



## Review

## Nutritional approach to preterm infants on noninvasive ventilation: An update



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## ABSTRACT

Nutrition and pulmonary function in very-low-birth-weight infants (VLBWIs) are strictly related. Preterm infants on noninvasive ventilation may have respiratory instability that can interfere with feeding tolerance. Moreover, feeding may impair pulmonary function. These infants have nutritional requirements different from nonventilated infants. The main challenge of the nutritional support in such patients is to guarantee adequate caloric intake while avoiding episodes of feeding intolerance. The aim of this study was to review the issues and strategies of enteral feeding of preterm infants on noninvasive ventilation.

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## Introduction

Nutrition and pulmonary function in very-low-birth-weight infants (VLBWIs) are strictly related. Although maintaining an optimal pulmonary function has priority in VLBWIs to secure vital functions, adequate nutritional support plays a major role because a state of malnutrition not only compromises growth in general, but has major adverse effects on the respiratory system. For example, inadequate early nutrition may contribute to the pathogenesis of bronchopulmonary dysplasia (BPD) by hampering the process of lung repair in the first month of life [1]. VLBWIs, growing along the lower quartiles during their neonatal stay, are at higher risk for neurodevelopmental damage as well as chronic pulmonary complications [2]. On the other hand, infants with respiratory problems often experience poor growth and delayed development [3].

As a matter of fact, infants with respiratory impairment on noninvasive ventilation (NIV) require an adequate nutritional assessment. Therefore, we performed a collective and narrative review to analyze the issues regarding feeding preterm infants with respiratory impairment.

## Methods

The following electronic databases were searched until January 2016 for published studies that fulfilled our criteria: Cochrane Central Register of Controlled Trials and PubMed (including MEDLINE). To identify potential systematic reviews/meta-analyses, we browsed The Cochrane Database of Systematic Reviews.

An initial screening of the title, abstract, and keywords of every record identified was performed. The next step was to retrieve the full text of potentially relevant studies. The following search terms were used: (enteral nutrition OR enteral feeding) AND (noninvasive ventilation OR continuous positive pressure airway pressure). Only studies in English and related to infants from birth to 23 mo of age were considered.

## Effects of noninvasive ventilation

Although lifesaving, invasive mechanical ventilation of VLBWIs represents a major risk factor for the development of BPD, ventilator-induced lung injury (VILI), and infection [4]. VILI is reported to be associated with alveolar structural damage, pulmonary edema, inflammation, and fibrosis. Mechanisms of lung injury include high airway pressure (barotraumas), large gas volumes (volutrauma), alveolar collapse and reexpansion (atelectrauma), and increased inflammation (biotrauma). In VLBWIs, BPD remains a leading cause of early death and morbidity. Improvements in survival rates among such infants have led to rates of BPD of  $\leq 60\%$  at the lowest gestational ages [5].

These concerns have prompted neonatologists to use noninvasive methods of ventilation; this approach has been increasingly gaining acceptance in most neonatal intensive care units (NICUs). Nasal continuous positive airway pressure (nCPAP) is an alternative to intubation and intermittent positive-pressure

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ventilation (IPPV). A meta-analysis of trials of early nCPAP versus intubation and ventilation showed that nCPAP reduces the risk for BPD [6]. These findings led to a more extensive use of techniques of NIV in NICUs.

Noninvasive forms of ventilation in neonates can be provided either as a single-level support such as CPAP and high-flow nasal cannula or bi-level support such as nasal intermittent positive pressure ventilation (NIPPV), which is a method of augmenting nCPAP by delivering ventilator breaths via nasal prongs. NIPPV may be synchronized with the infant's inspiration or delivered independently of the infant's breathing efforts, and it is usually delivered at pressures similar to those used during conventional ventilation. Different modes of ventilation may be applied non-invasively, leading to different NIPPV terminologies such as *nasal synchronized intermittent mandatory ventilation* [7], *nasal intermittent mandatory ventilation* [8], and *noninvasive pressure support ventilation* [9]. Various interfaces, such as facemasks and nasopharyngeal and nasal methods, have been used to deliver NIV. Short bi-nasal prongs are the most commonly used interface for NIPPV and bi-level positive airway pressure [10,11].

There is no agreement on the best NIV technique. In a recent trial comparing the effect of different modalities of NIV on the survival rate at 36 wk of postmenstrual age of extremely-low-birth-weight infants without BPD, there was no significant difference between noninvasive respiratory support with NIPPV and nCPAP [12].

### Feeding issues

It has been commonly reported that infants on NIV suffered from marked gaseous bowel distension; initially termed *CPAP belly syndrome*. This was described in infants who did not present abdominal distension at birth, but developed it after a 4- to 7-d course of nCPAP. These infants presented strikingly distended abdomens and visibly dilated loops. Findings on radiographs invariably included uniform dilation of small bowel and large bowel loops without evidence of thickening of the bowel wall, pneumatosis, or free air [13].

