Nutritional management of surgical newborns and infants in the acute phase and during follow up

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Abstract

The neonatal period represents a crucial stage of life since it is characterized by the development of organ structure and function. Early life is particularly susceptible to environmental factors through a programming effect. As a result, inadequate nutrition in early life leads to long-term mental and physical developmental alterations and increased mortality and morbidity. In this review, we will summarize available evidence with a particular focus on metabolic responses to surgical trauma, nutritional strategies that can be implemented in surgical infants and specific barriers to nutritional support after surgery.

Introduction

The neonatal period represents a crucial stage of life since it is characterized by the development of organ structure and function, particularly the brain. Even though older infants have already adapted to challenges posed by the postnatal environment, they are still growing; hence, they need to modulate their physiological and nutritional requirements with the aim of achieving growth and responding to noxious stimuli, such as infection and surgery, which interfere with the establishment of homeostasis.[1]

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Key words: Surgical infant; Nutrition; Newborns.

Conflict of interest: the author declares no potential conflict of interest.

Funding: funded by Merqurio Editore S.r.L, with the unconditional contribution of Nestlè Italiana S.p.A.

Received for publication: 19 April 2018.
Accepted for publication: 20 April 2018.

La Pediatria Medica e Chirurgica 2018; 40:197
doi:10.4081/pmc.2018.197

It is widely acknowledged that early life is particularly susceptible to environmental factors through a programming effect. As a result, inadequate nutrition in early life leads to long-term mental and physical developmental alterations and increased mortality and morbidity.[2]

Metabolic response to surgical trauma

Undergoing a surgical operation initiates a so-called *stress response* that determines a cascade of physiological events, including the activation of inflammatory pathways that enable the initiation of tissue repair. Accordingly, specific metabolic changes occur with the aim of increasing the availability of substrates necessary for essential organs and for the healing process.[3]

Newborns, particularly if they are premature and/or growth restricted, endure only a short period of starvation due to their rapid growth and limited energy and protein stores.[4] For instance, a preterm newborn with a birthweight of 1000 g has approximately 1.5% fat and 9% protein and an energy storage equal to 110 kcal/kg.[5] Hence, if adequate nutritional support is not promptly provided, malnutrition rapidly occurs. In contrast, a full-term newborn can tolerate a few days of undernutrition due to higher fat stores of approximately 600 g. Furthermore, energy requirements and metabolic rates are higher in newborns than in children or adults. Specifically, newborn energy intakes must meet the requirements for ensuring maintenance metabolism (40-70 kcal/kg/day) and growth (50-70 kcal/kg/day) and replacing energy losses (20 kcal/kg/day). A provision of 100-120 kcal/kg/day of enteral nutrition meets newborn energy requirements, whereas parenteral nutrition of 80-100 kcal/day is sufficient due to the lack of energy loss in excreta and the provision of a thermoneutral environment with an incubator that prevents the use of energy for thermoregulation. The total energy requirement of premature infants is higher than that of full-term infants, ranging from 110 to 160 kg/kg/day.[6,7] The major contributing factors to resting energy expenditure for stabilized surgical newborns are body weight; heart rate, which reflects haemodynamics and metabolic status; and postnatal age. Reported data on resting energy expenditure in newborns have been inconsistent, with values ranging from 33.3 to 50.8 kcal/kg/day, probably reflecting the different size of metabolically active tissues. Of note, preterm infants have been reported to have higher resting energy expenditure than full-term newborns.[3,6]

Regarding protein intake, infants need to be in positive nitrogen balance since proteins, when they are associated with adequate energy intake, allow for adequate growth and development. Newborn infants require 2.5-3.0 g/kg/day of proteins; protein requirements are even higher in preterm infants.[3,6]

Inadequate nutrition further impairs the stress-induced catabolic status of newborns that have undergone a surgical intervention or are critically ill, contributing to poor tissue repair and an increased risk of postoperative complications.[8]

Newborns show a different response to surgery compared to older children and adults. Indeed, while between 15 and 30% of adults are hypermetabolic in the postoperative period, newborns exhibit only a small increase in energy resting expenditure following major abdominal surgery, returning to normal values within 12-24 hours. The increase in resting energy expenditure is higher when a surgical operation occurs after 48 hours of life than when it occurs during the first 48 hours of life. It can be hypothesized that the endogenous opioids secreted in the perinatal period can downregulate endocrine and metabolic pathways following surgery. No significant changes in protein metabolism in newborns have been detected. These findings could reflect the utilization of energy and protein for tissue healing rather than growth and can explain the failure to thrive exhibited by infants with severe illnesses.[3,6,9]

