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Review Article

Enteral Feeding Advancements in Very Low Birth Weight Neonates - A Review Article

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Abstract
Optimal nutrition during the neonatal period is essential for growth and development throughout infancy and into childhood. Nutrients can be provided either parenterally or enterally but the aim in all infants to use full enteral feeding as soon as it is safe to do so. Because of poor co-ordination sucking and swallowing, very low birth weight infants (VLBW) are fed by gavage and are unable to regulate their own enteral intake. Therefore the rate at which feeding to be advanced must be determined by caregivers. Based largely on retrospective studies, there is concern that advancing feeding too rapidly may increase the risk of Necrotizing enterocolitis (NEC). It is thought that one possible way to prevent this condition is to limit the amount of milk feeds that infants receive each day for the first few weeks after birth. On the other hand there are potential disadvantages associated with slowing the advancement of enteral feed volumes, such as establishment of full enteral nutrition are delaying. So, controversy exists regarding role of advancement of eneral feeding. So the review has discussed the effect of slow versus rapid rates of advancement of enteral feeding volume in VLBW infants.

1. Introduction

The technological advances that have occured in the field of neonatal intensive care in the past decades have resulted in an incresed survival of premature and very low birth weight (VLBW) infants. Most very low birth weight infants who develop necrotizing enterocolitis (NEC) have received enteral milk feeds. The timing of the introduction and the rate of progression of enteral feed volumes may be modifiable risk factors for the development of NEC[1,2,3]. A recently published Cochrane meta-analysis which included five randomized controlled studies has not demonstrated any increased risk of NEC in

VLBW infants receiving a more rapid rate of feeding advancement[4]. Moreover relatively rapid advancement of enteral feeding in preterm infants may improve their growth and nutritional status[5,6,7], decrease the requirement and hazards of intravenous solutions[6], potentially shorten the length of hospitalization[6,7] and reduce the time to reach full enteral feeding[8,9].

2. Definition and prevalence of low birth weight

Low birth weight (LBW) is defined as a birth weight of a live born infant of less than 2,500 g regardless of gestational age[10]. These are further subdivided into: Very Low Birth Weight (VLBW) - birth weight <1,500 g and Extremely Low Birth Weight (ELBW) - birth weight <1,000 g. The global prevalence of LBW is 15.5%, which means that about 20.6 million LBW infants are born each year; 96.5% of them are in developing countries[11]. The prevalence of LBW in Bangladesh is 36%[12]. Low birth weight may directly or indirectly contribute to 60–80% of all neonatal deaths[13].

3. Cares of low birth weight neonates

Countries can substantially reduce their infant mortality rates by improving the care of low birth weight infants. Experience from both developed and developing countries has clearly shown that appropriate care of LBW infants, including feeding, temperature maintenance, hygienic cord and skin care, and early detection and treatment of infections can substantially reduce mortality in this highly vulnerable group. Interventions to improve feeding are likely to improve the immediate and longer-term health and wellbeing of the individual infant and to have a significant impact on neonatal and infant mortality levels in the population.

Better feeding of pre-term babies was one of the first interventions in the 1960s in the United Kingdom and was associated with reduced case fatality for pre-term babies in hospitals before the advent of intensive care[14]. Improving the survival of very low birth weight (VLBW) infants depends in large part upon understanding the physiologic capabilities of their immature organ systems and providing appropriate support as they mature. Advances in the nutritional support of these infants have contributed to the better outcomes we have come to expect today, even for the smallest infants.

4. Gastrointestinal development

The level of gastrointestinal (GI) maturity of an individual infant is a major determinant of whether the infant will be able to meet nutritional needs by sole use of the GI tract or if parenteral means will be necessary. The GI tract is not only an organ for digestion and absorption of nutrients; it also performs major endocrine, neural, and immunologic functions. Readiness to feed by mouth is a major developmental milestone for the premature neonate. Mechanical function of the GI tract, the major determinant of this readiness, includes suck–swallow coordination, gastroesophageal sphincter tone, gastric emptying, and intestinal motility. They function along a continuum in the GI tract to propel food to areas where digestive absorptive functions occur.

4.1 Suck–swallow coordination

Very premature infants prior to about 32 weeks' gestation have a suck–swallow pattern that differs from that of the more term infant[15]. The very preterm infant is not able to coordinate sucking activities during the swallowing process. Furthermore, preterm infants swallow preferentially at different phases of respiration than those of their full-term counterparts[15] and this results in an inefficient and potentially dangerous pattern that may result in aspiration of gastric contents into the trachea and lungs if these infants are fed by mouth. Thus, most of the very low birth weight (VLBW) infants are tube fed. Feeding directly into the stomach and/or intestine by gastric and transpyloric feeding, respectively, bypasses the immature suck–swallow coordination in these infants, but remains subject to other immaturities such as gastroesophageal reflux (GER), poor

gastric emptying, and immature small intestinal motility.

