gaspen | GEORGIA SOCIETY FOR PARENTERAL AND ENTERAL NUTRITION
A Chapter of the American Society for Parenteral and Enteral Nutrition

Newsletter

IN THIS ISSUE

President's Welcome

It's difficult to believe that the ASPEN 2019 Nutrition Science & Practice Conference has already come and went! This year's conference (for me) was all about adequate protein delivery, ERAS, and micronutrients. The keynote address made by Dr. Sanjeev Arora was extremely awe-inspiring as he discussed the creation of Project ECHO® (Extension for Community Healthcare Outcomes) to dramatically improve both capacity and access to specialty care for rural and underserved populations by linking expert inter-disciplinary specialist teams with primary care clinicians through teleECHO™ clinics. More information on Project ECHO® can be found here: https://echo.unm.edu/.

The purpose of this abbreviated newsletter is to highlight some of the programs and sessions members of our board attended at ASPEN 2019. We were fortunate to have three members of our board present at the conference – myself, Adina Hirsch, and Marlene Neville, and we wanted to use this newsletter to share some clinical pearls from the conference.

Aside from attending ASPEN 2019, our board has also been very busy planning our upcoming GASPEN annual meeting! The meeting will be held on Friday, September 20, 2019 at the WellStar Development Center and will provide seven hours of continuing education credit for dietitians, pharmacists, nurses, and physicians. This year's meeting will include topics such as: insulin management with parenteral and enteral nutrition, parenteral nutrition safety and EMR integration, disaster planning, and many more! You should have received a save-the-date, so make sure to mark your calendars!

As always, we welcome any suggestions and comments from GASPEN members for CE programs, newsletter articles, and any other ways that we can benefit our members. We also would like to welcome any GASPEN members who would like to become involved on our board.

I look forward to seeing everyone at the GASPEN Annual Meeting in September!

Khatija Jivani, PharmD, BCPS
GASPEN President

Meeting in Review

Critical Care – Update on Micronutrient Therapies in Sepsis

Session Review

Khatija Jivani, PharmD, BCPS

The high metabolic demand caused by sepsis can lead to altered mitochondrial and cellular function. Micronutrient therapies in sepsis may play a pivotal role in these processes and can lessen and may even prevent further damage in a septic patient. Many micronutrients have been researched over the years but robust results leading to a strong recommendation for or against using micronutrients are still lacking. The four micronutrients discussed in this summary include: Vitamin B1 (Thiamine), Vitamin C, Vitamin D, and Coenzyme Q12.

Vitamin B1 (Thiamine) has a short-life hence deficiency can occur in as little as 10 days. Septic patients can often be thiamine deficient, and research has shown a correlation between low thiamine levels and elevated lactate levels (after patients with liver dysfunction were removed). In a retrospective matched cohort study conducted by Woolum et al. in 2018, thiamine supplementation was shown to have a reduction in lactate with reduction in 28-day mortality. Since elimination is rapid, high doses of thiamine should be given ranging 200 to 500 mg as a single dose. It can also be given as a continuous infusion which may improve thiamine uptake by the body by 50 to 75%. Thiamine should also be supplemented in patients with congestive heart failure (CHF) as drugs such as loop and thiazide-type diuretics can cause thiamine-wasting. Additional studies regarding thiamine in critically ill patients are ongoing including thiamine deficiency in ICU delirium and thiamine supplementation in CRRT patients.