When children and particularly newborns are exposed to malnutrition during periods of critical illness and surgery, the concomitant metabolic requirements for growth and neurodevelopment cannot be fully met, leading to potential negative health consequences that track into adulthood. The provision of early nutritional support allows infants to preserve vital organ function and avoid loss of lean body mass.[9] On the other hand, it has to be taken into account that overfeeding leads to increased CO_2 production, making it more difficult to wean infants from respiratory support and contributing to the impairment of immune function and vital organs.[10]

Parenteral nutrition

Immediately after surgical intervention, it is often not possible to provide enteral feeding with adequate intake in order to support growth and development. Therefore, it is necessary to deliver parenteral nutrition, which enables the establishment of adequate macronutrients and micronutrients while intestinal motility and absorption improve and supplemental enteral feeding can be gradually introduced. The percentage of calories and protein given enterally is then increased at the expense of parenteral macronutrients intake. However, this transition from parenteral to total enteral nutrition may take a relatively long time.

Adequate protein intake is essential for preventing catabolism and promoting growth. Proteins should be provided in association with adequate energy intake in order to avoid their use as an energy source. Protein oxidation is actually an uneconomic metabolic process since energy production form carbohydrates and lipids provides higher energy at a lower metabolic cost. Careful attention should also be paid to patients with severe malnutrition or additional losses (*i.e.*, jejunostomy, ileostomy), who have particularly high protein requirements.[6,11,12]

Energy intake during parenteral nutrition is provided by carbohydrates and lipids. The quantity of glucose that can be infused safely differs according to infants' clinical condition and maturity. Specifically, infants born preterm and/or with a low birth weight may have an impaired ability to metabolize glucose. When glucose levels exceed metabolic needs, lipogenesis occurs, leading to new fat deposition and the worsening of respiratory acidosis due to the increased production of CO_2, along with further exacerbation of respiratory distress. The lipid oxidation rate is affected by glucose intake and resting energy expenditure. It has been reported that if glucose intake exceeds basal energy requirements, lipogenesis from glucose is higher than lipid oxidation, preventing the use of intravenous lipids as an energy source. Accordingly, glucose intake exceeding 18 g/kg/day is not recommended in stable surgical newborns receiving parenteral nutrition.[6,11,12]

Lipid emulsions are an essential part of parenteral nutrition, both as an energy supply delivered as an iso-osmolar solution at a low volume, both as a source of essential fatty acids, even though their long-term use has been associated with the development of cholestasis, cholelithiasis, hepatic steatosis and hepatic fibrosis. Liver disease may progress to biliary cirrhosis and portal hypertension (intestinal failure-associated liver disease, IFALD). Soy-based intravenous lipid solutions that contain high n-6 to n-3 polyunsaturated fatty acids ratios have been particularly implicated in determining hepatic dysfunction. Specifically, the factors associated with IFALD in infants receiving a high intake of n-6 polyunsaturated fatty acids with soybean oil-based lipid emulsions are a high intake of n-6, which leads to the production of proinflammatory mediators, high provision of phytosterols and limited alpha tocopherol supply. New lipid emulsions based on mixtures of different oils, including soybean oil, medium-chain triglycerides from coconut oil and/or olive oil and/or fish oil, may be recommended, along with the treatment and management of other risk factors, in order to reduce the risk of cholestasis or IFALD development.[13-15]

Immediately after the surgical intervention, attention should also be paid to electrolyte balance on parenteral nutrition with special consideration of infants with ileostomy, significant colon resection and/or impaired colonic function, who can lose a great amount of sodium in their faeces. If sodium losses are not adequately replaced, compensatory hyperaldosteronism can arise, and as a result, an increase in urinary potassium loss can occur.[11,12]

Although parenteral nutrition is of major importance for the management of surgical infants when there is need to bypass the gastrointestinal tract to provide nutrition and fluids, its use is associated with significant complications, such as the previously mentioned intestinal failure-associated liver disease, catheter malfunction and the development of catheter-related bloodstream infections and/or thrombosis. Hence, parenteral nutrition volume should be gradually reduced to discontinuation as soon as a slow and carefully monitored enteral nutrition approach can be implemented.

