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Glutamine: role in gut protection in critical illness.

Wischmeyer-Paul-E

Current opinion in clinical nutrition and metabolic care, Sep 2006, vol. 9, no. 5, p. 607-12

Abstract

AB PURPOSE OF REVIEW: Recent literature has focused on the role of the gut and increased gut permeability as a driver of systemic inflammation in critical illness. Thus, the therapeutic potential for an agent to prevent gut barrier compromise and attenuate gut-derived inflammatory response is significant. RECENT FINDINGS: In laboratory and clinical settings, glutamine can attenuate gut permeability following critical illness and injury. Further, recent literature has revealed other mechanisms by which glutamine may attenuate the systemic inflammatory response driven by the gut. These findings reveal that glutamine may act at multiple levels to attenuate gut injury and potential subsequent gut-derived systemic inflammatory response. These mechanisms focus around glutamine's ability to induce the cellular protective stress response in the gut. This leads to enhanced protection of the gut epithelial barrier and attenuation of generation of inflammatory mediators. SUMMARY: These mechanistic findings, combined with a limited amount of clinical data showing benefit on gut permeability in illness and injury, indicate more formal studies need to be carried out looking the role of glutamine in gut protection and as an antiinflammatory in critical illness.

The clinical efficacy of glutamine dipeptides on postoperative patients: an updated systematic review of randomized controlled trials from Europe and Asia (1997 - 2005).

Jiang-Zhu-Ming, Jiang-Hua


Abstract

AB OBJECTIVE: To examine the effects of parenteral supplementation of glutamine dipeptide on the outcomes of surgical patients. METHODS: The relevant data 1997 to March or May 2005 were retrieved from SCI, Medline, EMBASE, Chinese Cochrane Centre databases. The bibliographies of the retrieved papers and the personal file were searched as well. All the patients in the retrieved papers received parenteral nutrition, whether alanyl-glutamine dipeptide (Ala-Gln) was added was the only difference between the intervention and control groups. Methodological quality assessment was based on the Cochrane Reviewers' Handbook and Jadad's Score Scale. Statistical software RevMan4.2 was used for meta-analysis. The data were treated by intention-to-treat method. RESULTS: A total of 1074 relevant papers were screened. Thirteen prospective randomized controlled clinical trials (RCTs) from European & Asian studies met the inclusion criteria. Ten RCTs reported 355 cases of infectious complications showed that Ala-Gln administration significantly reduced the prevalence of infectious complications with a pooled relative risk (RR) of 0.42 (95% CI 0.24 - 0.72; P = 0.002). Eight studies with 273 cases reported the postoperative length of stay (LOS) and showed that Ala-Gln significantly reduced the postoperative LOS by 3.25 days (95% CI = -4.87 to -1.62; P = 0.00009). There was no significant effect of Ala-Gln on cost of hospitalization, though there was a trend to reduction (2 studies, pooled n = 52, P = 0.2). CONCLUSION: Parenteral Ala-Gln significantly reduces the post-operative infectious morbidity and LOS among surgical patients.

Glutamine: role in gut protection in critical illness.

Wischmeyer-Paul-E

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Abstract

AB PURPOSE OF REVIEW: Recent literature has focused on the role of the gut and increased gut permeability as a driver of systemic inflammation in critical illness. Thus, the therapeutic potential for an agent to prevent gut barrier compromise and attenuate gut-derived inflammatory response is significant. RECENT FINDINGS: In laboratory and clinical settings, glutamine can attenuate gut permeability following critical illness and injury. Further, recent literature has revealed other mechanisms by which glutamine may attenuate the systemic inflammatory response driven by the gut. These findings reveal that glutamine may act at multiple levels to attenuate gut injury and potential subsequent gut-derived systemic inflammatory response. These mechanisms focus around glutamine's ability to induce the cellular protective stress response in the gut. This leads to enhanced protection of the gut epithelial barrier and attenuation of generation of inflammatory mediators. SUMMARY: These mechanistic findings, combined with a limited amount of clinical data showing benefit on gut permeability in illness and injury, indicate more formal studies need to be carried out looking the role of glutamine in gut protection and as an antiinflammatory in critical illness.

Phanvijhitsiri-Kittiporn, Musch-Mark-W, Ropeleski-Mark-J, Chang- Eugene-B


Abstract
AB: Glutamine is considered a nonessential amino acid; however, it becomes conditionally essential during critical illness when consumption exceeds production. Glutamine may modulate the heat shock /stress response, an important adaptive cellular response for survival. Glutamine increases heat induction of heat shock protein (Hsp) 25 in both intestinal epithelial cells (IEC-18) and mesenchymal NIH/3T3 cells, an effect that is neither glucose nor serum dependent. Neither arginine, histidine, proline, leucine, asparagine, nor tyrosine acts as physiological substitutes for glutamine for heat induction of Hsp25. The lack of effect of these amino acids was not caused by deficient transport, although some amino acids, including glutamate (a major direct metabolite of glutamine), were transported poorly by IEC-18 cells. Glutamate uptake could be augmented in a concentration- and time-dependent manner by increasing either media concentration and/or duration of exposure. Under these conditions, glutamate promoted heat induction of Hsp25, albeit not as efficiently as glutamine. Further evidence for the role of glutamine conversion to glutamate was obtained with the glutaminase inhibitor 6-diazo-5- oxo-L-norleucine (DON), which inhibited the effect of glutamine on heat-induced Hsp25. DON inhibited phosphate-dependent glutaminase by 75% after 3 h, decreasing cell glutamate. Increased glutamine /glutamate conversion to glutathione was not involved, since the glutathione synthesis inhibitor, buthionine sulfoximine, did not block glutamine's effect on heat induction of Hsp25. A large drop in ATP levels did not appear to account for the diminished Hsp25 induction during glutamine deficiency. In summary, glutamine is an important amino acid, and its requirement for heat-induced Hsp25 supports a role for glutamine supplementation to optimize cellular responses to pathophysiological stress.

Glutamine: The first clinically relevant pharmacological regulator of heat shock protein expression?

