Review

The practical aspects of enteral nutrition in preterm infants

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Abstract

Preterm infants have higher nutrient requirements than term infants. Enteral tube feeding is the preferred route to feed preterm infants because premature infants are unable to coordinate sucking, swallowing, and breathing. There are two common tube feeding methods: intermittent (bolus) or continuous infusion. Minimal enteral nutrition or trophic feeding has many advantages for preterms and should be started as soon as possible if an infant is clinically stable. Mother's own milk is the best food for preterm infants. It also has many important non-nutrient advantages for preterm infants. However, breast milk alone may not meet their special nutritional needs. For this reason, it is common clinical practice to fortify human milk. Fortified human milk is an appropriate nutritional source for preterm infants compared to preterm formula and unfortified human milk. Fortification of maternal breast milk begins when feeding volume reaches 100 ml/kg/day. In the absence of mother's own milk, donor milk and premature infant formula may be used. The aim of this brief review is to discuss the current practical concepts about enteral feeding in preterm infants.

Keywords

Infant, preterm, enteral nutrition, breast milk, fortification.

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Introduction

With increasing survival of extremely premature infants, feeding practices in preterm infants are a growing concern for neonatologists because of their contribution to growth, long-term neurodevelopmental outcome and decreased morbidities. It is well known that preterm infants have higher

nutritional needs compared to term-born infants due to their accelerated growth rate and different metabolic situation.

In the 1960s and 1970s, the use of tube feeding allowed full enteral nutrition in preterm infants. However, because of very rapid advancement of feeding by this route, the number of very preterm infants who developed necrotizing enterocolitis (NEC) with enteral feedings increased. In the 1970s and 1980s feedings were routinely withheld for long periods (weeks) in order to prevent NEC. In the late 1980s it was seen that withholding of feedings did not prevent NEC but led to gut atrophy, with all its own problems. Early ("trophic") feedings were subsequently shown to be safe, i.e., without any increase in NEC.

The aim of this brief review is to discuss the current practical concepts about enteral feeding in preterm infants.

Minimal enteral nutrition

Early initiation of minimal enteral nutrition (MEN) or trophic feeding is highly recommended as a supplement to parenteral nutrition in the NICU population as soon as possible [1]. The goal of MEN is to "prime" the gastrointestinal tract with very low volume feedings. MEN increases the serum levels of gut hormones, including gastrin and gastric inhibitory polypeptide, and promotes intestinal maturation. Furthermore, MEN decreases indirect and direct hyperbilirubinemia and the risk of late onset sepsis [1-5]. Early small feedings can result in decreased feeding intolerance and a shorter parenteral nutrition period, enhancement of the postprandial response, better weight gain and improved bone mineralization [6]. There is no well-established practice for MEN, but some studies suggest that physiologic benefits occur at volumes as low as less than 1 ml/kg/day [7]. The preterm infants may benefit from minimal enteral feeding starting very slowly at 0.5-1 ml/kg two or three times a day. If the preterm infant is ready to begin trophic feeds, colostrum may be administered in trophic feeds. Although the grade of recommendation is weak, current data supports that MEN should be initiated within the first 2 days of life and advanced by 30 ml/kg/day in infants ≥ 1,000 g [8]. Feeding volumes are gradually increased regardless of the gastric residuals or as gastric emptying improves [9]. In most preterm infants weighing less than 1,500 g, parenteral nutrition is necessary to meet energy and nutrient

requirements while enteral feeds are introduced and progress together with MEN.

Methods of feeding

Tube feeding is the preferred and safest route in enteral nutrition because premature infants are unable to coordinate sucking, swallowing, and breathing. The orogastric route is better than the nasogastric one despite findings that it is more prone to displacement and vagal stimulation because the nasogastric tube causes an increase in the airway resistance [9].

Tube feeding can be administered via continuous drip using a pump or via intermittent feedings, using gravity drip through a feeding tube. In the intermittent feeding method, prescribed volume is usually given over 10 to 20 minutes every 2 or 3 hours. Intermittent feeding is preferred to continuous feeding because it is more physiological [10]. According to a new Cochrane systematic review analysis including 7 trials, involving 511 very low birth weight (VLBW) infants randomised to bolus or continuous feeding, it was found that there is no difference in time to reach full enteral feeds between the two feeding methods [11]. To date, the conflicting results of the studies comparing continuous and intermittent bolus feeding make it difficult to formulate universal recommendations regarding the best tube feeding method for premature infants of less than 1,500 grams [12]. During any kind of tube feeding, possible potential problems are reflux and aspiration, gastric perforation, vagal stimulation and bradycardia, as well as nasal erosion or palatal groove [13].