Enteral nutrition

Whenever possible, enteral feeding is preferred since even small quantities of enteral feedings prevent the deterioration of epithelial barrier function and disruption of tight junctions and promote the maintenance of normal intestinal villi, the release of hormones and local peptides, and the establishment of a healthy microbiome.[16] Furthermore, it has been reported that stimulation of the gastrointestinal tract through the delivery of enteral nutrition positively modulates immune function, thus contributing to reduced infection and inflammation risk.[17]

Breast milk is the preferred nutrition choice for all infants considering its particular content in terms of macronutrients, micronutrients and bioactive compounds and the several health benefits associated with breastfeeding, including the reduced risk for developing infections.[18] If mothers' milk is not available, donor human milk should be the second choice for at least preterm infants, who are more prone to developing gastrointestinal intolerance and infections and present gastrointestinal immaturity.[19]

When feeding human milk to preterm infants, fortification is necessary in order to meet the high nutritional requirements of these infants.[20,21] Even after necrotizing enterocolitis development, fortification is required in order to promote adequate growth

even though the optimal timing of its introduction has not been elucidated yet. The use of human milk-based fortifiers has been advocated so that infants can be fed an exclusive diet of human milk, which has been associated with more beneficial effects than feeding human milk fortified with cow's milk derived fortifiers.[12]

If human milk is not available, there is a lack of consensus on whether a hydrolysed formula, either as extensively or partially hydrolysed formula, should be used as a first choice rather than intact cow's milk formula.[12,22,23] It has also to be taken into consideration that the use of hydrolysed formulas has been associated with faster gastric emptying and intestinal transit time, which may not be beneficial in infants who have undergone bowel length reduction. On the other hand, hydrolysed formulas have been reported to promote more efficient protein digestion, even though available data are not conclusive.[24] Remarkably, human milk contains both proteases and antiproteases that probably modulate the proteolysis that occurs within the mammary gland. Higher concentrations of hydrolysed proteins, mainly caseins, have been found in preterm milk relative to term milk.[25] Within this context, it must be considered that the industrial hydrolysis process may release peptides with unknown biological functions.[26] Some commercial formulas contain free amino acids rather than proteins or peptides; their use is generally well tolerated and has been associated with a shorter duration of parenteral nutrition and reduced risk of developing allergies.[27] However, when taking care of preterm infants, clinicians should be bear in mind that specialized formulas have not been designed to specifically meet the high nutritional requirements of preterm infants.

Formulas with a high content of medium chain triglycerides (MCT) are preferred when fat malabsorption coexists. MCT are easily absorbed into the portal system since their digestion is less dependent on optimal bile secretion. Fat intake greatly contributes to better growth; moreover, fatty acids metabolized to short chains appear to promote gastrointestinal adaptation and functions.[12,22,23]

Enteral nutrition may be delivered through bolus feeding, continuous feeding or a combination of both. Bolus feeding mimics a physiological situation and promotes gastrointestinal motility, enterohepatic circulation of bile acids, gall bladder contraction and pulsatile release of gastrointestinal hormones. However, bolus feeding may result in increased feeding intolerance.[28] Bolus feedings are easier to deliver than continuous feeding since no feeding pump is required and feedings are given over 15 to 20 minutes, commonly every 3 hours. When feeding preterm infants and newborns immediately after surgical intervention, an interval of two hours between feedings may be preferred.[6] Continuous feeding is usually used in infants with delayed gastric emptying, gastroesophageal reflux or intestinal malabsorption or gastrointestinal intolerance. Continuous feeding may lead to increased nutrient absorption, energy efficiency, and splanchnic oxygenation;[28] however, it has also been associated with an alteration in normal physiology, such as an enlarged, non-contractile gall bladder.[29] Continuous feeding is generally delivered over 24 hours.

Promotion of the achievement of independent oral feeding, when the coordination of sucking, breathing and swallowing is possible, is of great importance. It is widely acknowledged that prolonged use of a naso- or oro- gastric tube in the neonatal period represents a non-physiologic stimulus that can negatively interfere with subsequent behaviour feeding.[30]

Barriers to nutritional support after surgery

The provision of adequate nutritional support during periods of critical illness and surgery is of major importance and has contributed to decreased mortality and morbidity rates in newborns.[6] However, nutritional management of surgical infants is challenging. After cardiac surgery, fluid restriction may be necessary, making it difficult to provide adequate amounts of nutrients. The parenteral route may be preferred since it enables the provision of a more concentrated form of nutrition, whereas enteral nutrition needs larger volumes of fluid to guarantee comparable nutrition, even though it offers significant advantages in terms of promoting gastrointestinal integrity and maturation. Furthermore, the occurrence of systemic hypotension and decreased cardiac output compromises blood flow to the splanchnic bed, which may determine reduced peristalsis and poor feeding tolerance.[9,31]

