Review of selected papers from the recent literature on parenteral and enteral nutrition

Amino acids for parenteral and enteral nutrition in premature and low-birthweight infants

SALLE et al. [1] report a controlled study in 31 infants of the use of 2 types of amino acid solutions for premature infant nutrition in the first days of life, one of the solutions being specially adapted for preterm babies. Plasma amino acid levels in premature infants receiving the adapted solution were close to those observed in cord blood. The results show that using amino acid solutions, adapted to preterm babies as a supplement to parenteral nutrition during the first days of life, allowed a progressive increase in nitrogen intakes without inducing dangerous plasma levels of some amino acids. Serum ammonia level was also lower.

Metabolic immaturity has changed the essentiality of, and quantitative need for a variety of amino acids. HELMS et al. [2] have compared changes in weight, nitrogen balance, direct bilirubin and plasma amino acid concentrations in 25 preterm neonates receiving a new paediatric amino acid formulation compared with a standard amino acid solution. All infants had gastro-intestinal diseases, such as necrotizing enterocolitis, gastrochisis, duodenal atresia or tracheo-oesophageal fistula. The weight gain was significantly greater in the group of twelve receiving the special solution, and nitrogen balance was significantly higher in this group. The plasma amino acid concentration was within a normal post-prandial, neonatal target range, whereas methionine, glycine and phenylalanine were above, and tyrosine was below the range in the 13 neonates receiving the standard crystalline amino acid solution.

SCHRÖDER and PAUST [3] have studied the effect of different quantities of amino acid infusion, in comparison with enteral feeding. They measured the plasma amino acid levels in preterm infants receiving standardized supplementary parenteral nutrition with 2 different amino acid volumes, using formula-fed preterm infants as controls. Taurine was not included in the infusate, and cystine was present in low amounts. The authors agree that a dosage of 1.8 g amino acid/kg/day is appropriate for supplementary parenteral nutrition in newborn infants and suggest that increasing the amino acid volume step-by-step within the first 3 post-natal days may facilitate the maintenance of plasma homeostasis. However, these measurements do not permit conclusions regarding actual amino acid requirements. A stable isotope technique may well allow a new approach to the defining of an optimal amino acid supply for the supplementary parenteral nutrition of sick preterm infants.

SHULMAN et al. [4] have encountered premature infants who have developed hypoproteinaemia, even though they have received the recommended parenteral intakes of protein and energy. One classical finding of protein deficiency is a change in hair colour and natural curl, the hair becoming brittle and sparse. When protein status improves the natural colour of the hair shaft contrasts with the depigmented band and creates a striped appearance, reminiscent of a flag. This “flag sign” is a reliable marker of protein deficiency. Infants who had developed the “flag sign” were compared with a control group in order to determine the clinical situations that might predispose them to protein deficiency. The results show
that necrotizing enterocolitis and surgery were significantly more frequent in the group of infants with the "flag sign". One may speculate that both conditions may have increased the metabolic rates and/or nitrogen losses in this group, compared with the controls. Serum albumin concentrations did not differ between the 2 groups, which may appear surprising. Previous studies however have shown that serum albumin is not the most sensitive marker for protein status in premature infants, and little association has been demonstrated between hypochromotrichia and serum albumin levels. The results of this study suggests that the protein requirements of these premature infants was probably higher than is commonly acknowledged.

The effects of 2 extremes of dietary intake on protein accretion in preterm infants have been studied by ROBERTS and LUCAS [5]. The results of this study confirm that the diet fed to premature infants has a significant influence on short-term growth rate. Infants fed with banked drip breast milk (BBM) do not achieve the 50th centile of intra-uterine growth rate, and grew 29% more slowly than those fed a preterm formula, despite a substantially greater intake of milk. The cause of the slower growth in the infants fed BBM was apparently the low concentrations of nutrients in the milk. The diet also exerted a major influence on body composition, whereas infants fed BBM gained weight at 71% of the rate of those fed preterm formula, calculated protein accretion on BBM being less than half that seen with formula feeding. As a result, the infants fed BBM had protein concentrations in new tissue that were 21% below the minimum level of the normal range for the third trimester in utero. The difference in protein deposition between the groups might indicate that the infants fed BBM deposit more fat and less lean body mass during growth than infants fed preterm formula. These findings indicate that the use of BBM as a sole diet for premature infants may result in a suboptimal pattern of nutrient accretion.

MELEGH et al. [6] have studied oral L-carnitine supplementation in 10 prematures requiring combined enteral and parenteral nutrition. The effect of this supplementation has been studied on the values for plasma ketone bodies and triglycerides. The results suggest that L-carnitine supplementation in low-birthweight newborns promoted ketone body formation from endogenous stores as well as from exogenous fat supply, and thus may enhance triglyceride utilization. The carnitine content of pooled milk, despite of its variability, was sufficient to maintain the plasma carnitine level in the control group during the observation period.

References


Fats in parenteral nutrition

BRANS et al. [7] have studied 39 low-birthweight neonates who required total parenteral nutrition, and who were submitted to one of three regimens of administration of fat emulsion for a period of 8 days. Free fatty acids in high concentrations may encroach on the bilirubin binding site and displace bilirubin from albumin. Liberation of bilirubin may result in a rising concentration of unbound bilirubin, potentially increasing the risk of encephalopathy. In this clinical study, however, the concentration of total free fatty acids seemed to have little effect on the concentration of apparent
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Unbound bilirubin, as measured by the peroxidase assay; yet there was no correlation between apparent unbound bilirubin concentrations and concentrations of free fatty acids. There was a trend towards greater variability in apparent unbound concentrations with the intermittent regimen, and previous studies have indicated that neonates who received intermittent infusions of fat emulsions showed evidence of considerable fluctuations in free fatty acid:albumin molar ratios, and also had very high ratios. This may be another argument in favour of continuous infusion of fat emulsion at a constant rate.