Jaile et al. [13] compared 25 premature infants on nCPAP with 29 premature infants who were not on CPAP. Gaseous bowel distension due to CPAP developed in 83% of infants weighing <1000 g versus 14% of those weighing  $\geq 1000$  g. Of the 29 infants not receiving nCPAP during the study period, gaseous bowel distension, indistinguishable from CPAP belly syndrome, developed in only 3 (10%). No cases of necrotizing enterocolitis (NEC) were reported in the study; however, the sample size was too small to draw conclusions about NEC.

### Correlates among ventilation, mesenteric flow, and gastric emptying

Several authors have reported a correlation between CPAP ventilation and mesenteric blood flow. Havranek et al. [14] reported that CPAP administration was associated with an attenuation of the postnatal increase in superior mesenteric artery blood flow velocity (SMA BFV) in preterm infants. [15]. Increases in SMA BFV were strictly related to feedings in stable infants [16] and attenuated increases in postnatal SMA BFV were associated with intestinal dysmotility [17] and feeding intolerance. In another study, the increase in SMA BFV after feeding was measured, showing a higher increase of BFV in SMA from 0 to 30 min after feeding, that was greater when infants were on CPAP than when they were not. The higher increase in SMA BFV from 0 to 30 min after feeding while on CPAP may relate to effects of this ventilation on gastric emptying time. The gut blood flow

depends on gastric emptying and feeding progression through the gastrointestinal (GI) tract [18–21]. The continuous positive airway pressure exerted by the CPAP may exert a pressure on the diaphragm thus increasing the velocity of gastric emptying [22].

The clinical implications of earlier maximum postprandial SMA BFV or shorter gastric emptying times in this population are not known. However, delayed gastric emptying in preterm infants is associated with feeding intolerance. As the method of ventilation may interfere with the GI function, feeding too may have an effect on pulmonary dynamics.

A number of authors have speculated about the effects of the abdominal body wall and of the abdominal contents on the mechanics of respiration. In a study by Yu and Rolfe [23], pulmonary function was measured at rest and after feeding (administered as tube feeding by the gravity method) in infants suffering from respiratory distress syndrome (RDS) and in healthy infants. They used a pneumotachograph with an adaptor during spontaneous breathing. In infants with RDS, the respiratory rate was raised, tidal volume decreased, and minute ventilation increased. Compliance was reduced to one-fourth the normal value. Resistance was essentially unchanged, but the decrease in compliance contributed to a greatly increased the work of breathing. The hypothesis is that the reduction in functional residual capacity after feeding might be associated with a raised transpulmonary pressure, which causes airway closure, either de novo or to a greater extent than before feeding.

There are still controversies regarding the best-tolerated feeding method because the effect of intermittent or continuous feeding on respiratory mechanics in VLBWIs remains unclear. Studies in the literature are small, rather old, and inconsistent.

Blondheim et al. [24] measured the dynamic respiratory function of two groups of infants randomly assigned to intermittent or continuous feeding groups. These authors found that bolus gavage of  $15 \pm 20$  mL/kg of milk decreased tidal volume, minute ventilation, and dynamic compliance and increased resistance within 10 min after feeding. In a more recent study, Brar et al. [25] found no adverse effect of intermittent versus continuous feeding on respiratory system compliance and resistance, tidal volume, or functional residual capacity after feeding in stable full enteral-fed VLBWIs, thus demonstrating that the two feeding methods were equivalent. Results from Blondheim et al. and Brar et al. are conflicting (one assessing that bolus feeding impaired respiratory patterns, the other stating that the effect of the two different feeding modalities on respiratory function was the same) as the accuracy in pleural pressure estimation used for dynamic measurement of respiratory mechanics was different. In the study by Blondheim et al., the infants examined were preterm VLBWIs with RDS; Brar et al. instead evaluated at-term infants. It is possible that the different pulmonary response to feeding might be influenced by prematurity.

Continuous feeding infusion may result in significantly higher losses of energy, mainly in the form of fat and protein from human milk, than intermittent infusion. It has been shown that human breast milk leaves a fatty residue in the burette and in the tube at the end of the infusion. There is some evidence that these losses are inversely related to flow rates. Fat and protein loss during tube feeding could adversely affect growth supplying lower energy amounts as well as deprive infants of the very low-chain polyunsaturated fatty acids needed for brain and nervous system development [26,27].

There may be some advantages to feeding in the prone position, although these benefits may be offset by the tendency of these infants to exhibit a higher body temperature while in this position [28].

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