Regarding surgical pulmonary diseases, growth failure in patients with congenital diaphragmatic hernia is a relatively common finding ascribed to the elevated work of breathing with increased metabolic demand secondary to pulmonary hypoplasia. Within this context, the optimization of oral nutrient intake may be difficult due to the occurrence of gastrointestinal intolerance with frequent vomiting episodes, gastro-oesophageal reflux disease and oral aversion due to the prolonged use of nasogastric tubes.[32,33]

Major difficulties are encountered even after surgical interventions on the gastrointestinal tract. The establishment of oral feeding in infants with oesophageal atresia is challenging due to the occurrence of postoperative anastomotic leaks, stenosis requiring dilatation and pulmonary complications.[33]

Gastrointestinal dysmotility, which may persist for several months after a surgical intervention, characterizes infants with gastroschisis after reduction of the intestines and abdominal closure, making it difficult to advance enteral volumes due to the occurrence of poor feeding tolerance.[34]

Short bowel syndrome

Surgical resection of the bowel may be necessary when several different conditions are diagnosed, such as necrotizing enterocolitis, intestinal atresia, gastroschisis, and malrotation with volvulus. It is important to bear in mind that, in nutritional management of infants, large fluid and electrolyte losses in ostomy have to be taken into account if recanalization of the intestinal tract must be postponed. Following surgical intervention, bowel length may be reduced to such an extent that it causes short bowel syndrome, which is defined as the need for prolonged parenteral nutrition for usually more than 3 months. However, it must be taken into account that, in addition to the reduction of the intestinal length, impaired intestinal function may coexist, further contributing to inadequate absorption of enteral nutrients.[11,12,23,35] In Table 1,[11] the

Table 1. Most common causes of short bowel syndrome in newborns and infants.

Cause	%
Necrotizing enterocolitis	35
Intestinal atresia	25
Gastroschisis	18
Malrotation with volvulus	14
Hirschsprung disease with proximal extension of aganglionosis into the small bowel	2
Other	6

most common causes of short bowel syndrome in newborns and infants are indicated.

The frequency of surgical short bowel syndrome was reported to be 0.7% among very low birth weight infants born during the period from 2002 to 2005 at the National Institute of Child Health and Development Neonatal Research Network Centres, and it showed an inverse relationship with birth weight.[36]

Surgical short bowel syndrome is one of the most common causes of intestinal failure, a condition characterized by reduction of the functional gut mass below a critical point necessary to support growth, hydration, and/or electrolyte balance. Salvia *et al.*[35] have reported an occurrence rate of intestinal failure of 0.1% among live-birth newborns and 0.5% among those admitted to the NICU.

Nutritional management of short bowel syndrome aims to promote gut adaptation and eventually achieve enteral independence while supporting growth and nutrition with parenteral nutrition. The clinical course of infants developing short bowel syndrome is characterized by three subsequent clinical stages. After approximately 1 week after surgical intervention, during which recovery from postoperative ileus occurs, the infant enters the acute phase, which lasts for up to 3 weeks. During this phase, efforts are focused on infant stabilization and on early restoration of fluid and electrolyte homeostasis by intravenous fluids and parenteral nutrition. The recovery phase may last several months and is characterized by gradual reduction of diarrhoea and ostomy output while enteral feedings are initiated and progressively increased according to feeding tolerance and reductions in the volume of parenteral nutrition. In this phase, however, parenteral nutrition guarantees the provision of adequate intake of macronutrients and micronutrients in order to support growth and development. In the maintenance phase, the volume of enteral nutrition is maximized and tolerated, whereas parenteral nutrition volume is minimized with the ultimate aim of discontinuation of parenteral nutrition. Oral feeding is also implemented. The time interval necessary to reach the maintenance phase is variable depending on the infant's clinical conditions and complications.[12,23]

Conclusions

On the basis of available data in the literature, optimization of nutrient delivery and metabolic support of infants undergoing a surgical intervention is mandatory in order to prevent the negative effects of malnutrition, which include increased mortality and morbidity in the short and long term, and to promote infant growth and development.

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