Depression and stimulation of polymorphonuclear leukocyte (PMN) function after fat emulsion infusion have been reported in adults. USMANI et al. [8] report the effect of intravenous fat emulsion on in vitro oxidative and chemotactic functions of PMN’s from healthy neonates. The study indicates no impairment of oxidative metabolic or chemotactic functions when neonatal and adult PMN’s are exposed to 25, 50 or 100 mg/ml concentrations of intravenous fat emulsion. Previous in vitro studies on PMN’s from adults have shown markedly decreased chemotactic activity, and suggest that impairment of PMN movement and oxidative metabolic functions could be responsible for the increased susceptibility to infections seen in patients receiving parenteral nutrition. The authors, however, found no abnormalities in chemiluminescent and chemotactic activity at any of 3 intravenous fat emulsion concentrations.

HELMS et al. [9] have demonstrated an enhanced lipid utilization in infants receiving oral L-carnitine during long term parenteral nutrition, evidenced by increased ketogenesis in the group receiving 50 μmol/kg/day of L-carnitine. This supplementation increased total plasma carnitine concentration, but values remained at the lower end of the normal range for similarly aged breast-fed infants or those receiving formula containing L-carnitine. The increased mean plasma β-hydroxybutyrate represents modestly improved endogenous fat utilization in the carnitine supplemented group. The data suggest that not only preterm infants, but also term infants receiving long-term total parenteral nutrition (TPN) are unable to produce adequate quantities of carnitine. It remains to be determined whether this inability to generate carnitine relates to continued immaturity of endogenous biosynthesis, selective inhibition of synthesis by a component or components of the nutritional solution, or alterations in liver function.

References


Minerals in parenteral nutrition

AIKEN and LENNEY [10] have studied 15 infants with birth weights below 1,500 g, who required intravenous feeding from birth, receiving 2 feeding regimens differing only in their calcium and phosphate content. In 5 infants the diet provided calcium and phosphate intakes of 0.55 and 0.44 mmol/kg/day, and ten received 1.08 and 0.89 mmol/kg/day respectively. Infants given low calcium and phosphate intakes had lower plasma and urinary phosphate, but similar urinary calcium excretion to those given high intakes. Plasma calcium concentrations were higher in infants on the low-intake regimen. In the cases given high calcium and phosphate intakes, plasma phosphate concentration was inversely related to weight gain. The biochemical findings in the group receiving low intakes suggest the development of phosphate deficiency. Calcium and phosphate retention with high intakes may be limited by a number of factors, amongst which are inappropriate calcium:phosphate ratio and renal immaturity. The results suggest that a major factor limiting calcium
and phosphate retention from intravenous feeding in immature infants may be renal tubular leakage of these ions, particularly phosphate in association with sodium leakage. The practice of infusing a high calcium, alternating with a high phosphorus content of the infusate, has been advocated as a means to avoid precipitation of larger quantities of calcium and phosphorus. However, this practice has the potential risk of causing hypercalcaemia and hypercalciuria during high calcium infusion, and hypocalcaemia during high phosphorus infusion.

KOO et al. [11] determined the calcium and phosphorus homeostasis in 18 infants who received high or low calcium and phosphorus with parenteral nutrition, and with a fixed, low dose of vitamin D. The results show that high calcium (60 mg/dl) and phosphorus (46.5 mg/dl) in parenteral nutrition solutions can result in stable serum 1,25(OH)₂D₃, and tubular reabsorption of phosphorus, presumably reflecting minimal stress to the calcium and phosphorus homeostatic mechanism, without further increase in urinary calcium excretion. The finding of higher serum 1,25(OH)₂D₃ concentrations in infants who received low calcium and phosphorus infusate supports the thesis that the calcium and phosphate intake was probably deficient. The authors conclude that the use of high calcium and phosphorus nutrient infusate, which more closely resembles the quantity that may be delivered from human milk, appears to be appropriate for infants requiring parenteral nutrition.

Serial changes in selected serum constituents in low-birthweight infants on peripheral parenteral nutrition with different zinc and copper supplements have been studied by LOCKITCH et al. [12] in 105 infants of birth weight 2,000 g or less. Mean serum zinc, retinol-binding protein (RBP) and prealbumin (TBPA) declined significantly over time, while alkaline phosphatase rose. Only the group receiving the higher zinc supplement maintained a mean serum zinc concentration within the normal range at 7 weeks. Preterm infants required higher levels of zinc supplements than the 40 μg/kg/day suggested in the early days of parenteral nutrition. However, many infants with very low serum zinc concentrations did not show any dermatitis. Higher intravenous supplements of zinc prevent a marked decrease in serum concentrations, but do not affect serum copper concentrations in the preterm infant.

LEACH [13] has studied the role of manganese in enteral and parenteral nutrition. The essentiality of manganese rests upon the results of animal experiments, and on one unsubstantiated case of manganese deficiency in a human subject in whom symptoms included delayed blood clotting, hypocholesterolaemia and changes in beard colour. The estimated dietary requirement for the paediatric age group is established as 0.5 to 0.7 mg/day. Most manganese excretion is in the bile, and the liver is apparently the key organ in maintaining manganese homeostasis. Unsupplemented parenteral fluids can contain significant quantities of manganese, so that levels of contamination should be known before adding manganese salts to give the desired manganese intake. Recommended daily intravenous intake in stable patients in the paediatric age group is 5 to 10 μg/kg. Because bile is a major route of manganese excretion, it should probably not be included in the parenteral fluids of patients with biliary obstruction. Chloride and sulphate salts are the more soluble forms of these elements, and precipitation of calcium and phosphorus result in co-precipitation of manganese.