Vitamin C (Ascorbic acid) is an antioxidant and may play a role in maintaining vascular integrity in patients with sepsis by maintaining tight junctions. It may also prevent oxidation of steroids, which can result in improved uptake of steroids into the cell. In the retrospective study conducted by Marik et al. in 2017, the combination of hydrocortisone, Vitamin C, and thiamine in the treatment of severe sepsis and septic shock showed a 32% reduction in mortality. Research has also shown that Vitamin C levels tend to decrease significantly due to consumption over 96 hours in a critically ill patient. In another study conducted by Zabet et al. entitled the Effect of high-dose Ascorbic acid on vasopressor's requirement in septic shock, researchers found that Vitamin C dosed at 25 mg/kg intravenously every 6 hours for 72 hours was associated with lower vasopressor doses, less time on vasopressors, and reduced mortality when compared to placebo. Other studies have shown trends in reduced encephalopathy, reduced SOFA scores with reduced inflammatory mediators, and less vascular injury with Vitamin C supplementation. The Vitamin C, Thiamine And Steroids in Sepsis (VICTAS) Study is currently enrolling patients and is expected to be complete in 2021. High dose Vitamin C may lead to oxalate nephropathy and may even lead to hemolysis in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Vitamin C administration may also cause a false elevation in point-of-care glucose measurements and mask hypoglycemia but readings should return to normal 24 hours after discontinuation of Vitamin C.

Vitamin D is critical in regulation of cell proliferation and differentiation, hormone secretion, and immune function. It may also have anti-inflammatory, antimicrobial, and/or antineoplastic effects. Severe Vitamin D deficiency is usually defined as levels less than 10 ng/mL. Research has shown that there may be a relationship between low Vitamin D levels and healthcare-associated infections.

In a study conducted by Youssef et al. in 2012, researchers concluded that patients with severe Vitamin D deficiency prior to admission had almost a 3-fold relative risk of developing hospital-acquired infections. In another study, low pre-operative Vitamin D levels prior to Roux-en-Y gastric bypass surgery was associated with a significant increase in risk of developing surgical site infections. However, studies have also shown that Vitamin D supplementation can result in a U-shaped relationship with an increase in all-cause mortality seen in patients with levels greater than 60 ng/mL. Critically ill patients may have lower Vitamin D bioavailability despite adequate levels. In critically ill or septic patients, levels should be monitored using 1,25-dihydroxyvitamin D levels. In a pilot randomized-controlled trial conducted by Quraishi et al. in 2015 showed that high-dose cholecalciferol supplementation (200,000 IU and 400,000 IU) rapidly increased Vitamin D levels leading to improved bioavailability and utilization of Vitamin D. No difference was seen in C-reactive protein (CRP) levels between the groups. When comparing Vitamin D2 (ergocalciferol) and Vitamin D3 (cholecalciferol), Vitamin D3 is preferred since it is more effective for boosting circulating levels. Studies have shown that Vitamin D3 supplementation may reduce all-cause mortality and low daily doses may be sufficient to prevent deficiency in the general population. Bolus doses as high as 750,000 IU have been studied but show a rapid peak and decline within 3 months of administration and was also associated with a further decrease in levels likely attributed to Vitamin D wasting, suggesting that mega doses in critically ill patients may not be optimal.

Co-Enzyme Q 10 (CoQ10) is an antioxidant that is transported on low-density lipoproteins (LDLs) and is primarily synthesized endogenously. Ubiquinol, the reduced form, is more bioavailable than the oxidized form, ubiquinone. Levels may be low in patients with sepsis compared to control and be inversely associated with inflammatory markers. In a prospective clinical trial of patients with sepsis given 200 mg of CoQ10 versus placebo, researchers did not see a difference in inflammatory markers over a period of 0 to 72 hours except for interleukin-6 (IL-6). There was no difference in ICU or hospital length of stay or hospital mortality, however, these findings may be a result of study limitations. CoQ10 doses used in heart failure patients have been as high as 1,200 mg/day, and this study only dosed patients at 200 mg/day. Also, CoQ10 is unavailable in parenteral form and this may have affected bioavailability. In a study looking at therapeutic hypothermia post-cardiac arrest, researchers found that the CoQ10 group had a significant improvement in overall survival with a trend towards better neurological outcome, but no serum levels were drawn to assess the adequate dose or level to target. An absorption study evaluating a dose of 300 mg twice daily for 7 days in cardiac arrest patients is currently ongoing. There is a concern that intravascular CoQ10 levels may be low in patients on concomitant statin therapy and may improve statin-induced myopathy, especially in septic patients.