Wischmeyer-P-E
CURR-OPIN-CLIN-NUTR-METAB-CARE, 2006, Vol/Iss/Pg. 9/3 (201-206)

Abstract
AB PURPOSE OF REVIEW: It is well known that enhanced heat shock protein expression protects organisms against morbidity and mortality following experimental injury/illness. Presently, chemical/gene therapy based laboratory methods of enhancing heat shock protein expression are impractical for clinical application. Our laboratory has shown glutamine enhances heat shock protein expression following models of experimental illness/injury. The purpose of this review is to examine recent data supporting the use of glutamine as a clinically relevant enhancer of heat shock protein expression. RECENT FINDINGS: Recent studies indicate glutamine induces heat shock protein-70, HO-1 (heat shock protein-32), and heat shock protein-27 in models of illness/injury. Enhanced expression of heat shock proteins correlates with improved outcome in these models. Further, in-vitro data reveal glutamine enhances DNA binding of heat shock factor-1 (heat shock protein transcription factor) to its promoter. Finally, recently published pilot data show that glutamine enhances serum heat shock protein-70 expression in critically ill patients and this enhanced expression correlates with improved outcome. SUMMARY: Currently, extensive data support glutamine as a gene level regulator of heat shock protein expression. Glutamine depletion, following critical illness/injury, is likely to lead to a state in which organisms are unable to induce heat shock proteins appropriately. Further, pharmacologic supplementation of glutamine potentiates the heat shock protein response prior to and following a stress. Pharmacologic trials utilizing glutamine to enhance heat shock proteins in humans are indicated.
The Prospective Study on Application of Parenteral Nutrition with Alanyl-glutamine Dipeptide in Chemotherapy of Gastrointestinal Neoplasms Patients.

Peng-Yi-Liang, Gong-Qian-Fen, Wand-Zi-Qiang
Ai zheng, Aug 2006, vol. 25, no. 8, p. 1044-7

Abstract

**AB BACKGROUND & OBJECTIVE:** There is an argument on whether or not glutamine-supplemented parenteral nutrition is beneficial to chemotherapy in gastrointestinal neoplasm patients. The aim of this study was to prospectively evaluate the effect of parenteral nutrition with alanyl-glutamine dipeptide on gastrointestinal neoplasm patients receiving chemotherapy. **METHODS:** This study was a prospective, randomized double-blind clinical trial. Seventy-two patients were randomly divided into study group and control group (each group had 36 patients). The side effects during chemotherapy were observed. Serum albumin, serum pre-albumin, IgG, IgA, IgM, C3, C4 level were measured before chemotherapy and on day 4 and day 8 after chemotherapy. Nitrogen balance was also calculated simultaneously. **RESULTS:** (1) Less side effects during chemotherapy in study group were revealed compared to those in control group (P<0.05). (2) Serum albumin and pre-albumin levels were both decreased in the two groups on day 4 after chemotherapy, and were markedly decreased in control group on day 8 after chemotherapy (P<0.05). (3) IgG, IgM, IgA levels were all decreased compared to the test results before chemotherapy on day 4 after chemotherapy. C3 and C4 levels were higher in study group compared with control group on day 8 after chemotherapy (P<0.05). (4) Nitrogen balance in study group was better than that in control group (P<0.05). **CONCLUSIONS:** Alanyl-glutamine dipeptide is beneficial to chemotherapy in gastrointestinal neoplasm patients. It could reduce the side effects of chemotherapy, which helps to improve the nutritional status, the immune function and the survival quality of patients during chemotherapy.

Metabolic effects of parenteral nutrition enriched with n-3 polyunsaturated fatty acids in critically ill patients.

Tappy-Luc, Berger-Mette-Monica, Schwarz-Jean-Marc, Schneiter-Philippe, Kim-Seungki, Revelly-Jean-Pierre, Chiolero-Rene
Clinical nutrition, Aug 2006, vol. 25, no. 4, p. 588-95

Abstract

**AB BACKGROUND & AIMS:** n-3 fatty acids are expected to downregulate the inflammatory responses, and hence may decrease insulin resistance. On the other hand, n-3 fatty acid supplementation has been reported to increase glycemia in type 2 diabetes. We therefore assessed the effect of n-3 fatty acids delivered with parenteral nutrition on glucose metabolism in surgical intensive care patients. **METHODS:** Twenty-four surgical intensive care patients were randomized to receive parenteral nutrition providing 1.25 times their fasting energy expenditure, with 0.25 g of either an n-3 fatty acid enriched- or a soy bean-lipid emulsion. Energy metabolism, glucose production, gluconeogenesis and hepatic de novo lipogenesis were evaluated after 4 days. **RESULTS:** Total energy expenditure was significantly lower in patients receiving n-3 fatty acids (0.015 +/- 0.001 vs. 0.019 +/- 0.001 kcal/kg/min with soy bean lipids (P<0.05)). Glucose oxidation, lipid oxidation, glucose production, gluconeogenesis, hepatic de novo lipogenesis, plasma glucose, insulin and glucagon concentrations did not differ (all P>0.05) in the 2 groups. **CONCLUSIONS:** n-3 fatty acids were well tolerated in this group of severely ill patients. They decreased total energy expenditure without adverse metabolic effects.
Vitamins and trace elements: Practical aspects of supplementation.

Berger-Mette-M, Shenkin-Alan

Abstract
AB: The role of micronutrients in parenteral nutrition include the following: (1) Whenever artificial nutrition is indicated, micronutrients, i.e., vitamins and trace elements, should be given from the first day of artificial nutritional support. (2) Testing blood levels of vitamins and trace elements in acutely ill patients is of very limited value. By using sensible clinical judgment, it is possible to manage patients with only a small amount of laboratory testing. (3) Patients with major burns or major trauma and those with acute renal failure who are on continuous renal replacement therapy or dialysis quickly develop acute deficits in some micronutrients, and immediate supplementation is essential. (4) Other groups at risk are cancer patients, but also pregnant women with hyperemesis and people with anorexia nervosa or other malnutrition or malabsorption states. (5) Clinicians need to treat severe deficits before they become clinical deficiencies. If a patient develops a micronutrient deficiency state while in care, then there has been a severe failure of care. (6) In the early acute phase of recovery from critical illness, where artificial nutrition is generally not indicated, there may still be a need to deliver micronutrients to specific categories of very sick patients. (7) Ideally, trace element preparations should provide a low-manganese product for all and a manganese-free product for certain patients with liver disease. (8) High losses through excretion should be minimized by infusing micronutrients slowly, over as long a period as possible. To avoid interactions, it would be ideal to infuse trace elements and vitamins separately: the trace elements over an initial 12-h period and the vitamins over the next 12-h period. (9) Multivitamin and trace element preparations suitable for most patients requiring parenteral nutrition are widely available, but individual patients may require additional supplements or smaller amounts of certain micronutrients, depending on their clinical condition.