Enteral feeding tubes for preterm infants may be placed in the stomach (gastric tube feeding) or the upper small bowel (transpyloric tube feeding). In a meta-analysis of nine studies comparing transpyloric with gastric tube feeding in preterm infants, it was found that there were no statistically significant differences in the incidence of other adverse events, including NEC, intestinal perforation, and aspiration pneumonia. The authors concluded that there was no benefit in the routine use of transpyloric feeding in preterm infants [14].

Intermittent bolus feeds may be administered using a syringe to gently push milk into the stomach or using a syringe attached to the tube and allowing drip in by gravity. In one small crossover study, Symon and Cunningham compared nasogastric feeding methods (push versus gravity) [15]. They reported a trend towards a higher respiratory rate

following push feed. There was no statistical difference in the time taken to give the feeds regardless of the method used. The review concluded that there is insufficient evidence to recommend one of these methods [16].

Continuous feeds may be useful in infants who have not tolerated bolus feedings. However, the use of the continuous feeding method reduces fat delivery to the infant compared with intermittent bolus methods [17]. If the clinical condition mandates continuous feeding, three strategies will arrange fat delivery [18]. First, the syringe should be oriented with tip upright and be delivered first. Second, the feeding tube should be shortened, thus preventing loss of fat on tubing surfaces. Third, the syringe should be emptied completely at end of the infusion. This practice will prevent the loss of fat [18].

During enteral feeding, the use of an umbilical catheter does not increase the risk of NEC [19-21].

In a prospective, randomized clinical trial, Davey et al. have shown that premature infants in stable condition who were fed with an umbilical artery catheter (UAC) in place did not have an increased incidence of feeding problems compared with infants who received enteral feedings until 24 hours after removal of UACs [19].

Preterm human milk

Milk produced by mothers of preterm infants is qualitatively and quantitatively different from that of mothers who give birth at term. These differences are more evident in the early stages of lactation and tend to decrease after some weeks [22]. Neither preterm milk nor preterm formula adequately meet the requirements for premature infants. Maternal breast milk may lack some nutrients including protein, calcium, phosphorus, iron, and vitamins [23]. However, because of the many important non-nutrient advantages (anti-infective properties, positive modulation of the immune response, protective effect against NEC, enhancement of neurodevelopmental outcome, etc.), breast milk is the preferred source rather than bovine-based products or formula for feeding preterm infants [24]. The mother of the preterm infant should be encouraged to start expressing breast milk immediately after delivery. When mother's own milk is unavailable, donor human milk or preterm formula may be used in preterms after the first few hours of parenteral nutrition. Studies show that feeding preterm infants pasteurized donor human milk also reduces the risk of developing NEC when

compared with feeding infant formula [25, 26]. But donor human milk's composition is similar to the nutrient content found in mature milk. A systematic meta-analysis of donor human milk studies found slower growth and smaller increments in length and skinfold thickness in the premature infants fed pasteurized donor milk compared with formula [27]. Also, storage and processing of mother's own milk and donor milk changes some of the immunologic and nutritional properties [28]. However, mother's milk may be stored at refrigerator temperature of 4°C for 96 hours without compromising its overall integrity, including bacterial colony counts, white blood cell counts, osmolality, pH and concentrations of sIgA, lactoferrin, protein, total fat, and free fatty acids [29]. Recently, it was shown that prolonged refrigeration did not affect the fatty acid composition of breast milk, and preserved both its overall oxidative status and the activity of human milk lipolytic enzymes [30].

Preterm infant formula

When human milk is not available, premature formulas will be the primary source of nutrition. Compared to regular term formulas, the premature formulas have higher whey protein, predominantly a higher content of medium chain triglycerides as the fat, more glucose polymers in addition to lactose, and a higher Ca and P content for better bone mineralization [31].

Preterm infants born at more than 34 weeks of gestation and > 2 kg may feed on standard term formula if human milk is not available. Nutrient enriched "discharge formula" is an alternative. These formulas include more energy and nutrient than standard formula and less than preterm formula. They may increase growth rates up to 18 months corrected age, but current evidence on "post-discharge formula" for preterm infants after hospital discharge is not enough to recommend it [32]. In preterm infants, feeding with preterm formula compared with donor breast milk results in a higher rate of short-term growth but also a higher risk of developing NEC. There are limited data on the comparison of feeding with formula milk versus fortified donor breast milk [26].

