Enteral nutrition for preterm infants: by bolus or continuous? An update

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Abstract

Optimization of nutritional management of preterm infants is crucial for achievement of their long-term health. Enteral nutrition is preferred to total parenteral nutrition (TPN) because the former avoids complications related to vascular catheterization, sepsis, adverse effects of TPN, and fasting. Due to the lack of ability of preterm infants to coordinate suckling, swallowing, and breathing, tube feeding is necessary for most infants less than 1500 g to ensure sufficient feeding tolerance, to support optimal growth and to reduce the risk of aspiration. Therefore, feeding by orogastric or nasogastric tube using either continuous or intermittent bolus delivery of formula or human milk is common practice for these infants. Theoretical risks and benefits of both continuous nasogastric milk feeding and intermittent bolus milk feeding have been proposed. According to the literature, continuous nutrition could be preferred in smaller infants (as those with a birthweight below 1250 g) or hemodynamically impaired infants; in stable growing infants nutrition can be administered intermittently as in healthy term infants.

Introduction

Approximately 8% of infants are born with a weight at birth less than 2.5 kg.[1] These infants face uncertain futures, ranging from insufficient postnatal growth to compromised neurodevelopmental outcomes.[2] Thus, optimization of their nutritional management is crucial for achievement of their long-term health and well-being. There is a correlation between the neurocognitive outcome and growth, for this reason an adequate nutrition is essential for the optimal growth and health. Most of severe preterm infants are discharged weighing less than the tenth percentile for age despite improvements in their nutritional management.[3] Some of them remain small to adulthood and exhibit adverse long-term developmental outcomes including learning impairments and reduced work capacity.[4,5] Because growth failure of low birth weight (LBW) infants has been attributed, in part, to the provision of inadequate levels of protein and energy, more aggressive nutritional support is now being advocated.[6] Evidence suggests that this approach is justified because early provision of amino acids to extremely LBW infants is associated with improved growth;[7] moreover provision of adequate amount of amino acid increases whole body protein synthesis and accretion rates in LBW infants.[8] Parenteral feeding allows rapid nutrition when enteral nutrition is not possible due to respiratory problems, limited gastric capacity, reduced intestinal mobility, and a perceived risk for necrotizing enterocolitis.[6] When an infant is medically stable, minimal enteral feeding is provided to *prime* the intestine and gradually the infant is moved from parenteral to enteral feeding until achievement of full enteral feedings.

Enteral nutrition is preferred to total parenteral nutrition (TPN) because the former avoids complications related to vascular catheterization, sepsis, adverse effects of TPN, and fasting. Moreover, enteral feeding in the first days of life promotes endocrine adaptation and the maturation of motility patterns, provides luminal nutrient, and probably benefits immune function. Potential clinical benefits are therefore earlier tolerance of enteral feeds, reduced risk of infection, and earlier discharge.

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Materials and Methods

The following electronic databases were searched until April 2017 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.

The following search terms were used: "Feeding Methods"[Mesh] AND "Infant, Premature"[Mesh]. Only studies in English, performed in the last 10 years and related to infants

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from birth to 23 months of age were considered. We retrieved 789 items. 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. Among the items, we searched papers focused on the modality of delivering nutrition searching with keyword *continuous feeding* and *bolus feeding* and only 70 items were retrieved.

Results and Discussion

The benefits of bolus *vs* continuous feeding in LBW infants have been debated for some time since both the modalities of feeding present advantages and disadvantages; theoretical risks and benefits of both continuous nasogastric milk feeding and intermittent bolus milk feeding have been proposed. Bolus (or intermittent feeding) is defined as provision milk through a tube into the stomach over 10 to 20 minutes every two to three hours; continuous nutrition is administering enteral formula via nutritional pump continuously 24 hourly.

Intermittent bolus feeding simulates the feeding pattern of infants when they are breast or bottle fed and has been advocated to promote more physiological feeding-fasting surging of hormonal levels than continuous feedings, as normally seen in healthy term infants, and may stimulate gastrointestinal tract development and enhance protein accretion.[10,11-13] Several studies have shown that intermittent bolus feedings reduce the time to achieve full enteral feeds, decrease feeding intolerance and increase weight gain,[14] but contrary results have also been published.[15] Feeding stimulates whole body protein synthesis in the human neonate.[16] This feeding-induced stimulation of protein synthesis is crucial to support the rapid growth rate of early postnatal life and thus reducing the risk of impaired neurocognitive function.[17] More detailed experimental evidence from studies using neonatal pigs, a well-recognized animal model for human infants, demonstrated that intermittent bolus feeding, compared to continuous orogastric feeding, promotes better weight gain, intestinal growth and development.[18] It has been demonstrated on pigs, that circulating insulin and amino acid levels increase minimally and remain constant in continuously fed pigs compared to fasted pigs, whereas the intermittent bolus feeds elicit a pulsatile insulin and amino acid pattern with a stimulation of protein synthesis in all tissues with the greatest response occurring in skeletal muscle.[17] These results are supported by previous studies on humans, showing that preterm infants who receive bolus feeding exhibit marked cyclical surges in hormone levels.[19]

Feeding by bolus has been reported to be associated with metabolic instability in preterm infants. A case series of preterm infants fed intermittently and monitored with continuous glucose monitoring revealed intraday glycemic fluctuations with repeated abnormal glucose levels in some preterm infants. These fluctuations resolved within several weeks in all case. The clinical significance of large glycemic variability regarding future complications of preterm infants, however, remains to be determined.[20]

Intermittent nutrition may also adversely affect pulmonary function and may cause greater gastric distension, which can increase airflow, respiratory instability and be more difficult for the immature gastrointestinal tract to handle this kind of nutrition resulting in increased feeding intolerance and feeding-related apneas.[21] Blondheim *et al.*[22] measured impaired pulmonary functions (*i.e.*, greater pulmonary resistance, reduced pulmonary compliance, lower tidal volume, and minute ventilation) in the bolus-fed infant, but the incidence of cardiorespiratory events was not evaluated.