Competency Training: Optimizing Practice as a Nutrition Support Clinician in the Modern Era

Session Review

Marlene Neville, MMSc, RD, LD, CNSC

This session examined the current trends of nutrition support education across the multi-disciplinary spectrum; provided a review of the current literature and national guidelines concerning nutrition support competency training; presented current nutrition support practices among varied practice settings; and proposed an interdisciplinary method to include optimal nutritional support training, recognized standards of practice, and order writing privileges, as designated by state licensure guidelines. The ASPEN Model papers were referenced for standardized competencies for parenteral nutrition (PN) prescribing, order review, preparation / compounding, and administration. Strong recommendations were made to include PN support education in the curricula of healthcare professional schools. In addition, institutions were urged to develop, implement, and mandate competency training programs for all disciplines involved in PN. Course speakers encouraged the audience to conduct systematic evaluations of the best methods to implement these PN competency training programs and share / publish their results.

Micronutrient Contamination of Parenteral Nutrition Solutions in the United States

Session Review

Adina Hirsch, PharmD, BCNSP

Parenteral nutrition (PN) solution contamination has been a concern for several years as it confounds the amounts of micronutrients that patients requiring PN receive and puts patients at risk for micronutrient toxicities.

Every year, ASPEN awards several early career investigators who have submitted original abstracts with the VARS Award, in memory of Harry M. Vars, a leader in nutrition support research. This year, one of the VARS paper finalists, Logan Olson, PharmD, BCCCP from Mayo Clinic, Rochester, was awarded the Promising Investigator Award for his research (**Quantitative Assessment of Trace Element Contamination in Parenteral Nutrition Components**) on micronutrient contamination of PN solutions in the United States.

Methods: The lab at Mayo Clinic, Rochester quantified trace element (TE) contamination of 65 PN products in the US (32 components) for zinc (Zn), manganese (Mn), copper (Cu), chromium (Cr), and selenium (Se) contamination. Products tested included amino acid solutions, injectable lipid emulsions, multivitamins (MVI), insulin, ranitidine, unfractionated heparin (UFH), sterile water for injection (SWFI), 70% dextrose (D70W) and several electrolyte products as well as L-carnitine and cysteine.

GASPEN at ASPEN 2019

(left to right): Khatija Jivani and Adina Hirsch

Results: TE contamination was found in 71% of the PN products tested. The majority of contamination detected was with Mn and Cr. No TE contamination was found in SWFI, potassium chloride, D70W, ILE, UFH, vitamin K, or MVI (vial 2). Significant levels of Cr contamination were detected in magnesium sulfate and potassium and sodium phosphates. Significant levels of Mn contamination were detected in magnesium sulfate, sodium and potassium phosphates, calcium chloride, and calcium gluconate.

Conclusions: There is significant contamination of both Cr and Mn in PN products. The authors recommended that multi trace element (MTE) products in the United States be reformulated to remove Cr and to decrease or remove Mn in adult, pediatric and neonatal MTE products.

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American Society for Parenteral and Enteral Nutrition

Future ASPEN Nutrition Science & Practice Conferences

2020
March 28th to 31st
Tampa Convention Center
Tampa, FL

2021
March 20th to 23rd
Colorado Convention Center
Denver, CO

New Products

Adina Hirsch, PharmD, BCNSP

Selenious Acid Injection (American Regent, Inc.)

In April 2019, the FDA approved selenious acid injection for adult and pediatric patients as a source of selenium for parenteral nutrition (PN) when oral or enteral nutrition is not possible, insufficient, or contraindicated. Prior to FDA approval, there were no FDA-approved parenteral selenium products in the United States.