Monitoring for feeding intolerance is essential, including abdominal examination and daily circumference, gastric residuals, presence of vomiting or abnormal stooling [33]. Gastric residuals are accepted as markers of gastrointestinal immaturity. However, bloody residuals appear to be

the best predictors of NEC and should be taken into account if clinically suspected [34]. Gastric residuals should be recorded prior to the next feeding. Gastric residual volume should not exceed 25-50% of the volume fed. However, large gastric residuals without other signs of NEC should not be the indication to withhold feedings [1]. With abnormal gastric residual volume, the position of the feeding tube should be checked and the body position and medical condition of the infant controlled.

Fortification

Unfortified human milk does not provide sufficient quantities of nutrients such as protein, calcium, phosphorus, iron and vitamins as well as other nutrients needed for rapid growth and normal development of the preterm infant [35]. For mother's own milk or banked donor milk, nutrient fortification is necessary. It is common clinical practice to fortify human milk with multicomponent products to compensate for the lack of calories, proteins, minerals and vitamins. Human milk fortifier is indicated in preterm infants less than 31 gestational weeks of age and/or birth weight less than 1,500 g. Use of fortifiers is not recommended prior to one week of age. Once an infant has tolerated breast milk for longer than 1 week, or reached 100 ml/kg/day, the use of fortifiers is continued until infant weight reaches 2 kg [36]. The commonly used human milk fortifiers are powdered products that are different from liquid fortifiers in that they do not further dilute maternal milk when added. Powdered human milk fortifiers have some advantages compared to the liquid fortifiers. Powdered fortifiers have higher protein, calcium, phosphorous, and zinc contents compared to the liquid form.

The optimal method for human milk fortification is still undefined [35]. Fortification can be made in three different forms [36]: standard, which is the most common used method in neonatal intensive care units (adding fixed concentrations of fortifier to maternal milk), tailored (based on milk analysis; extra protein is added to human milk according to weekly determinations of milk protein content to achieve target protein intakes at all times) [36] and adjustable (adjusting the fortification according to blood urea nitrogen [BUN] values of the preterm infant) [37, 38]. Tailored fortification appears to be the most convenient method currently available; cost and the need to analyse milk samples are limitations of this method [36].

As concerns multinutrient fortification of human breast milk, the limited available data from only one small study (39 infants participated) [39] suggest that after hospital discharge feeding preterm infants with multinutrient fortified breast milk compared with unfortified breast milk increases growth rates during infancy [40]. If the preterm infants are receiving 150 ml/kg/day of preterm formula or fortified breast milk, there is no need of vitamin supplements.

Clinical monitoring of nutrition

For optimal early nutrition in preterm infants, the goal is to achieve a growth rate similar to that of fetuses of the same gestational age. The rate of weight gain that must be achieved is 15-20 g/kg/day which is the equivalent to the rate of intrauterine fetal growth during the third trimester. But the reality is that premature infants are often unable to attain this rate due to the immaturity of the gut and mother's breast milk is not sufficient. In a large prospective study involving 1,660 preterms born between 24 and 29 weeks of gestation with birth weight < 1,500 g, it was found that most infants had not achieved the median birth weight of the reference fetus at the same postmenstrual age at hospital discharge [41].

In addition to weight-assessment, adequate growth is monitored by serial measurements of routine parameters: length and occipitofrontal circumference during follow up management of preterms must increase by 0.5-0.8 (~1) cm/week and 0.8-1.1 (~1) cm/week, respectively [26, 41-44]. Growth parameters are charted on specific growth curves for premature infants [37]. Achieving these goals requires 120 cal/kg/day enterally. The energy requirements may increase in some medical problems. As an example, infants with bronchopulmonary dysplasia (BPD) may require higher caloric intake (130-150 cal/kg/day) because of increased work of breathing [45, 46].

The preterm infant's nutritional evaluation includes weight, fluid and nutrient intake daily, length and head circumference weekly and biochemical markers such as Hb, Hct, BUN, Ca and P biweekly [47].

There is no conclusive evidence about most aspects of feeding practices. According to a recent international survey, feeding practices show marked variations in neonatal intensive care units in different countries [48]. These variations are not largely based on evidence. There is limited evidence on current feeding practices. Further large studies are

needed to find optimal enteral feeding in our current enteral feeding practices (route, feeding methods, fortification methods, etc.) for preterm infants.

Declaration of interest

The Author declares that there is no conflict of interest.

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