Risks and benefits of nutritional support during critical illness.

Debaveye-Yves, Berghe-Greet-Van-den

Abstract
AB: Critically ill patients who depend on intensive care for more than a few days reveal profound erosion of lean body mass, which is thought to contribute to high morbidity and mortality. Despite a shortfall of evidence that supplemental feeding actually alters clinical outcome of these life-threatening disease states, this observation evoked an almost universal, albeit often inappropriate, use of nutritional support (NS) in the critically ill, administered via the parenteral or the enteral route. Lack of knowledge and overenthusiasm subsequently resulted in complications associated with both parenteral nutrition (PN) and enteral nutrition (EN), which led to the standing controversy over which should be preferred. With time, however, it became clear that EN and PN are not mutually exclusive and that critically ill patients requiring NS should be fed according to the functional status of the gastrointestinal tract. In addition, tight blood glucose control with insulin is advised in fed critically ill patients because overall metabolic control appears to surpass any outcome benefit attributed to the route of feeding. Recently, various special nutritional formulas have been suggested to prevent or treat multiorgan failure in the critically ill, among other pathways via modulation of immune function. Although special nutritional formulas may be promising in a variety of clinical settings, based on currently available data, these cannot be recommended for routine use in critically ill patients.
Severe refeeding hypophosphatemia in a CAPD patient: a case report.

Lin-Kang-Kuei, Lee-Jia-Jung, Chen-Hung-Chun
Renal failure, 2006, vol. 28, no. 6, p. 515-7

Abstract
AB: Refeeding syndrome is defined as severe electrolyte and fluid shifts associated with metabolic abnormalities in malnourished, refeeding patients. Hypophosphatemia is its predominant concern, though its occurrence is unusual in uremic patients due to the concomitant hyperphosphatemia. This case study reports a 56-year-old woman on continuous ambulatory peritoneal dialysis (CAPD) therapy who was admitted for peritonitis. Ileus and diarrhea developed during admission; enteral feeding was given initially and then shifted to total parenteral nutrition (TPN) because of poor digestion. A lower concentration of phosphate was administered in the TPN formula initially due to high initial serum phosphate level. However, severe hypophosphatemia (0.3 mg/dL) developed on the second day after TPN supplementation. Continuous intravenous phosphate (total 6 mmol of phosphate) was supplied immediately. Unfortunately, the sudden onset of conscious loss and cardiac arrest happened on the third day of TPN. It should be emphasized that severe refeeding hypophosphatemia can also develop early in uremic patients with hyperphosphatemia.

Use of fish oil in parenteral nutrition: rationale and reality.

Calder-Philip-C

Abstract
AB: Excessive or inappropriate inflammation and immunosuppression are components of the response to surgery, trauma, injury and infection in some individuals and can lead, progressively, to sepsis and septic shock. The hyperinflammation is characterised by the production of inflammatory cytokines, arachidonic acid-derived eicosanoids and other inflammatory mediators, while the immunosuppression is characterised by impairment of antigen presentation and of T-helper lymphocyte type-1 responses. Long-chain n-3 fatty acids from fish oil decrease the production of inflammatory cytokines and eicosanoids. They act both directly (by replacing arachidonic acid as an eicosanoid substrate and by inhibiting arachidonic acid metabolism) and indirectly (by altering the expression of inflammatory genes through effects on transcription factor activation). Thus, long-chain n-3 fatty acids are potentially useful anti-inflammatory agents and may be of benefit in patients at risk of hyperinflammation and sepsis. As a consequence, an emerging application for n-3 fatty acids, in which they may be added to parenteral (or enteral) formulas, is in surgical or critically-ill patients. Parenteral nutrition that includes n-3 fatty acids appears to preserve immune function better than standard formulas and appears to diminish the extent of the inflammatory response. Studies to date are suggestive of clinical benefits from these approaches, especially in patients post surgery, although evidence of clinical benefit in patients with sepsis is emerging.
Peripherally inserted central venous catheters are not superior to central venous catheters in the acute care of surgical patients on the ward.

Turcotte-Simon, Dube-Serge, Beauchamp-Gilles

Abstract
AB BACKGROUND: Peripherally inserted central venous catheters (PICC) have supplanted central venous catheters (CVC) for the administration of intravenous antibiotics and total parenteral nutrition to patients in our hospital. From the literature, it appears that this change has occurred in a number of other surgical units. Accounting for the change are the expected advantages of low complication rates at insertion, prolonged use without complications and interruption, and cost- and time-savings. METHODS: We have proceeded with a review of the literature to understand and justify this change in practice. Our hypothesis was that the routine adoption of PICC instead of CVC for the acute care of surgical patients has occurred in the absence of strong scientific evidence. Our aim was to compare the associated infectious, thrombotic, phlebitic, and other common complications, as well as PICC and CVC durability. Articles concerning various aspects of PICC- and CVC-related complications in the acute care of adult patients were selected from the literature. Studies were excluded when they primarily addressed the use of long-term catheters, outpatient care, and pediatric patients. Data were extracted from 48 papers published between 1979 and 2004. RESULTS: Our results show that infectious complications do not significantly differ between PICC and CVC. Thrombotic complications appear to be more significant with PICC and to occur early after catheterization. Phlebitic complications accounted for premature catheter removal in approximately 6% of PICC. Finally, prospective data suggest that approximately 40% of PICC will have to be removed before completion of therapy, possibly more often and earlier than CVC. CONCLUSIONS: We believe that there is no clear evidence that PICC is superior to CVC in acute care settings. Each approach offers its own advantages and a different profile of complications. Therefore, the choice of central venous access should be individualized for surgical patients on the ward. More comparative prospective studies are needed to document the advantages of PICC over CVC.