Groups of children with chronic diarrhoea, children and infants on total parenteral nutrition, infants with inborn errors of metabolism and premature infants, are the 4 groups that have been identified as being at risk of developing acute trace metal deficiency. ZLOTKIN [14] points out that the first generation of total parenteral nutrition formulation included hydrolysates of protein, that were "contaminated" with trace metals. Their use was infrequently associated with trace metal deficiencies. The newer formulations, prepared from individually-produced crystalline amino acids, are virtually free of trace metals. Their use has been associated with clinical manifestations of both copper and zinc deficiency. Concerning manganese,
one may calculate that to replete stores in a 1-kg infant at intra-uterine rates of manganese accretion, intakes of approximately 10 µg/kg/day would be appropriate. Compared with the American Medical Association (AMA) recommendations, this value is within the range of recommended intakes: 2 to 10 µg/kg/day. Preterm infants receiving zinc at 438 µg/kg/day and copper at 63 µg/kg/day achieve intra-uterine retention rates. These dosages are significantly higher than the AMA recommendations.

PERIS VIDAL et al. [15] have performed zinc balances on 5 different occasions in 3 children receiving total parenteral nutrition for 4 or more weeks. Excessive urinary zinc loss was a constant finding, and one patient also showed increased fecal loss. It is concluded that total parenteral nutrition solutions, when administered for long periods, must be supplemented with zinc, in order to obtain positive balances and a retention of zinc of between 50 to 100 µg/kg/day. The supplements to obtain this retention will be 100 to 200 µg/kg/day. In cases of zinc deficit and/or high digestive losses, the zinc supplement in parenteral nutrition must be increased up 200 to 500 µg/kg/day.

Phosphorus intake has been evaluated by VILEISIS [16] in 27 appropriate weight-for-gestational-age, clinically ill neonates who required total parenteral nutrition for 2 weeks. All received approximately 30 mg/kg/day elemental calcium. A low-phosphorus-intake group with 30 mg/kg/day showed signs of phosphate depletion with hypercalcemia, hypophosphatemia and absence of phosphaturia. A high-phosphorus-intake group with 50 mg/kg/day did not have signs of phosphorus depletion. However, they had high urinary cyclic adenosine monophosphate excretion and marked phosphaturia, suggesting secondary hyperparathyroidism. One group with a moderate phosphorus intake of 40 mg/kg/day had evidence of neither phosphate depletion nor secondary hyperparathyroidism. This dose appears to be appropriate for the very sick, poorly growing infant receiving total parenteral nutrition.

Trace elements were determined by DAHLSTROM et al. [17] in serum from 18 children aged 4 to 65 months who received long-term parenteral nutrition. In the group with TPN as their only source of nutrition, serum selenium values were decreased when compared with healthy children. During the study, no known clinical signs or symptoms of selenium deficiency were observed. However, subsequent to the end of the study, 2 patients who had very low serum selenium values developed thinning of hair, lightening of the hair and skin colour, and a progressive increase in erythrocyte mean corpuscular volume over a 6-month period. Selenium deficiency with clinical myopathy has been described after only 30 days on TPN, and 2 cases of fatal cardiomyopathy caused by selenium deficiency during long-term parenteral nutrition have also been reported. The authors did not find any recognized clinical symptoms of selenium deficiency, although the serum selenium values were generally 30 to 40% lower than in the control children. Serum chromium levels were also decreased when compared with healthy controls. Glucose intolerance correlated with chromium deficiency has been found in children with marasmus protein-calorie malnutrition but, in the present study, the children were well nourished. The only sign that might be related to manganese deficiency in this study was that of bone demineralization seen on skeletal radiograph in some of the children. Their serum manganese level was 30 to 40% lower than in control children. However, these findings could also be part of the metabolic bone disease correlated with the aluminum toxicity previously described in adults and children after long-term parenteral nutrition. In general, feeding 30 to 70% of calories by mouth did not normalize trace element levels in serum in these children, perhaps because of poor absorption secondary to their short or diseased intestines or inadequate oral intake.

References


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Vitamins and parenteral nutrition

DEVITO et al. [18] have measured the serum vitamin E levels in 17 very low-birthweight infants in the first two weeks of life, before and after the institution of intravenous vitamin E supplementation in a dosage of 4.5 mg/day as a component of a paediatric multivitamin preparation. Serum vitamin E levels were 0.22 ± 0.16 mg/dl before supplementation and rose to 2.55 ± 0.65 mg/dl in 9 infants of more than 900 g, and rose to 3.68 ± 0.70 mg/dl in 6 infants of less than 900 g birth weight. The post-supplementation serum vitamin E levels were in the range in which a reduction of incidence or severity of retinopathy of prematurity and intraventricular cerebral haemorrhage had been reported by others. No toxic effects of the preparation, nor of the increased vitamin E levels, were found. Vitamin E can be administered enterally. However, large doses of vitamin E by the oral route have been associated with abdominal distension and necrotizing enterocolitis. In addition, enterally administered vitamin E may not be well absorbed, due to the fat malabsorption of very low-birthweight infants, and the solvents utilized in preparation of vitamin E for oral use may have toxic effects in these infants. The authors believe that the parenteral route for vitamin E administration should be applied.