Continuous nasogastric feeding is reported to improve energy efficiency (by increasing energy absorbed and decreasing energy expenditure), to reduce feeding intolerance, to improve nutrient absorption, duodenal motor function, and growth.[23] It is also reported to improve weight gain in infants less than 1250 g, as well as resulting in an earlier discharge for ELBW infants.[24]

Continuous feeding may also be beneficial from the perspective of glycemic stability since there is no variability induced by feedings but, on the other hand, continuous infusion of milk into the gastrointestinal tract could alter the cyclical pattern of release of gastrointestinal tract hormones, which might affect metabolic homeostasis and growth.[25] The slower infusion rate of continuous feeding is thought to be preferable in cases with delayed gastric emptying. Nevertheless it has been shown in a study by Corvaglia[26] that continuous feeding was associated with a greater number of prolonged apneas and apnea-related hypoxic episodes and these findings were consistent with those of Dollberg *et al*.[27] Another disadvantage of continuous administering of feeding is that provision of nutrients could be impaired since a substantial portion of the nutrients provided is lost due to the delivery system.[9] It has been demonstrated that the use of the continuous feeding method reduces fat delivery to the infant compared with intermittent bolus methods.[28] To improve fat delivery the feeding tube should be shortened, thus preventing loss of fat on tubing surfaces and the syringe should be emptied completely at end of the infusion.[29]

A Cochrane review,[30] comparing clinical effects of continuous versus intermittent bolus nasogastric milk feeding in VLBW infants, concluded that the present evidence is inadequate for determining an optimal feeding strategy because of the small sample sizes and methodological limitations. There was no difference in time to achieve full feedings between feeding methods regardless of tube placement. Reports of the incidence of NEC were similar. A trend toward earlier discharge for infants less with a birth weight less than 1000 fed by the continuous tube feeding method compared to intermittent nasogastric tube feeding method was revealed; one study[24] demonstrated that infants with a birthweight less than 1000 g or between 1000 and 1250 g gained weight faster when fed by the continuous nasogastric tube feeding. However, there is not enough evidence to determine the best feeding method for low birth weight premature infants. More research is required in this area.

In 2015, a trial was performed on infants born with a birthweight <1750 g that were randomly assigned to either intermittent bolus feeding or continuous feeding; in this study, it was compared the time necessary to achieve full enteral feeding and parameters of feeding tolerance. This randomized controlled trial demonstrates that for preterm LBW infants, there are no differences in days to reach full enteral feeding, weight gain, or safety between continuous or bolus feeding; it was also revealed that the mean daily gastric residual volumes were significantly lower in the bolus group than in the continuous group, as was the total number of patients with feeding interruptions as demonstrating a better feeding tolerance in infants fed by bolus.[31] However, recent studies have demonstrated that only frankly pathologic residuals (as hemorrhagic, heavily bilestained or bloodstained residuals) increase the risk of NEC. There is no literature consensus about the amount of residue that is clinically relevant.[32-34] Hence, the importance of gastric residuals as a diagnostic sign is declining, since it can be considered more a sign of GI maladaptation than of insurgence of NEC and therefore it is not possible to conclude that bolus feeding exerts a better impact on feeding tolerance than continuous feeding.

Some few, of small size and not randomized, studies assessing the impact of different modalities of feeding (bolus versus continuous feeding) on splanchnic oxygenation were performed and they reported conflicting results. Dani *et al*.[35] demonstrated that bolus milk feeding induces an increase in splanchnic oxygenation without increasing oxygen blood extraction in both healthy AGA and SGA infants, whereas continuous feeding does not affect gastrointestinal oxygenation. Corvaglia *et al*.[36] reported a significant decrease of splanchnic oxygenation occurring in the second half of continuous feeding and a slight trend toward increase in splanchnic Tissue Oxygenation Index during the final 10 minutes of continuous feeding. The study by Dave[37] showed that CSOR increased 1 hour after orogastric bolus feeding in stable preterm infants, but the authors did not compare the effect of bolus versus continuous feeding. An RCT comparing the effect 2 different feeding regimens on the blood flow velocity (BFV) in the superior mesenteric artery showed that BFV average measurements significantly increased both after bolus and after continuous gavage, but increase in all BFV parameters were significantly higher after bolus than after continuous nutrition suggesting that feeding by bolus is more protective of the gastrointestinal tract. A possible explanation is that a small or absent increase in mesenteric blood flow cannot support the additional metabolic demand on the gut imposed by feeding.[38]

Conclusions

Bolus and continuous feedings are both suitable feeding strategies for preterm infants, both presenting clinical benefits as well as disadvantages. To date, the conflicting results of the studies comparing continuous and intermittent bolus feeding make difficult to formulate universal recommendations regarding the best tube feeding method for premature infants with birth weight less than 1500 g.[39] During any kind of tube feeding, potential problems are reflux and aspiration, metabolic impairment, gastric perforation, vagal stimulation and bradycardia, as well as nasal erosion or palatal groove.[40] Continuous nutrition could be preferred in smaller infants (as those with a birthweight below 1250 g) or hemodynamically impaired infants; in stable growing infants nutrition can be administered intermittently as in healthy term infants.

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