal Models

Large animal models of BPD have proven to be a challenge and very expensive owing to the need for longer term survival. Studies have, therefore, focused primarily on hyperoxia-exposed neonatal rodents who exhibit lung injury somewhat analogous to the BPD seen in preterm infants. Unfortunately, few studies have focused on vulnerability of respiratory control in the face of neonatal lung injury in such a model. Ratner and associates[3,4] have demonstrated that intermittent hypoxia (IH; to which infants with BPD are clearly predisposed) superimposed open hyperoxic lung injury aggravates both alveolar arrest and neurologic handicap in neonatal mice. More recent studies in neonatal rats have documented that an early period of sustained postnatal hypoxia followed by subsequent chronic IH causes a markedly attenuated ventilator response to acute hypoxic exposure.[5] The conditions precipitating this vulnerability of respiratory control may be analogous to the oxygenation status of preterm infants exposed to low baseline levels of oxygen, as described elsewhere in this article.

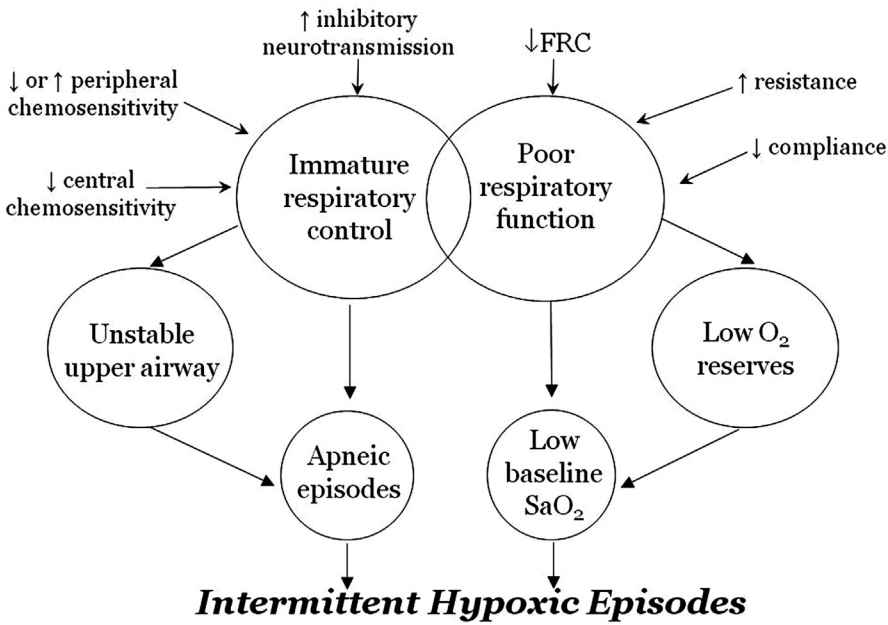

Fig. 1. Multiple factors contribute to both immature respiratory control and poor respiratory function, are potentially aggravated by bronchopulmonary dysplasia, and enhance vulnerability for development of intermittent hypoxic episodes. ↑, increased; ↓, decreased; FRC, functional residual capacity; SaO_2, oxygen saturation.