An evaluation of a paediatric multiple vitamin preparation for TPN in infants and children has been reported by MOORE et al. [19], who studied the blood levels of water-soluble vitamins. The daily amounts of intravenous vitamin in preterms were: B1 0.78 mg, B2 0.9 mg, niacin 11 mg, B6 0.65 mg, B12 0.65 µg, folate 91 µg, biotin 13 µg, pantothenate 3.2 mg and ascorbic acid 52 mg. In non-preterm infants the daily vitamin intakes were: B1 1.2 mg, B2 1.4 mg, niacin 17 mg, B6 1 mg, B12 1 µg, folate 140 µg, biotin 20 µg, pantothenate 5 mg and ascorbic acid 80 mg. Blood levels generally reflected excessive intake of vitamin C, vitamin B12, folate, niacin and pantothenate. It is likely that intake of these vitamins was greater than the needs of the premature infant.

MOCK et al. [20] have reported 3 children who developed biotin deficiency during parenteral alimentation. Infants with acquired biotin deficiency can present a distinctive peri-oral dermatitis, conjunctivitis, alopecia, hypotonia and developmental delay. Biotin deficiency can reproduce many of the clinical findings, seen in infants with the juvenile form of multiple carboxylase deficiency. The presence of a characteristic pattern of organic aciduria and reduced urinary excretion of biotin are better criteria than plasma biotin concentrations for predicting a positive response to biotin supplementation, and parenteral administration of 100 µg biotin/day results in resolution of clinical findings in infants who develop acquired biotin deficiency. The Nutrition Advisory Group of the American Medical Association has recommended parenteral administration of 20 µg of biotin/day for children on parenteral alimentation. Data presented in the present report provide preliminary evidence that this recommendation ought to be revised upwards.

References
Diarrhoea and parenteral/enteral nutrition

COLLET et al. [21] have reported a prospective study on continuous enteral nutrition as treatment for infants with travellers' diarrhoea and severe malnutrition, using standardized, progressive, semi-elemental drip feeding after rehydration. Total parenteral nutrition was unnecessary. The volume administered was 150 ml/kg/day from the 1st to the 6th day. The concentration of the semi-elemental diet was progressively increased, and maltodextrin was added after the 7th day from 1.5 g/kg/day to 7.5 g/kg/day. Out of 24 children, this therapy was successful in 18, and in the 6 remaining children relapse was treated with the same protocol, also with success.

WALKER-SMITH [22] reports the use of a semi-elemental formula designed for children with diarrhoea. The clinical use of such diets is based on the following premises: they are more easily absorbed, do not stimulate gastro-intestinal secretion, and have a low residue. This kind of diet may be indicated in 2 broad clinical situations: firstly where there is a defect of protein hydrolysis, and secondly where there is a defect of absorption or severe small-intestinal mucosal damage. The formula contained whey protein hydrolysate. Infants who received it showed a significantly greater weight gain which was associated with a greater retention of fat.

ORENSTEIN [23] studied 13 infants with intractable diarrhoea who were classified as having severe or moderate malabsorption on the basis of D-xylose absorption. Within each group designated severe and moderate, patients were randomly assigned to continuous enteral nutrition with an elemental formula or to an alternative therapy: total parenteral nutrition (TPN) for the severe, or intermittent oral nutrition with the elemental formula for the moderate patients. As Orenstein has reported, continuous elemental nutrition was associated with faster resolution of the malabsorption and diarrhoea, fewer complications and less expensive hospitalization than with total parenteral nutrition. Present evidence suggests that enteral nutrients are necessary for an optimal gastrointestinal function. Fasting leads to mucosal atrophy and a decline in absorptive capacity, even if malnutrition is prevented by the parenteral administration of nutrients. The mechanisms for this mucosal stimulation by feeding are still uncertain, but they probably include intraluminal supply of nutrients for the enterocyte, intraluminal stimulation of absorption, and non-luminal factors such as the neural and hormonal effects of feeding.

SMITH et al. [24] have observed that improved nutritional management reduces length of hospitalization in intractable diarrhoea. Sixteen patients were managed by one of two specific refeeding protocols, to compare the efficacy of two enteral formulae in the nutritional restoration of infants with intractable diarrhoea. Infants initially needing intravenous rehydration or parenteral nutrition were given nothing by mouth until faecal output was reduced to less than 100 g per day. They then received continuous infusion of the enteral formula by naso-gastric tube. Starting with 0.25 kcal/ml and 50 ml/kg, fluids were increased to 165 ml per kilo over 3 to 6 days. The concentration of the formulae was increased every 24 to 48 h from 0.25 to 0.50 up to 0.67 kcal/ml, as determined by a faecal volume being less than 100 g per day, and the absence of faecal reducing sugars. Nutritional support reduced the length of hospitalization.

References

Cystic fibrosis and enteral nutrition

O’LOUGHLIN et al. [25] have examined the effect of nutritional rehabilitation in cystic fibrosis patients with severe disease. Thirteen malnourished patients were studied over 7 to 16 months. They received naso-gastric supplementation with a semi-elemental formula infused at 100 to 150 ml/h over 8 to 10 hours, using a peristaltic pump by night. The formula contained hydrolyzed soy and whey protein with added essential amino acids, carbohydrates in the form of oligo- and polysaccharides, and long- and medium-chain fatty acids. Essential fatty acids constituted 4% of the total calories. The study demonstrated that a caloric intake sufficient to promote weight gain in patients with cystic fibrosis led to improvement in growth, body composition and clinical status. Nocturnal naso-gastric supplementation significantly increased caloric intake to 129% of the recommended dietary allowance. Naso-gastric feeding is minimally invasive and can be performed at home, allowing patients to lead a relatively normal life.