Intradialytic parenteral nutrition in hemodialysis patients: Acute and chronic intervention.

Avery-Lynch-Margaret

Abstract
AB: Protein and calorie malnutrition have been encountered more frequently than expected in the hemodialysis patients. Intradialytic parenteral nutrition (IDPN) has been documented to improve nutritional status in hemodialysis patients in both acute and chronic settings (Henrich, 1996). The aim of this study was to support the usage of IDPN in our malnourished hemodialysis patients. Serum concentration of albumin is one of the main indicators of mortality in the dialysis population. The serum albumin concentration for six out of eight of our hemodialysis (HD) patients receiving IDPN increased significantly. There was a mean increase of 7.0 g/L of plasma albumin for the eight patients assessed. These results demonstrate that IDPN is an effective nutritional intervention for malnourished hemodialysis patients.
Stability of total parenteral nutrition when added with alanyl-glutamine.

CHIN-J-CLIN-NUTR, 30 JUN 2006, Vol/Iss/Pg. 14/3 (163-166)

Abstract
OBJECTIVE: To evaluate the stability of total parenteral nutrition (TPN), especially the fat emulsion, when added with alanyl-glutamine. METHODS: The appearance was observed under various temperatures. The pH and osmotic pressure were measured when alanyl-glutamine was added into three different TPN prescriptions. The diameter and surface looking for fat emulsion particles were measured. RESULTS: There were not obvious changes in appearance, pH and osmotic pressure. The size and surface of fat emulsion particles were stable when TPN was mixed with alanyl-glutamine. No side effect was reported when such TPN was used in 100 person-times in clinical practice. CONCLUSION: Total parenteral nutrition prescription is stable after being added with alanyl-glutamine.

Structured triglyceride emulsions in parenteral nutrition.

Chambrier-C, Lauverjat-M, Bouletreau-P

Abstract
AB: Over the past 3 decades, various concepts for IV fat emulsions (IVFE) have been developed. A randomized, structured-lipid emulsion based on an old technology has recently become available. This structured-lipid emulsion is produced by mixing medium-chain triglycerides and long-chain triglycerides, then allowing hydrolysis to form free fatty acids, followed by random transesterification of the fatty acids into mixed triglyceride molecules. Studies in animals have shown an improvement in nitrogen balance with the use of these lipid emulsions. Only 8 human clinical studies with these products have been performed. The results of these human clinical studies have been less promising than the animal studies; however, an improvement in nitrogen balance and lipid metabolism exceeds results associated with infusion of long-chain triglycerides (LCT) or a physical mixture of long-chain triglycerides and medium-chain triglycerides (LCT-MCT). Structured-lipid emulsion seems to induce less elevation in serum liver function values compared with standard IVFEs. In addition, structured-lipid emulsions have no detrimental effect on the reticuloendothelial system. Further studies are necessary in order to recommend the use of structured-lipid emulsions. The clinical community hopes that chemically defined structured triglycerides will make it possible to determine the distribution of specific fatty acids on a specific position on the glycerol core and therefore obtain specific activity for a specific clinical situation.
Choline deficiency is associated with increased risk for venous catheter thrombosis.

Buchman-Alan-L, Ament-Marvin-E, Jenden-Donald-J, Ahn-Chul

Abstract
AB BACKGROUND: Patients with intestinal failure who require long-term parenteral nutrition (PN) develop catheter thrombosis as a complication. This patient group may also develop choline deficiency because of a defect in the hepatic transsulfuration pathway in the setting of malabsorption. This study was undertaken to determine whether choline deficiency is a risk factor for development of catheter thrombosis. METHODS: Plasma free and phospholipid-bound choline concentrations were measured in a group of 41 patients that required long-term PN. Episodes of catheter thrombosis from onset of PN to the time of blood testing were recorded. RESULTS: Sixteen (39%) patients developed catheter thrombosis, and 5 of these had recurrent catheter thrombosis. Plasma free choline was 7.7 +/- 2.7 nmol/mL in patients with no history of catheter thrombosis and 6.2 +/- 1.7 nmol/mL in patients with previous catheter thrombosis (p = .076 by Wilcoxon rank-sum test). The partial correlation between plasma free choline concentration and the frequency of clots after controlling for catheter duration was r = -0.33 (p = .038). The relative risk for catheter thrombosis in subjects with a plasma free choline concentration <8 nmol/mL was 10.0, 95% confidence interval (1.134-88.167). Plasma phospholipid-bound choline concentration was 2191.7 +/- 679.0 nmol/mL in patients with previous catheter thrombosis and 2103.3 +/- 531.2 nmol/mL in patients without history of catheter thrombosis (p = NS). CONCLUSION: Choline deficiency is a significant risk factor for development of catheter thrombosis in patients with intestinal failure who require PN.

The Use of IV Fat in Neonates.


Abstract
AB: IV fat emulsion (IVFE) is an integral part of the parenteral nutrition (PN) regimen in neonates. It provides a concentrated isotonic source of calories and prevents or reverses essential fatty acid deficiency. Continuous administration of IV fat with PN regimens prolongs the viability of peripheral IV lines in infants who might have limited venous access. IVFE must be administered separately from the PN solution in neonates. The acidic pH of a PN solution is necessary for maximum solubility of calcium and phosphorus. If fat emulsion is added to the PN solution, as is done in 3-in-1 (total nutrient admixture) solutions, the high amount of calcium and phosphorus needed by these infants may result in an unseen precipitate with serious consequences. Continuous fat infusion over 24 hours is the preferred method in neonates. The administration rate of 0.15 g/kg/hour for IVFE in the neonate should not be exceeded. Essential fatty acid deficiency can be prevented in neonates by providing IVFE in a dose of 0.5-1.0 g/kg/day. Carnitine is not routinely required to metabolize IVFE in the neonate. Infants should receive 20% lipid emulsion to improve clearance of triglycerides and cholesterol. Serum triglyceride levels should be maintained at <150-200 mg/dL in neonates. There are concerns about potential adverse effects of early administration of IV fat in very-low-birth- weight infants weighing <800 g. We hold the IV fat dose at 1.0-1.5 g /kg/day until the second week of life in infants <30 weeks gestation.
Early treatment with ursodeoxycholic acid for cholestasis in children on parenteral nutrition because of primary intestinal failure.