Selenious acid injection is available in multi-dose 10-mL vials (60 mcg/mL). Dosing per prescribing information is as follows (section 2.5):

- Adults: 60 mcg/day
- Pediatric patients 7 kg and above: 2 mcg/kg/day (up to 60 mcg/day)
- Pediatric patients less than 7 kg: 2 to 4 mcg/kg/day

Dosing may be higher in patients depending on their clinical situation. Of note, selenious acid is not intended for direct intravenous infusion. It is indicated to be administered as part of a PN admixture only.

Reference: Selenious Acid for Injection [package insert]. Shirley, NY: American Regent, Inc.; 2019.

Omegaven® (Fresenius Kabi, LLC, USA)

In July 2018, the FDA approved Omegaven® (100% Fish Oil Injectable Lipid Emulsion (ILE)) as a source of calories and fatty acids in pediatric patients with parenteral nutrition associated cholestasis (PNAC). Omegaven® is not indicated for the prevention of PNAC. Prior to FDA approval, Omegaven® was available only under compassionate use by the FDA.

Omegaven® is a 10% ILE (0.1 g/mL) supplied in single dose vials of 50-mL (5 g/50 mL) and 100-mL (10 g/100 mL). Omegaven® provides 1.12 kcal/mL (11.2 kcal/g). Dosing and administration per prescribing information is as follows (section 2.1):

- 1 g/kg/d (also maximum dose)
- Rate of infusion should not exceed 1.5 mL/kg/hr or 0.15 g/kg/hr
- Use a 1.2 micron in-line, DEHP-free vented infusion set
- Complete the infusion of Omegaven® within 12 hours if administered via Y-site and 24 hours if part of a PN admixture

Reference: Omegaven® [package insert]. Graz, Austria: Fresenius Kabi; 2018.

NEW INDICATION: GATTEX® (teduglutide; Shire-NPS Pharmaceuticals, Inc.)

In May 2019, the FDA expanded the approval of GATTEX®, a GLP-2 analog for the treatment of patients with short bowel syndrome (SBS) who are dependent on parenteral nutrition, to include the pediatric population aged one year and older.

Dosing and administration per prescribing information is as follows (section 2.2):

- For subcutaneous use only
- The recommended dosage for both adults and pediatric patients is 0.05 mg/kg once daily by subcutaneous injection
- Alternate administration sites between one of the four quadrants of the abdomen or into alternating thighs or arms

Reference: Gattex® [package insert]. Lexington, MA: Shire-NPS Pharmaceuticals, Inc.; 2019.

Parenteral Nutrition Component Shortages Update

Yolanda Whitty, PharmD, BCPS

Per ASPEN's Clinical Practice Committee Shortage Subcommittee:

- Do not ration parenteral nutrition (PN) nutrients if the supply is sufficient to provide the full daily dose.
- Follow the recommendations for PN management on the ASPEN Product Shortage Management website.
- Return to appropriate dosing as soon as the shortage has been resolved.
- Avoid suboptimal dosing due to potential cost incentive and lack of perceived adverse effects to patients.

Current shortages of PN components are summarized in the table below.