MOORE et al. [26] have studied 8 children aged 2 months to 13 years, with cystic fibrosis and growth failure, who were given home nocturnal naso-gastric feeding of an elemental diet for 3 months, and re-evaluated 3 months afterwards. The formula was delivered by an enteral pump. The study confirmed the effectiveness of tube-feeding in promoting growth in children with cystic fibrosis. During tube-feeding the children consumed significantly more calories than before and there was catch-up growth. By the time the tube-feeding ended the rate of growth in height had declined to normal values for age. Improved nutritional status does not necessarily prevent bouts of respiratory illness in patients with advanced pulmonary disease. Chest X-ray scores did not improve. The children adapted well to the tube-feeding, but in 2 patients tube enterostomies were performed to promote comfort and facilitate the delivery of the feeding. Because of inherent problems following general anaesthesia in cystic fibrosis patients with severe lung disease, both procedures were done under local anaesthesia.

References


Glycogenosis and continuous gastric night-time feeding

Two children of 32 months and 6.5 years respectively with type I glycogen storage disease and treated at home with continuous nocturnal intragastric feeding, have been reported by CHOURAQUI and LELUYER [27]. A high glucose formula was used. A high carbohydrate meal was given soon after stopping the nocturnal infusion and this was followed by frequent day-time feeding. In this way, the children were rapidly discharged from hospital and soon returned to school. The regimen stabilized blood glucose levels, avoiding hypoglycaemic complications, and improved tolerance to fasting and exercise. Moreover it decreased serum triglyceride, cholesterol, uric acid and lactate levels as well as liver size. The increase in linear growth rate was remarkable, and was associated with an increase in insulin:glucagon ratio. No complications resulted from the gastric tube. The method proved to be effective, simple, practical and acceptable to children and their parents. In addition, it is relatively inexpensive and represents a reliable long-term alternative to porto-caval shunt for patients with type I gly-
cogen storage disease. The nocturnal infusions should be continued until after adolescence.

Reference

Short bowel syndrome and parenteral/enteral nutrition

Thirteen children aged 2 to 16 years, studied by RICOUR et al. [28], had a sub-total resection of small bowel, following a mid-gut volvulus in 10 cases. Thirty-six cumulative patient years of parenteral nutrition and 11 years of constant-rate enteral nutrition were performed. The results demonstrate that the nutritional management of children who have undergone extensive small bowel resection depends, as in infants, on the length of the residual intestine. If at least 30 cm remain, in most cases the remarkable adaptability of the intestine can allow complete recovery from within a few months to a few years. In contrast, if resection is total or near total, with less than 20 cm remaining, life-long dependence on artificial nutritional support is unavoidable unless intestinal transplantation becomes feasible. When the intestinal resection is not complete, the prognosis depends on the adaptive capacity of the residual bowel, which in turn is influenced by anatomical, caloric and nutritional factors. The role of the ileum in the residual segment could be essential because of its specialized absorptive functions, particularly of bile acids, for which the jejunum cannot substitute. The loss of the ileo-caecal valve could enhance bacterial colonization of residual small bowel, accentuating malabsorption, not only of nutrients but also of water and electrolytes. Enteral nutrition has an important role in the regulation of the adaptation of the residual bowel. The induction of this adaptation is multifactorial. Introduction of nutrients into the intestinal lumen modifies the bacterial ecology, as well as intestinal motility, and biliary and pancreatic secretions. Enteral nutrition is indispensable for facilitating this adaptation, and should be begun as early as possible, being progressively increased by adjusting each nutrient according to digestive tolerance.

Reference

Tumours and parenteral/enteral nutrition

RICKARD et al. [29] review the problem of the nutritional care of children with neoplastic disease. Present data suggest that bone marrow suppression may be attenuated and treatment improved by the use of central parenteral nutrition in selected children with advanced cancer, e.g. acute non-lymphocytic leukaemia or advanced neuroblastoma. Enteral nutrition is the preferred method of feeding children with cancer who are at low nutritional risk but, in the experience of the authors, enteral feeding programmes have not been effective either in preventing or reversing protein energy malnutrition in most high risk children during initial, intense treatment. In a study of 21 children with advanced cancer, who received a comprehensive enteral nutrition programme, energy intake averaged only 41% of the recommended dietary allowance. In a few older school-age and teen-age children, the authors found continuous naso-gastric feeding to be beneficial. The patients receiving naso-gastric tube feeding were carefully selected so that they had minimal gastro-intestinal complaints, adequate platelets, family education, and continuing support. The authors prefer not to use naso-gastric tube feeding in the older infant, toddler or pre-school groups of children, because of the psychological trauma associated with the insertion and maintenance of tubes. Additionally nausea and vomiting, as well as decreased intestinal motility and absorption from oncological ther-
apy, makes tube feeding less advisable and less effective. Parenteral nutrition is both safe and effective in children with advanced neoplastic disease. Its effectiveness in reversing protein-energy malnutrition and restoring immunity has been proved. An improvement in transferrin concentration at 9 to 14 days of parenteral nutrition suggested that transferrin was more responsive than albumin. Parenteral nutrition support is continued for several days beyond cessation of chemotherapy or irradiation treatment, which induces anorexia, nausea and vomiting.