4.2 Gastric emptying

Gastric emptying is slower in premature than in term infants[16] and leads to a greater residual volume of gastric contents. Several studies suggest that therapeutic agents that increase gastric emptying rates in children and adults are also effective in premature infants. However, the efficacy and safety of this agent would need to be studied in larger randomized trials.

4.3 Intestinal motility

The small bowel motility patterns are poorly developed before 28 weeks' gestation. Gastroanal transit ranges from 8 to 96 hours in premature infants as compared with 4 to 12 hours in adults. Small intestine showed disorganized motility patterns between 27 and 30 weeks' gestation, which progress to a more mature pattern at 33 to 34 weeks' gestation[17].

5. Enteral feeding in very low birth weight infants

Feeding the LBW infant involves decisions about what milk to feed, what nutritional supplements to give, how to feed, how much and how frequently to feed, what support is needed, and how to monitor. Current available guidelines on feeding the LBW infant are generally based on research in developed countries and may not be applicable in developing country settings. Further, many of the current feeding guidelines are not practical in resource-poor settings[18]. Experience from both developed and developing countries has clearly shown that appropriate care of low birth weight (LBW) infants, with adequate attention to feeding can improve their survival.Very low-birth-weight infants are an extremely heterogeneous group of newborns and include those with very immature gestational age and those who are more mature but extremely growth retarded. Feeding related complication are markedly increased in VLBW, because most VLBW infants are also premature, it may be difficult to differentiate problems due to prematurity from those due to very small size. In general, the lower a baby's birth weight, the greater are the risks for complications.

5.1 Initiation of enteral feeding

A lack of enteral nutrients affects intestinal motility, perfusion, and hormonal responses[19]. It is possible that a prolonged delay in starting feeds in preterm neonates may be partly responsible for the common problems of feed intolerance encountered in these newborns. However, enteral fasting during the early neonatal period also has potential disadvantages. Because gastrointestinal hormone secretion and motility are stimulated by enteral milk, delayed enteral feeding could diminish the functional adaptation of the immature gastrointestinal tract[20]. Consequent intestinal dysmotility may exacerbate feed intolerance leading to a delay in establishing enteral feeding independently of parenteral nutrition.

Enteral fasting might also cause hyperbilirubinaemia by increasing enterohepatic recirculation of bilirubin and delaying hepatic enzyme maturation. Prolonging the duration of use of parenteral nutrition may be associated with infectious and metabolic complications that have adverse consequences for survival, duration of hospital stay, growth and development[21, 22].

5.2 Trophic feeds or minimal enteral nutrition (MEN)

Trophic feeding (also referred to as minimal enteral nutrition, gut priming and hypocaloric-feeding) means feeding small volumes up to 24ml/kg/day[23,24,25]. Trophic feeding was developed and adopted into clinical practice as an alternative to complete enteral fasting for very preterm or VLBW infants during the early neonatal period[26].

5.3 Progressive enteral feeding

Progressive enteral feeding is defined as the intention to advance feed volumes in excess of

trophic feeding[27]. In current clinical practice, the introduction of progressive enteral feeds for very low birth weight infants is often preceded by a period of enteral fasting or "trophic feeding"[23,24,25]. Data from observational studies suggest that using feeding regimens that include delaying the introduction of progressive enteral feeds for about five to seven days after birth reduces the risk of necrotizing enterocolitis[25,28]. However, there may also be potential disadvantages associated with delaying the introduction of progressive enteral feeds. Because gastrointestinal hormone secretion and motility are stimulated by enteral milk, delayed enteral feeding could diminish the functional adaptation of the gastrointestinal tract[20]. It has been argued that the risk of necrotizing enterocolitis should not be considered in isolation of these other potential clinical outcomes when determining feeding policies and practice for very low birth weight infants[22,25].

A Cochrane review[27] which included five randomized controlled trials (RCT) in which a total of 600 infants participated very preterm or very low birth weight infants participated with only a minority of participants being of extremely low birth weight or extreme preterm gestation,do not provide evidence that delayed introduction of progressive enteral feeds reduces the risk of NEC in VLBW infants.

5.4 Volume during enteral feeding advancement

There are no fixed guidelines about volume during advancement**.** The enteral feeding volume increment that have been used in the earlier studies have been variable[29,6,5,30,31,7,8,9]. The volume increments in slow advancement groups have ranged from 10 ml/kg/day to 23ml/kg/day. The volume increments in rapid advancement groups have ranged from 15 ml/kg/day to 45ml/kg/day.

