



Case Report: Zinc Deficiency in Long Term TPN Therapy

The following is a case report describing one patient's experience with zinc deficiency. It was prepared by Emily J. Blackwell, University of Appalachia College of Pharmacy Pharm.D. Candidate (2008) under the guidance/supervision of Cynthia Bogartz, Pharm.D. at Infusion Partners of Knoxville, Tennessee.

Special points of interest:

- Many patients are susceptible to zinc deficiency
- Remicade drug label updated with new warnings (see page 2)

The Importance of Proper Zinc Supplementation in TPN Therapy—Case Report of a 55 Year-Old Female with Diagnosis of Short Bowel Syndrome (SBS)

Introduction: The significance of zinc supplementation in human nutrition was recognized relatively recently in 1961 due to the emergence of “adolescent nutritional dwarfism” as a result of zinc deficiency. Since that time, proper zinc supplementation has become a major public health concern due to inadequate growth in infants and children, especially in developing countries. However, growth retardation is only one of the many possible effects that may result because of inadequate dietary zinc supplementation.

Zinc is an integral trace element involved in many cellular processes such as:

- protein development
- hormone release
- growth and development
- gene transcription
- immune response
- nerve impulse transmission

Signs and symptoms of zinc deficiency include:

- growth retardation
- diarrhea
- poor appetite/loss of taste
- increased incidence of infections
- delayed wound healing (e.g. pressure ulcers)
- rough, scaly skin (hemorrhagic dermatitis, hair loss)

Individuals at risk for this deficiency include patients with:

- severe/persistent diarrhea
- malabsorption syndromes
- strict vegetarian diets
- inflammatory bowel disease
- alcoholic liver disease
- total nutrition obtained parenterally

The normal serum concentration range for zinc is 70-130 mcg/dL. The recommended values for zinc supplementation include the following:

Recommended daily allowance (RDA):	11 mg/day (males) 8 mg/day (females)
Small bowel losses	Replace 12 mg/L
Stool or ileostomy output	Replace 17 mg/L
Wound healing	Replace 5 mg/day

Inside this issue:

Crohn's Disease Updates	2
Drugs in the News	3
More Warnings for Exjade	3
Drug Warning Updates	4
New Autoimmune Disease Vaccine	4

Discussion: A 55 year-old female diagnosed with Short Bowel Syndrome (SBS), and subsequent malabsorption with chronic diarrhea, developed protein deficiency while receiving long-term 12-hour cyclic Total Parenteral Nutrition (TPN) therapy. Infusion Partners received the initial referral on 2/08/05 and the patient began TPN on 2/11/05. TPN labs were checked weekly. Protein deficiency was noted beginning in August 2006, based on pre-albumin serum levels of 12-15 mg/dL (normal range 16-38 mg/dL). The patient's TPN prescription was gradually adjusted to include increased calories and protein, to a maximum quantity of 2.2 g/kg/day of protein and total calories of 32 kcal/kg or 1800 kcal/day. The TPN at this time included 5 mg of zinc per day. The patient's pre-albumin levels continued to drop over the next several weeks, at an average of 1 mg/dL/week, from 15 mg/dL to 13 mg/dL. On 4/16/07 the patient reported other

signs and symptoms of zinc deficiency such as loss of appetite and taste, eczema, hair loss, and fatigue. Labs reported on this date included a serum zinc level of 55 mg/L (normal range 70-150 mg/L) and therefore an additional 5 mg of zinc was added to the patient's daily TPN.

The patient reported no improvement in the signs/symptoms of zinc deficiency by mid-May 2007, and therefore an additional 10 mg/day of zinc supplementation was added to the patient's TPN prescription on 5/15/07. This provided the patient with a total of 20 mg zinc per day. On 6/11/07 the patient's labs showed that the zinc level had improved to 118 mg/L. Pre-albumin levels also improved over the next 2-3 weeks and currently are sustained in the range of 16-18 mg/dL. Total protein (amino acids) in the TPN was therefore decreased from 2.2 g/kg/day to 1.86 g/kg/day.

By June 2007, the patient reported improvement in the signs and symptoms of zinc deficiency. As her sense of taste and appetite improved, the patient also began to increase her oral intake. This allowed her to decrease from a 7 day per week TPN regimen to a 4 day per week regimen on 6/19/07.