RICKARD et al. [30] also showed an unfavourable nutritional course in paediatric cancer, defined as a weight loss of 5% or more, and/or a decrease in subcapular skinfold measurements greater than twice a coefficient of variation of 0.3 mm. In several children who had no evidence of oedema, low energy intakes, i.e. more than 2 standard deviations below the mean of healthy children, and decreases in subcapular skinfold measurements, were the first indicators of nutritional depletion which occurred even with weight gain. Serum proteins which have shorter half-lives and different synthetic rates from albumin, such as transferrin, pre-albumin and retinol-binding proteins, may be useful indicators of subclinical protein-energy malnutrition. The authors suggest that sequential monitoring of the indices of nutritional status in children with newly-diagnosed neoplastic disease during the initial phases of treatment, should be included in nutritional study protocols. Common risk factors associated with the development of protein-energy malnutrition include irradiation of the gastro-intestinal tract in intense, frequent courses, at intervals of 3 weeks or less, chemotherapy in the absence of corticosteroids, major abdominal procedures, advanced disease during initial intense treatment, and lack of family- or health-care support. Decreased oral intakes with potentially increased energy requirements ultimately result in protein-energy malnutrition. In general, parenteral nutrition is required for 3 to 4 weeks during the initial intense treatment or periods of abdominal pelvic irradiation in patients at high nutritional risk, whereas enteral nutrition may be satisfactory during the later phases of treatment, except for periods of abdominal irradiation, tumour resection, or multiple relapse in patients at low nutritional risk.

References

Burns and parenteral/enteral nutrition

GORDON [31] describes a protocol of nutritional support for burn patients according to certain principles. A high protein, high calorie diet is indicated for every patient who is able to eat; an oral nutritional supplement is indicated for all patients who consistently do not meet 75% of their protein or caloric requirements from the high protein, high calorie diet. For patients unable or unwilling to obtain 75% of their calorie and protein requirements orally, tube feeding with enteral formula is indicated, as it also is for intubated patients with adequate bowel function. Initial tube feeding osmolality should be 200 to 400 mosmol/kg H₂O. The concentration of tube feeding formulae should be calculated so that the osmolality is less than 400 mosmol/kg H₂O. The concentration can be increased gradually after the desired volume is reached. Paediatric patients should start with 1 to 2 ml/kg body weight/h, increasing the volume of feeding to 5 to 15 ml/h. When larger volumes are tolerated, the concentration should be increased until the requirement is met. Water requirements can be supplied by intermittent flushes with a prescribed amount of water. Tube feeding can also be used to supplement intravenous hyperalimentation therapy. Correct placement of the tube should be checked by both the physician and a registered nurse who must agree together that the feeding tube is correctly in place. Signs of adverse reactions
should be watched for; tube feeding should be discontinued where there is choking, regurgitation, vomiting or abdominal distension. The feeding tube should be flushed with 20 ml water every 2 hours to ensure patency, and the patient should be in semi-Fowler’s position. Tube feeding should be stopped one hour before meals, if it is used to supplement a regular diet.

The adequacy of a modular tube feeding diet for burn patients has been studied by BELL et al. [32]. The nutritional regimen in paediatric burn patients provides calories at twice the predicted basal metabolic rate, 2.5 g/kg/day protein and 5 mg/kg/min carbohydrate. Lipids are provided to meet the caloric deficit after protein and carbohydrate administration. Modular diet is an appropriate method of nutritional supply. The selected patients had more than 30% initial total body surface area burned, were older than 2 years, and received at least two thirds of the total calories from the modular diet for a minimum of 6 days. Findings suggest that serum data have limited meaning for assessment of nutritional adequacy in burn patients, because no specific pattern evolved from this study. Serum albumin levels have traditionally been used to assess nutritional status in burn and non-burn patients. The authors found that none of the observed serum albumin levels in this study were within normal limits for any patient receiving any percentage of the modular diet. When the modular diet comprised at least two thirds of the total calories for the burn patients, a stool frequency was minimal, and probably one of the most important factors contributing to the management of stool frequency was the use of volumetrically controlled feeding pumps. One must be cautious not to draw conclusions about nutritional status based on nitrogen balance information alone, except to note that the presence of positive nitrogen balance is preferable.

References


Home parenteral/enteral nutrition

BLAIR et al. [33] have reported that home elemental nutrition (HEN) was used in 11 children and adolescents with complicated Crohn’s disease, to relieve their immediate symptoms and make them more fit for definitive surgery. HEN resulted in symptomatic relief, good weight gain and reduction in prednisone requirements. The 7 patients who subsequently underwent definitive bowel resection suffered no surgical complications. The feeds were administered daily over a 12-hour period, usually at night, for an average of 2.8 months. Elemental diets have the advantage of requiring no digestion and of being absorbed in the upper gastro-intestinal tract above the areas usually affected by Crohn’s disease. They create a medical bypass, allowing the bowel to rest, and, as a result, symptoms from intestinal obstruction are relieved and the distal entero-cutaneous fistulae close. In addition the medical bypass achieved may allow exclusion of whole proteins, and thus perhaps the allergens that have been implicated as possible causes of Crohn’s disease. The benefits of HEN are generally temporary and, in most cases, the disease will flare up again when a normal diet is resumed. For this reason, it can only be recommended for preoperative treatment to minimize the risk of surgery. In the experience of the authors, HEN compares favourably with that reported with the use of TPN, and the psychological benefits of HEN are also significant.

TAYLOR and MANNING [34] report the use of home parenteral nutrition (HPN) in a 12-month-old infant with short bowel syndrome. Mean daily fluid, protein and caloric intake were 160 ml/kg, 0.34 g nitrogen/kg and 94 kcal/kg respectively, giving a total calorie: nitrogen ratio of 276 kcal/g, 32% of calories being given as fat. Limited oral feeds were offered, using comminuted chicken, a glucose polymer and medium-chain triglycer-
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ides, but daily intake rarely exceeded 200 ml and 120 kcal. HPN has been continued for 12 months. It offers the main advantage for children that, apart from the saving of expense and the diminished risk of infection, avoids the adverse psychological effects of prolonged hospitalization.