Intravenous (IV) Parenteral Nutrition Component Shortages

PN Component	Reason for Shortage	Availability of Alternatives
Ascorbic acid injection, 500 mg/mL, 50-mL vials	5/13/19: Mylan Institutional did not provide a reason for the shortage.	McGuff Pharmaceutical has 50-mL vials available.
Amino acid products 15% Plenamine™ 1,000-mL, 10% TrophAmine® 500-mL, and 10% Premasol® 500- and 2,000-mL	5/21/19: ICU Medical discontinued several products. BBraun did not provide a reason for shortage.	BBraun has HepatAmine®, ProcalAmine®, and FreAmine® III available. ICU Medical has Aminosyn® II 10% and 15% and Aminosyn®-PF 7% and 10% available. Baxter has Clinisol®, Travasol®, Premasol®, Prosol®, Clinimix®, and Clinimix-E® available.
Copper chloride injection, 0.4 mg/mL 10-mL vials	5/26/19: Pfizer has shortage due to manufacturing delays; they are the sole supplier of copper chloride injection.	Pfizer has product available in limited supply.
Magnesium sulfate, 500 mg/mL 10- and 20-mL vials	5/23/19: American Regent is not marketing the product. Fresenius Kabi and WG Critical Care have shortages due to increased demand. Pfizer has shortage due to manufacturing delays.	Exela Pharma Sciences has the 10-mL vials. Fresenius Kabi has the 2-, 10-, 20-, and 50-mL vials.
Multiple vitamins for infusion, adult & pediatric	4/22/19: Pfizer has shortage due to manufacturing delays.	Baxter has all presentations fully available at this time.
Potassium acetate, 2 mEq/mL 50-mL vials	5/26/19: American Regent is not marketing product. Pfizer has shortage due to manufacturing delays.	Potassium acetate 2 mEq/mL 20-mL vials are available from Exela Pharma Sciences and Pfizer.
Potassium phosphate 3 mMol/mL 15-mL vials	5/26/19: American Regent is not marketing product. Fresenius Kabi has shortage due to increased demand. Pfizer has shortage due to manufacturing delays and recall on seven lots of the 15-mL vials due to sterility concerns.	Fresenius Kabi has 5-, 15-, and 50-mL potassium phosphate vials and Glycophos® 1 mMol/mL 20-mL vials available. Pfizer has the 15-mL vials available in limited supply.
Sodium chloride 23.4%, 100- and 200-mL vials	5/20/19: Fresenius Kabi and Pfizer have shortages due to increased demand.	Fresenius Kabi has 30-mL vials available and estimates that the 200-mL vials will be available early-June 2019. Pfizer estimates that the 200-mL vials will be available December 2019.
Sodium phosphate, 3 mMol 5- and 15-mL vials	5/3/19: American Regent is not marketing product. Fresenius Kabi has shortage due to increased demand. Pfizer has shortage due to manufacturing delays.	Fresenius Kabi has Glycophos® 1 mMol/mL 20-mL vials available. Pfizer estimates a release date of March 2020 for the 15-mL vials.

Note: Where applicable, use oral/enteral formulations for administration via oral/enteral routes and restrict IV agents to PN use only, if possible. Reserve pediatric multivitamin supply for children < 2.5 kg or < 36 wk gestational age. Avoid use of pediatric products in adult PN.

1. Product Shortage Management. ASPEN. https://www.nutritioncare.org/Guidelines_and_Clinical_Resources/Product_Shortages/Product_Shortage_Management/.
2. Drug Shortages List. ASHP. https://www.ashp.org/drug-shortages/current-shortages/drug-shortages-list?page=CurrentShortages#top. Accessed May 29, 2019.

Save the Dates

- **2019 GASPEN Annual Meeting 0.7 CEU/7 Contact Hours**
  Learn about evidence-based practices for managing adult and pediatric patients receiving parenteral and enteral nutrition in the inpatient and outpatient settings!

  Friday, September 20th; 7:15 AM to 4:45 PM ET
  WellStar Development Center | Atlantic Auditorium
  2000 N Park Pl SE, Atlanta, Georgia 30339

- ASPEN Clinical Nutrition WEBINAR SERIES **FREE Webinars**

  ENFit®: Overcome Implementation Challenges
  Tuesday, June 4th; 3:00 to 4:00 PM ET

  Parenteral Nutrition Prescribing in the Age of Drug Shortages
  Tuesday, June 18th; 4:00 to 5:30 PM ET
  Both available at www.nutritioncare.org

Get Involved!

We encourage our members to volunteer for committees, become involved as board members, speak at meetings and present posters and abstracts.

Feel free to contact our board members for more information.

Contact Us

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Correction: *The article published in the Winter 2019 GASPEN Newsletter on the Southeast Chapter of Critical Care Medicine meeting on November 13, 2018 was written by Lindsay Sellers, PharmD, PGY2 Pharmacy Resident at Augusta University Medical Center.*