Abstract

AB BACKGROUND: There is conflicting evidence as to whether ursodeoxycholic acid (UDCA) reduces the incidence of parenteral nutrition-associated cholestasis.
AIM: To investigate the efficacy of UDCA on parenteral nutrition-associated cholestasis in children with intestinal failure due to short bowel syndrome or to other causes.
METHODS: Children with cholestasis received 30 mg/kg/day UDCA. Improvement or normalization of parenteral nutrition-associated cholestasis was evaluated at 6 months of therapy and at the last follow-up. In a subgroup of children, serum UDCA levels were measured while receiving UDCA and after 4 weeks withdrawal.

RESULTS: Twelve children were treated with UDCA. Full remission or partial improvement of parenteral nutrition-associated cholestasis occurred in 11 of 12 children. In three of four children, withdrawal of UDCA was associated with a rebound rise of cholestasis. Only one of 12 treated children showed no improvement and in this patient, in contrast to four other patients, plasma levels of UDCA did not increase during treatment. CONCLUSIONS: Ursodeoxycholic acid was effective in controlling parenteral nutrition-associated cholestasis. The efficacy of UDCA also in children with short bowel is related to intestinal absorption.
Outcomes of early nutrition support in extremely low-birth-weight infants.

Donovan-Ramona, Puppala-Bhagya, Angst-Denise, Coyle-Bryan-W


Abstract

AB BACKGROUND: Early nutrition intervention, both parenteral and enteral, is becoming a standard of care for the extremely low-birth-weight infant (ELBW; <1000 g) in many neonatal intensive care units (NICU) across the United States. However, there are no published or widely accepted guidelines regarding nutrition support strategies for this population. Most NICU clinicians have developed their own guidelines, so nutrition practices vary widely. In an effort to standardize our practice, we implemented nutrition support guidelines for ELBW infants, initiating both parenteral nutrition (PN) and minimal enteral feedings (MEFs) within the first 24 hours of life, whenever possible. The purpose of this study was 2-fold: (1) to evaluate the adherence to the nutrition guidelines and (2) to compare pre- and postguideline outcomes such as time to regain birth weight, time to reach full enteral feedings, and average daily weight gains. METHODS: The study was conducted at a level III NICU from January 2002 until February 2003. Charts of 70 infants with a birth weight ≤1250 g were reviewed as part of a quality-assurance project to monitor adherence to the newly established guidelines. Another 23 charts of ELBW infants who were admitted and cared for in the NICU before the initiation of the nutrition guidelines were reviewed as a control group. Data collected from the charts included the hour of life PN and MEFs were started, the day of life infants reached full enteral feedings, infant weights for the first 4 weeks of life, incidence of early hyperglycemia, occurrence of necrotizing enterocolitis, and length of neonatal birth hospital stay. Student's t-tests were used to compare clinical outcomes between infants receiving early nutrition support (<≤ 24 hours of life) vs those who were started later. RESULTS: Of eligible infants, 82.6% began receiving nutrition support within 24 hours of life. The average time to begin PN was 22 hours after the adoption of the guidelines vs 64.4 hours before guideline implementation (p < .01). In the postguideline group, MEFs were initiated at mean 27.1 hours of age vs 80.4 hours in the preguideline group (p < .01). Those who were started on early nutrition support reached full enteral feedings significantly sooner than those who received delayed nutrition support (12.7 days vs 45.8 days; p < .01). Early nutrition support also resulted in earlier regain of birth weight (day 13.3 vs 15.4 days, p < .05). Although not statistically significant, infants who received earlier nutrition support showed trends toward greater overall weight gain in weeks 3 and 4 of life and a lower incidence of elevated serum blood glucose. CONCLUSIONS: The implementation of early nutrition support guidelines influenced the timeliness of initiating nutrition support in our unit. Early initiation of nutrition support in ELBW infants produces a rapid regain of initial weight loss, improves weight gain, and enhances earlier achievement of full enteral feedings.
Early and aggressive nutritional strategy (parenteral and enteral) decreases postnatal growth failure in very low birth weight infants.


Abstract
AB OBJECTIVE: To compare postnatal growth and nutritional deficits after the implementation of two different nutritional strategies in two consecutives periods of time. METHODS: An early and aggressive nutritional regimen was used in a cohort of 117 very low birth weight (VLBW) infants. Amino acids were administered at the rate of 1.5 g/kg /day along with 5.6 mg/k/min of glucose flow on day 1 of life, and progressively increased to 4 g/kg/day and 13 mg/kg/min. Intravenous lipids were started at 0.5 g/kg/day at 24 h from birth, and increased to 3.5 g/kg/day; enteral feeding was begun at day 1 of life. Uni- and multivariate analyses were used to compare this group with the conventional group of 65 VLBW infants conservatively fed. RESULTS: Univariate analysis showed that in the aggressive group there was a 66% reduction in the risk of post natal malnutrition at 40 weeks of postmenstrual age (OR 0.34; 95% CI 0.17-0.67). This difference persisted in the multivariate analysis. Energy and protein deficits were lower in the aggressive group (P < 0.001). CONCLUSIONS: Early and aggressive introduction of total parenteral nutrition and enteral feeding resulted in better growth in weight, length and head circumference, and a reduction of nutritional deficits at 40 weeks of postmenstrual age.

Photoprotection of parenteral nutrition enhances advancement of minimal enteral nutrition in preterm infants.