Home parenteral nutrition has been used by AMARNATH et al. [35] in 9 children and adolescents with chronic intestinal disease and growth failure, treated for 7 to 63 months with an average height gain of 9 cm. Patients or parents or both were trained in the techniques of HPN for an average of 2 weeks in the hospital, and venous access was achieved by the placement of a catheter into the superior vena cava through either the cephalic or jugular vein. Most patients continued to eat some food, but their intakes were initially markedly decreased because of fear of pain, diarrhoea or vomiting. When symptoms lessened, oral intake increased, HPN was gradually reduced, and stopped completely when the patient was able to tolerate 100% of his caloric requirement by mouth.

References

Antibiotics and parenteral nutrition

KAMEN et al. [36] have analysed antibiotic stability in parenteral nutrition solutions, to evaluate the compatibility of commonly used antibiotics with standard hyperalimentation solutions and to determine whether these drugs could be administered together with parenteral nutrition. If there were no incompatibilities, this would allow significantly more TPN to be delivered without a need for extra fluid in patients receiving antibiotics several times daily. They found amikacin, azlocillin, cefaman-dole, cephalothin, gentamicin, mezlocillin, mox-alactam, naftillin, oxacillin, penicillin, piperacil-lin, ticarcillin and tobramycin to be stable for 6 h and to be compatible with the solution. Ampicillin has been shown previously to have limited stability in dextrose solutions. The authors do not, however, advocate the direct addition of antibiotics to the TPN solution bottle, but rather the administration of selected antibiotics into the tube during infusion of the TPN solution.

Reference

Nutrient deficiencies in parenteral nutrition

RUDMAN and WILLIAMS [37] have reviewed nutrient deficiencies during TPN and report that II types of nutrient deficiencies have been described. They stress that of essential fatty acids. Both linoleic and linolenic acids are essential nutrients. The high glucose content of TPN and the consequent hyperinsulinaemia prevent mobilisation of both fatty acids stored in the adipose tissue, and thus predispose to be the rapid appearance of an essential fatty acid deficiency state, even though substantial amounts may be present in the adipocytes. The only related clinical findings are an increase in serum liver enzymes and fatty infiltration and inclusion bodies in the hepatocytes. Concerning a possible deficit of other nutrients, it becomes very clear that the metabolism of intravenously administered nutrients is not identical with that of those administered by mouth, because of the role of both the gut and the liver in processing them. The difficulties encountered by patients given TPN in synthesizing some normally dispensable amino acids, as well as substances such as tyrosine, cysteine, carnitine and choline, are further evidence for the crucial function of the entero-hepatic circulation.
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Reference


Computer programmes in parenteral nutrition

The need for individualized parenteral nutrition in paediatric patients makes the formulation and preparation of these solutions more complex and prone to error. YAMAMOTO et al. [38] report a computer programme which helps with comprehensive management of parenteral nutrition by concurrent formulation and preparation of the appropriate solutions. This programme, designed to run on a personal computer, is very comprehensive and flexible. Fluid calculations are automatically performed and are printed on the listing in ml/day and ml/kg/day, divided between oral and parenteral nutrition and the total fluids. Calorie calculations are performed in a similar fashion. The programme for calorie calculations is very detailed and include provisions for the use of medium-chain triglyceride oil supplements, high calorie formula, and formula diluted with glucose water, sterile water, breast milk or other substances. It determines appropriate intravenous rates of administration of parenteral nutrition.

Reference


Complications during parenteral nutrition

RUBIN et al. [39] describe a previously unreported complication of TPN through a silastic central venous line. A low-birthweight infant with severe hyaline membrane disease, requiring lung ventilation at 12 days of life, showed signs and symptoms of necrotizing enterocolitis. The chest X-ray showed a left upper lobe consolidation which was attributed to pneumonia, but an intravenous contrast injection into the silastic line showed the line passing from the left brachial vein through the subclavian vein and the superior vena cava into the right atrium. From the right atrium, it passed across the foramen ovale into the left atrium, then into the left upper pulmonary vein. The contrast escaped into the lung parenchyma and filled the bronchial tree. The central venous catheter was immediately removed. A diagnosis was made of chemical pneumonitis, secondary to a leak of intravenous feeding solution directly from the pulmonary vasculature into the lung parenchyma. The authors suggest that an X-ray, 2 to 3 days after placement, should always be performed to confirm that the position of the catheter has not changed.

In the case reported by STINE and HARRIS [40] in a premature infant 5-weeks old, an infected subdural collection of intravenous fat emulsion was diagnosed when the infant was receiving TPN through a facial vein cut-down. In the opinion of the authors, the subdural collection occurred as a result of septic thrombosis of the internal jugular vein, with subsequent retrograde flow and infiltration of fat emulsion from the bridging veins into the subdural space.

MACTIER et al. [41] review the problems of central venous catheterization in very low-birthweight infants. They point out that it is impossible to assess the role of a central venous line in the development of septicaemia in this very high risk population. Of 42 prematures with central venous line, one developed a hydrocephalus, considered to be due to superior vena cava thrombosis. Six central venous catheter tips removed from infants with systemic infection were cultured. Three yielded the same organism as the blood culture, one grew a different organism and two were sterile. The authors prefer to use peripherally inserted, small diameter, long silicon lines for parenteral nutrition whenever possible.