Among these available studies, seven were randomized controlled studies and two were case control studies. InBook et al.[29] enteral feeding volumes were advanced at 10 ml/kg/day versus 20 ml/kg/day as slow and rapid group advancement. In Rayyis et al.[5] feeding advancement in infants weighing <1500 grams were 15 ml/kg/d in slow advancement and 35 ml/kg/d in rapid advancement group. In Caple et al.[6] feeding advancement in infants weighing 1000 to 2000 grams were 20 ml/kg/d in slow advancement and 35 ml/kg/d in rapid advancement group. In Salhotra and Ramji[7]feeding advancement in infants weighing <1250 grams were 15 ml/kg/d in slow advancement and 30 ml/kg/d in rapid advancement group. In Krishnamurthy et al.[8] feeding advancement in infants weighing <1500 grams were 20 ml/kg/d in slow advancement and 30 ml/kg/d in rapid advancement group. In Karagol et al.[9] feeding advancement in infants weighing 750 to 1250 grams were 20 ml/kg/d in slow advancement and 30 ml/kg/d in rapid advancement group. Though statistically not yet proven most clinician preferred slow advancement of feeding due to fear of NEC[28].

6. Necrotizing enterocolitis (NEC) and its relation with feeding

NEC is a syndrome of acute intestinal necrosis of unknown etiology, affects about 5% of very preterm (< 32 weeks) or very low birth weight (VLBW) (< 1500 grams) infants (Holman et al. 1997). The incidence of NEC varies across different neonatal units and periods, ranging from 1 to 22% in very low birth weight (VLBW) infants (Lin and Stoll 2006). In the latest NICHD neonatal network cohort (1999– 2001), about 7% of VLBW babies developed proven NEC (> stage II), with about half undergoing surgery[32]. The associated mortality rate is > 20%.

Infants who develop NEC experience more nosocomial infections, have lower levels of nutrient intake, grow more slowly, and have longer durations of intensive care and hospital stay than gestation comparable infants who do not develop NEC[33]. NEC is also associated with a higher incidence of long-term neurological disability, which may be a consequence of

infection and under-nutrition during a critical period of brain development[34].

NEC rates were inversely related to birth weight. Intestinal immaturity due to prematurity, poor intestinal motility, umbilical catheter placement, systemic infections, early enteral feeding (EEF) and rapid increment of enteral feedings are cited as major risk factors for NEC in addition to indomethacin and corticosteroid use[30].

7. Studies about different feeding advancement

Book et al.[29] reported in a prospective study increments of enteral feeding of 10 to 20 mL/kg per day have been reported as safe. One of the latest study from India reported neonates in the rapid feeding advancement group achieved full volume feedings before the slow advancement group (median 7 days vs. 9 days), had significantly fewer days of intravenous fluids (median 2 days vs. 3.4 days) ($p < 0.001$), shorter length of stay in hospital (median 9.5 days vs. 11 days) ($p = 0.003$) and regained birth weight earlier (median 16 days vs. 22 days) ($p < 0.001$). There were no statistical differences in the proportion of infants with apnea, feed interruption or feed intolerance[8].

Another earlier study in India Salhotra and Ramji[7] were enrolled 53 infants for the study (27 in the fast advancement group and 26 in the slow advancement group). The infants in the fast group reached full enteral intake of 180 ml/kg/day significantly earlier (10 ± 1.8 days) than in the slow group (14.8 ± 1.5 days). The two groups were comparable for episodes of feed intolerance, apnea, NEC. Infants in the fast group regained birth weight significantly earlier (median 18 days) than in the slow advancement group (median 23 days). The authors concluded that stable VLBW neonates can tolerate rapid advancements of enteral feeding without increased risk of adverse effects.

Caple et al.[6] were enrolled total of 155 infants, 72 infants in the intervention group and 8 intervention group and 83 in the control group. Infants in the intervention group achieved full volume feedings sooner (7 vs 10 days, median), regained birth weight faster (11 vs 13 days, median), and had fewer days of intravenous fluids (6 vs 8 days, median). Three infants in the intervention group and 2 control infants developed NEC for an overall incidence of 3.2%.

Morgan et al.[4] identified five randomized controlled trials in which a total of 588 infants participated in a meta analysis published in The Cochrane library in 2013. The trials were undertaken in neonatal care centers in North America[5,6], in India[7,8] and in Turkey[9] within the past 10 to 15 years. Few participants were extremely preterm, extremely low birth weight or growth restricted. The trials defined slow advancement as daily increments of 15 to 20 ml/kg and faster advancement as 30 to 35 ml/kg. Meta-analyses did not detect statistically significant effects on the risk of necrotizing enterocolitis or all-cause mortality. Infants who had slow advancement took significantly longer to regain birth weight (reported median differences two to six days) and to establish full enteral feeding (two to five days).

Authors' concluded that the available trial data suggest that advancing enteral feed volumes at slow rather than faster rates does not reduce the risk of necrotizing enterocolitis in very preterm or VLBW infants. Advancing the volume of enteral feeds at slow rates results in several days delay in regaining birth weight and establishing full enteral feeds but the long term clinical importance of these effects is unclear. The applicability of these findings to extremely preterm, extremely low birth weight or growth restricted infants is limited. Further randomized controlled trials in these populations may be warranted to resolve this uncertainty.

8. Conclusion

This review on feeding advancement did not provide evidence that slowly advancing enteral feed volumes reduces the risk of NEC in very preterm or VLBW infants.

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