Khashu-Minesh, Harrison-Adele, Lalari-Vikki, Gow-Andrew, Lavoie-Jean-Claude, Chessex-Philippe
Seminars in perinatology, Jun 2006, vol. 30, no. 3, p. 139-45

Abstract
AB BACKGROUND: Light exposure of TPN generates peroxides which induce vasoconstriction. Mesenteric vasoconstriction may affect feeding tolerance. Since photo-protection of TPN decreases peroxide generation, we hypothesized that shielding TPN from light may improve the establishment of minimal enteral nutrition in preterm infants. METHODS: Infants were randomized to TPN being light exposed (LE) or protected (LP) from birth. Feeding volumes were monitored through 7 days of life in those initiated on minimal enteral nutrition (MEN). Comparisons between LP and LE were performed by ANOVA. RESULTS: Daily increments and cumulative volumes of enteral feeds (mL/kg birth weight/d) during the first week of life were significantly higher in LP (n = 18) than LE (n = 19). CONCLUSION: Photo-protection of parenteral nutrition enhances advancement of MEN in preterm infants. Further research is needed to substantiate these findings and determine whether this confers long-term nutritional advantages.
Effects of glutamic acid and taurine on total parenteral nutrition.

Tsuchioka T, Fujiwara T, Sunagawa M
Journal of Pediatric Surgery, Sep 2006, vol. 41, no. 9, p. 1566-72

Abstract

AB BACKGROUND: The objective of the present study was to ascertain whether simultaneous administration of glutamic acid (Glu) and taurine (Tau) to patients on total parenteral nutrition (TPN) could improve intestinal mucosal atrophy and suppress bacterial translocation. METHODS: A 5-day TPN study was conducted in 5-week-old Sprague-Dawley rats. Commercially available Glu was used for TPN in group G and was enhanced with Tau (500 mg kg(-1) day(-1)) in group GT. Oral nutrition was provided in group C controls. At 5 days, amino acid and cytokine levels in plasma and endotoxin levels in portal blood were measured. The histology of the small intestine, liver, and lung were analyzed. RESULTS: Mucosal thickness and villus height in the small intestine were lower for group G than for groups C and GT. Taurine level in group GT was higher than in group G. Arginine and citrulline levels in groups G and GT were lower than in group C. Taurine level in the small intestine was greater in group GT than in group G. Citrulline concentration was lower in group G than in groups GT and C. Endotoxin level in portal blood and cytokine (tumor necrosis factor alpha, interleukin-1beta, and interleukin-6) levels in blood tended to be lower for group GT than for group G, but no significant differences were noted. Immunostaining showed strong positive reactions to vascular cell adhesion molecule-1 in the liver and lung for group G, and milder reactions for group GT. CONCLUSIONS: Simultaneous administration of Glu and Tau improved small intestinal mucosal thickness and villus height during TPN. Levels of Tau in the small intestine and plasma increased, and the level of citrulline in the small intestine improved. Decreased expression of adhesion molecules in the liver and lung and improved microcirculation in the liver were also confirmed.

Lipid injectable emulsions: 2006.

Driscoll-David-F
Nutrition in Clinical Practice, Aug 2006, vol. 21, no. 4, p. 381-6

Abstract

AB: Lipid injectable emulsions are an essential source of fatty acids, as well as a daily source of calories. They have been used in the clinical setting for almost 40 years, but despite this, there are no established official standards governing pharmaceutical quality. After 15 years of development, the United States Pharmacopeia (USP), which writes such standards for all FDA-approved pharmaceuticals, is poised to adopt an official monograph for lipid injectable emulsions that sets pharmaceutical requirements on all manufacturers placing limits on pH, free fatty acid concentrations and globule size (both mean droplet size and the population of large fat globules larger than 5 micrometers). Recent animal data has shown pathophysiologic changes in vital organs for lipids that fall outside the USP-proposed globule size limits. From a clinical perspective, newer lipid injectable emulsions show great promise in certain patient settings, most notably in the intensive care unit in both adults and infants. The clinical use of alternative oils, such as medium-chain triglycerides, fish oil and olive oil show benefits over conventional soybean oil formulations. In adults, for example, the administration of omega-fatty acids via soybean oil-based lipids produces a heightened inflammatory response via production of 2-series prostaglandins, whereas substitution of a portion of the lipid with omega-3 fatty acids via fish oil can favorably dampen the inflammatory response. In infants, for example, substitution of soybean oil with fish oil has recently been shown to reverse parenteral nutrition-associated liver disease. These advances should lead to safer infusion therapy in patients receiving lipid injectable emulsions.
A review of the quality of life of adult patients treated with long-term parenteral nutrition.

Baxter-Janet-P, Fayers-Peter-M, McKinlay-Alastair-W
Clinical nutrition, Aug 2006, vol. 25, no. 4, p. 543-53

Abstract
AB BACKGROUND AND AIMS: Some previous studies have assessed quality of life (QoL) in home parenteral nutrition (HPN) using generic instruments or non-validated questionnaires. A systematic search of electronic databases and relevant publications identified 50 publications. This paper reviews the QoL of patients receiving HPN and discusses the factors affecting QoL. RESULTS: There is little available data about the QoL of HPN patients. Both HPN and the underlying disease may affect QoL, and an evaluation of QoL requires the separation of these two issues. CONCLUSIONS: There is a need for a standardised, scientifically validated, treatment-specific instrument to measure QoL in this population. The use of a treatment-specific QoL questionnaire should become part of the routine clinical management of HPN patients.

Prospective evaluation of a peripherally administered three-in-one parenteral nutrition product in dogs.

Chandler-M-L, Payne-James-J-J

Abstract
AB OBJECTIVES: Peripheral parenteral nutrition is an option for short-term nutritional support in dogs which cannot be supported with enteral nutrition. The objective of this study was to examine the use of a three-in-one, 840 mOsmol/l peripheral parenteral nutrition product containing amino acids, lipids and glucose in separate compartments in dogs. METHODS: Nine dogs were administered the three-in-one product, and two dogs were administered the amino acid part of the product, via a peripheral vein. Dogs were monitored for mechanical and metabolic complications. RESULTS: Mechanical complications (apparent thrombus or thrombophlebitis) caused failure of infusion at a median of 36 hours. None of the dogs appeared to develop catheter-related sepsis. Using a 10-hour infusion period appeared to decrease the incidence of line failure. Mild and clinically non-significant hyperglycaemia was the only metabolic complication. In four of the dogs, serum folate, cobalamin and homocysteine concentrations were determined before and after peripheral parenteral nutrition administration. Oral and parenteral administration of methionine has been previously associated with lowered serum folate concentrations. Low serum folates and the subsequent hyperhomocystenaemia have been associated with venous endothelial damage and venous thrombus in other species. Serum cobalamin also affects homocysteine metabolism. Median serum folate, cobalamin and homocysteine concentrations were not affected by the short-term administration of this three-in-one product. Clinical SIGNIFICANCE: Using the product for 24 hours/day may require catheter replacement due to line failure. Other than line failure, which may be improved by 10- to 12-hour infusion times, this product was found to be safe and practical for short-term peripheral parenteral nutrition in dogs.