Metabolic derangements occurring in children requiring parenteral nutrition have been studied by BAKER et al. [42]. From a total of 201 children receiving parenteral nutrition for 5378 days the sepsis rate was 3.7% in central lines used only for parenteral nutrition and 4.8% in multi-purpose central lines. In patients supported centrally,
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Hypoalbuminaemia was the most commonly found abnormality, followed by hypocalcaemia, hypophosphataemia and hypomagnesaemia, reflecting a malnourished state. One third of the patients had abnormal liver function tests and in half of these, factors causing liver dysfunction other than parenteral nutrition were present. Abnormal renal function tests occurred in 10% of patients. Hyperglycaemia occurred in 20% of all patients, and was quickly corrected by adjusting either the concentration of dextrose or the solution flow rate.

NELSON et al. [43] report that, in 60 paediatric patients treated with parenteral nutrition during 1866 patient days in a period of 21 months, surgical residents were responsible for dressing changes during the first 16 months, and a specially trained nurse was responsible during the final 5 months. Twenty percent of the lines became infected. The infection rate was significantly higher in the lines cared for by residents, 28.8% compared with 3.3% in the lines cared for by the nurse. This occurred in spite of the lines being in place significantly longer in the "nurse" group. These data indicate that a specially trained person using aseptic techniques can reduce infection rates in patients receiving central venous parenteral nutrition.

Levels of serum bile acids, and liver disorders, during TPN in 56 children studied by GOROSTIZA et al. [44] showed more frequent increases in serum bile acid levels (77%), than other parameters such as transaminases (57%), or bilirubin (37%). Qualitative analysis showed that only the primary bile acid levels increased, suggesting cholestasis. Conversely, during sepsis of digestive origin, an increase in secondary bile acid serum levels is observed, reflecting the intestinal bacterial overgrowth. Liver disorders were more frequent in patients with malnutrition and were more severe in low-birthweight infants.

The pathogenesis of the damage to the liver in patients receiving parenteral nutrition is unknown. Lipofuscin, often found in hepatic cells, may be an important clue. BERGER et al. [45] studied a premature infant submitted to TPN, who, on the 30th day, developed cholestatic jaundice. A percutaneous needle biopsy of the liver showed the presence of granules suggestive of lipofuscin pigment. The accumulation of this pigment has been considered to be a complication of receiving fat emulsions, but the authors' review of previous reports found that lipofuscin had been found in the liver even when only amino acids and glucose electrolye mixtures had been infused. Nutritional deficiencies, for example of selenium and vitamin E, that develop with parenteral feeding could weaken the anti-oxidant defences and allow damage by free radicals. Lipofuscin is a complex of lipids, proteins and malonaldehyde, that develops when subcellular membranes are damaged by peroxidation of free radicals.

The fat over-load syndrome has been reported in relation to excessive accumulation of serum lipids. A major feature of this syndrome has been a bleeding tendency, which in some cases has been related to hepatic dysfunction, and a decrease in blood clotting factor synthesis. CAMPBELL et al. [46] report a 7-year-old child who required nutritional management with TPN and presented with fever, pallor, scattered petechiae and haematemesis. Transaminases were increased, and the lipid level was 920 mg/dl. Serial laboratory studies demonstrated a prolonged bleeding time, which was associated with marked platelet dysfunction. The study provides evidence that the bleeding problem in lipid over-load was due to platelet dysfunction only, and not to a coagulation defect. The platelet dysfunction was reversible, and the exact aetiology remains unknown.

References
Aluminum and parenteral nutrition

KOO et al. [47] have studied the response to aluminum loading from parenteral nutrition solutions in 20 infants of gestational ages up to 29 to 41 weeks. Serum aluminum concentrations ranged from 6 to 318 μg/1, compared with a median of 18 μg/1 for normal infants and children. Currently used parenteral nutrition solutions are contaminated with aluminum. Urine aluminum concentration was higher with higher aluminum loading and was not different in term and preterm infants. The aluminum contents in the final parenteral solution with high calcium and phosphorus were 306 ± 26 μg aluminum/l. The presence of an in-line filter in the parenteral nutrition solution did not affect the aluminum concentration in the infusate. The renal excretory capacity for aluminum may be overwhelmed by excessive or prolonged aluminum loading during the early newborn period. The authors suggest that the renal elimination of aluminum in infants is incomplete as assessed by lower urine aluminum excretion versus load, elevated serum aluminum concentration and bone deposition of aluminum.

The study of plasma and urinary aluminum concentration, in 18 premature infants receiving intravenous therapy and in 8 term infants receiving no intravenous therapy, reported by SEDMAN et al. [48] shows that the bone aluminum concentration was 10 times higher in the group that had received at least 3 weeks of intravenous therapy. Such infants may be at risk of aluminum intoxication secondary to increased parenteral exposure and poor renal clearance.

References


Miscellaneous

CORAN et al. [49] comment that the nature of weight gain, seen in infants receiving TPN, continues to be controversial. The question is whether weight gain represents an increase in body mass or water retention. The authors have studied 18 infants receiving intravenous nutrition following major surgery, for periods ranging from 1 to 17 weeks. Total body water and extracellular fluid volume were determined. The results of this examination demonstrate that total body water and extracellular fluid volume do not increase intravenous nutrition, but remain unchanged or decreased in spite of the fact that weight gain occurs. These findings support the hypothesis that weight gain, during intravenous nutrition in infants, is due to tissue accretion rather than fluid retention.

PUTET et al. [50] have continuously measured the energy consumption and nutritional evaluation over 24 h in two comparable groups of children under cyclic or continuous TPN. Energy consumption and nitrogenous retention were equal in both groups. In cases submitted to cyclic TPN, night and day utilization of nutrients was significantly different, with important utilization of glycogen and lipid stocks during the day. Thus cyclic TPN allows a greater mobilization of the energy stores, and greater physical activity during the day than continuous TPN; it might change the quality of the weight gain and avoid an unnecessary storage of lipid deposits.

References