Abstract

AB: Taurine deficiency in patients on long-term parenteral nutrition may be involved in cholestasis. We aimed to assess plasma taurine and tauro-conjugated bile acids in adults with short-bowel syndrome and their response to intravenous taurine. Thirty-two adult patients, who had been on taurine-free parenteral nutrition for a mean of 59 (SE 14) months for short-bowel syndrome, were studied retrospectively. In a second study, a subgroup of ten patients with chronic cholestasis received taurine-enriched (6.0 (SE 0.6) mg/kg per d) parenteral nutrition for 55 (SE 13) months. Post-absorptive plasma taurine and bile acid concentrations were measured and liver function tests routinely sampled. At baseline, plasma taurine was lower in patients with a jejunal length of less than 35 cm (group A, n 16) than in those with a jejunal length of 35 cm or more (group B, n 16): 43 (SE 3) v. 58 (SE 4) mumol/l (P=0.01). The groups were no different in terms of chronic cholestasis (12/16 v.13/16 patients), total bile acids (26 (SE 13) v.14 (SE 5) mumol/l) or the ratio of tauro-conjugated:glyco-conjugated bile acids (5 (SE 2) v.8(SE 4) %, usual range 30-60 %). After supplementation, there was an increase in plasma taurine level (63 (SE 8) v. 43 (SE 4), P=0.007) but was no change in either total bile acids or the ratio of tauro-conjugated: glyco-conjugated bile acids. There was a significant decrease in aspartate aminotransferase level. Long-term parenteral nutrition for short-bowel syndrome is associated with an impaired tauro-conjugation of bile acids (enterohepatic pool), irrespective of plasma taurine level (systemic pool) and despite long-term taurine intravenous supplementation.
The incidence and impact of dextrose dose on hyperglycemia from parenteral nutrition (PN) exposure in hematopoietic stem cell transplant (HSCT) recipients.

Sheean-Patricia, Braunschweig-Carol

Abstract

AB BACKGROUND: Short-term, transient hyperglycemia is associated with adverse outcomes in acutely ill populations. Because parenteral nutrition (PN) is dextrose based, we hypothesized that exposure to PN would be associated with hyperglycemia and that greater levels of dextrose infusion would be associated with higher glucose concentrations. Our objective was to examine the temporality, incidence, and dose response from dextrose load upon hyperglycemia using several serum glucose cut points in PN vs non-PN HSCT recipients. METHODS: The medical records of adults admitted for initial autologous or allogeneic hematopoietic stem cell transplant (HSCT) at 2 university-affiliated hospitals between September 1999 and December 2003 were used in this retrospective cohort. To minimize the impact of disease acuity on serum glucose, patients with diabetes mellitus, steroid administration, patients with recently treated infections, or patients who died during therapy were eliminated from the study. Serum glucose values were recorded once per day from the first morning venous blood draw (2 AM-6 AM) to achieve uniformity among patients, to avoid measurements occurring more frequently among hyperglycemic patients, and to minimize the influence of oral intake. Hyperglycemia was examined using several serum glucose cut points (110, 125, 150, 175, and 200 mg/dL). Wilcoxon rank-sum tests were used to detect differences in hyperglycemic events between PN and non-PN subjects, and mixed-effects regression models were used to detect the association between PN exposure and hyperglycemia. To address the temporality and incidence of hyperglycemia between PN vs non-PN participants, before and after time frames were created. Preinfusion (before) and actual infusion (after) times were used for these intervals for PN patients; however, the average hospital days before (before) or during (after) PN infusion were used for comparison in non-PN recipients (ie, autologous non-PN before = hospital days 1-10, after = hospital days 11-21). RESULTS: Of the 208 patients who qualified for inclusion 49% (n = 101/208) received PN, which provided on average 26 kcal per kg, 1.3 g of protein per kg, and 2.7 mg/kg/min of dextrose (range 1.3-3.9 mg/kg/min). The proportion of hyperglycemic days before was not different between groups; however, it was significantly greater after in PN vs non-PN patients, regardless of serum glucose cut point. A dose response between dextrose administered (mg/kg/min) and serum glucose concentrations was not seen. When longitudinally presented, the temporal relationship between serum glucose and PN initiation was reflected approximately on hospital day 9. Using regression models that account for repeated measures, the odds of having hyperglycemia (yes/no; glucose >110 mg/dL) after PN exposure were nearly 4 times (odds ratio 3.9; 95% confidence interval, 2.7-5.5) that of non-PN exposed, after controlling for donor type, race, age, and conditioning chemotherapy. PN was the only variable to significantly interact with time (p < .0001), signifying not only the change in odds over time but also as powerful evidence that PN was the causative agent of hyperglycemic events. CONCLUSIONS: The broad use of PN at levels within current clinical guidelines in HSCT adults was associated with profound hyperglycemia; however, greater dextrose dose, within the narrow levels administered in this cohort, was not associated with higher glucose concentrations.
Paediatric Parenteral Nutrition. Part II: Getting To Grips With Pharmaceutical Aspects.

Allwood M
Complete Nutrition, August 2006, vol 6 (4), 8-10

Abstract
Introduction: The compounding of PN formulations required to meet the particular demands of paediatric patients, and in particular neonates, pose some particular problems for the pharmacist. These challenges are particularly associated with the following factors: the small volumes required; high requirements for calcium, magnesium and phosphate; amino acid mixtures which must include cysteine/cystine; the accuracy of making small volume additions, often fractions of a ml, of particular additives and heparin additions to bags.

Apparent increase of insulin peak area in HPLC analysis of a preparation consisting of a mixture of insulin and total parenteral nutrition.

Ichikawa-Etsuko, Kimura-Michio, Mori-Hiromi, Yamazaki-Futoshi, Hirano-Kazuyuki
Chemical & pharmaceutical bulletin, Aug 2006, vol. 54, no. 8, p. 1196-9

Abstract
AB: The peak area of insulin in a mixture of K.C.L.(R) injection and hyperalimentation fluid was found to increase in a time dependent manner up to 24 h in measurement by a high-performance liquid chromatograph. The increase of peak area corresponding to the insulin was detected at wavelengths of both 210 and 280 nm. This increase was only observed in the presence of the sugars, tryptophan, riboflavin, and insulin, and ascorbate was shown to counteract the increase. These results suggest the possibility that insulin forms a mixture caused by the oxidation reaction in a hyperalimentation fluid.
Longitudinal trends in quality of life after starting home parenteral nutrition: a randomised controlled study of telemedicine.

Chambers-Alison, Hennessy-Enid, Powell-Tuck-Jeremy
Clinical nutrition, Jun 2006, vol. 25, no. 3, p. 505-14

Abstract
AB BACKGROUND AND AIMS: This study defines and quantifies longitudinal changes in quality of life (QoL) at the time of first discharge home on home parenteral nutrition (HPN) and over the first year. METHODS: Results were compared in patients in standard contact with a nutrition nurse specialist by telephone, with results of those in contact via telemedicine in a randomised controlled trial. Participants were recruited from nine UK HPN centres. Patients were randomised to receive telemedicine upon initial discharge or after 1 year. The SF36 was the principal instrument chosen to determine QoL throughout the year on three predetermined occasions. EQ5D and hospital anxiety and depression scores were also recorded. RESULTS: Thirty participants were recruited to the study from March 2001 to June 2003. In all domains, QoL scores were significantly lower than normative data at discharge. QoL scores significantly improved over the first 6 months in physical functioning, physical role (RP), vitality (VT), social functioning (SF), emotional-role (RE) domains, and mental component summary (MCS). At 6 months RE, mental health (MH) and MCS were no longer significantly lower than normative data. There was no significant change in bodily pain (BP), general health (GH), MH, and physical component summary (PCS). Opiate use significantly reduced SF36 domains RP, BP, VT, SF, MH, and MCS at 6 months and was associated with more subsequent inpatient episodes and central line reinsertions. Patients with an acute onset of intestinal failure had less pain and better GH scores at 6 months, and had less inpatient episodes after discharge than patients with a more chronic onset. Telemedicine had no impact on QoL or subsequent clinical outcome. CONCLUSIONS: Aspects of QoL improve over the first 6 months of HPN. Opiate use and chronic diagnosis have a negative impact on some elements of QoL and clinical outcome variables.
The effect of heparin in peripheral intravenous nutrition via a fine-bore midline: A randomised double-blind controlled trial.

James A. Catton, John Davies, Brian M. Dobbins, Jonathan M. Wood, Michael J. McMahon, Dermot Burke

Abstract

BACKGROUND & AIMS: Peripheral intravenous nutrition (PIVN) delivered via a fine bore midline offers a viable alternative to central venous feeding. The major complication is the onset of peripheral vein thrombophlebitis (PVT). Feed additives such as heparin and hydrocortisone have been advocated in its prevention. Concern over the safety of heparin has prevented its widespread use; this study examines its true benefit.

CONCLUSION: When intravenous feeds are delivered in to a peripheral vein via a fine bore midline, the addition of heparin to the feed extends the total period of feeding attainable.

Home parenteral nutrition and the psyche: psychological challenges for patient and family.

Stern-Julian

Abstract

AB: The paper discusses the case histories of three patients who have faced the emotional implications of being initiated onto long-term parenteral nutrition (PN). In each case the patient’s personal and family history, relationship to their illness and the presence or relative absence of resentments and grievances have influenced their ability to tolerate the training and the transition to home PN (HPN). In addition, the emotional importance of food and feeding from a developmental and social perspective is explored, together with the numerous psychological and social ‘losses’ experienced by all patients on PN and the adaptations required within the family setting. The ‘meaning’ of PN to the individual and the need for both internal and external support are identified and, based on clinical experience, a number of features are described that may be indicative of the relative abilities of different patients to cope with HPN. Finally, the role of a dedicated Psychological Medicine Unit closely allied to a nutrition service is discussed.
Managing children and adolescents on parenteral nutrition: challenges for the nutritional support team.

Johnson-Tracey, Sexton-Elaine

Abstract
AB: Managing infants, children and adolescents, ranging from premature infants to 18-year-old adolescents, on parenteral nutrition (PN) is a challenge. The ability of children to withstand starvation is limited and, unlike adults, children require nutrition for growth. PN in children is often required secondary to a congenital bowel problem rather than because of an acquired condition. Conditions requiring PN include motility disorders, congenital disorders of the intestinal epithelium and short-bowel syndrome (SBS). Intestinal failure may be temporary and children with SBS may be weaned from PN. However, other children require permanent PN. There are no comprehensive guidelines for the nutritional requirements of children and adolescents requiring PN. Practice in individual centres is based on clinical experience rather than clinical trials. Requirements are assessed on an individual basis according to age, nutritional status and clinical condition. These requirements need regular review to ensure that they remain appropriate for the changing age and weight of the child. Assessments of intakes use different methods, e.g. reference tables and predictive equations. Complications of PN include infection, accidental damage to, or removal of, the line and cholestatic liver disease. Home parenteral nutrition (HPN) is associated with fewer line infections and allows continuation of nutritional support in a more normal environment, encouraging normal development and participation in family activities. However, having a child at home on HPN is associated with physical and psychological stresses. A feeling of depression, loneliness and social isolation is common amongst children and their families. Home-care services are essential to supporting children at home and should be tailored to, and sensitive to, the individual needs of each family.