Conclusion: It is important for clinicians to be aware of the importance of zinc supplementation during long term TPN therapy. Many patients, especially those patients with increased GI losses, are susceptible to zinc deficiency. These patients may experience a consequent protein deficiency which may not respond to increased protein in the TPN. Zinc supplementation may be an appropriate therapy for patients with low serum zinc levels who have met their respective protein requirements, yet have not met their pre-albumin goal. The addition of adequate zinc to this patient's TPN regimen also provided an added quality of life benefit in that her TPN requirement was reduced from 7 days a week to 4 days a week, once the zinc deficiency-related alterations in appetite and taste were corrected.



Patients on long term parenteral nutrition may experience deficiencies in micronutrients

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Crohn's Disease Updates

Tysabri: Use in Crohn's Disease?

Remicade: New Adverse Reaction added to Label

TYSABRI: New Indication Coming for Crohn's Disease?

The FDA's Gastrointestinal Drugs Advisory Committee and Drug Safety and Risk Management Committee recently voted to allow Tysabri (natalizumab) to have an additional indication for treatment of moderate-to-severe Crohn's disease. The FDA has yet to make this recommendation final. If the indication for Crohn's disease is permitted, a risk management plan similar to the TOUCH program for Tysabri use in multiple sclerosis patients would be required. Natalizumab has also been studied in the treatment of rheumatoid arthritis.

Source: American Society of Health-System Pharmacists News, 9/15/07

REMICADE: Post-marketing Adverse Events

The following adverse events, some with fatal outcome, have been reported during post-approval use of REMICADE: neutropenia (see WARNINGS, Hematologic Events), interstitial lung disease (including pulmonary fibrosis/interstitial pneumonitis and very rare rapidly progressive disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, pericardial effusion, systemic and cutaneous vasculitis, erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal necrolysis, Guillain-Barré syndrome, psoriasis (including new onset and pustular, primarily palmar/plantar), transverse myelitis, and neuropathies (additional neurologic events have also been observed, see WARNINGS, Neurologic Events) and acute liver failure, jaundice, hepatitis, and cholestasis (see WARNINGS, Hepatotoxicity). Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to REMICADE exposure.

Source: FDA MedWatch Summary June 2007, Remicade label revision dated April 2007



The FDA MedWatch service is free & available to everyone at <http://www.fda.gov/medwatch/>

Drugs in the News

New Generics Available:

- Ampicillin and Sulbactam from GeneraMedix, Inc. in 1.5 and 3 gram vials
- Cefotetan Disodium for Injection from Abraxis Pharmaceutical Products (APP) in 1 and 2 gram vials. This drug has not been available since 2006, when it was withdrawn from the market due to problems with sourcing of raw materials.
- Epirubicin Hydrochloride Injection from Teva as a 2 mg/ml concentration. Vial sizes are 50 mg and 200 mg. This product is an AP-rated generic equivalent of Pfizer's Ellence Injection. The brand name product is indicated for use as a component of adjuvant therapy in patients with axillary node tumor involvement following resection of primary breast cancer.

Legislation Introduced to Help Americans Suffering from Pain

Representatives Lois Capps (D-CA) and Mike Rogers (R-MI) have introduced the National Pain Care Policy Act of 2007 to Congress. This legislation is intended to improve pain care research, education, training, access, outreach, and care. It would authorize an Institute of Medicine Conference on Pain Care, provide comprehensive pain care education and training for health care professionals, and begin a public awareness campaign on pain management. Many organizations have expressed support for this proposed legislation, including the American Cancer Society Action Network and the American Pain Foundation.

USP to Release Sterile-Compounding Chapter Revision in Parts

David W. Newton, PhD, Chair of the United States Pharmacopeia Sterile Compounding Expert Committee, told attendees at the American Society of Health-System Pharmacists 2007 Summer Meeting that revisions to Chapter 797 would be released in two parts. The chapter has been extensively revised. The new version will have 23 sections instead of 14, and will include more information on definitions, air quality standards, testing methods, facility design, cleaning, and disinfection procedures.

The first part of the revision will be released soon and will take effect about 6 months after its release. The second part of the revision will update the sections on disinfectants, cleaning and environmental monitoring, and will be released later in the year.

More Warnings for Exjade

Novartis has notified healthcare professionals that new warnings have been added to the labeling for Exjade (deferasirox). Exjade is an oral drug used to treat transfusional hemosiderosis, the chronic iron overload that can result from blood transfusions.

Cases of acute renal failure, some of them fatal, have been reported in patients taking this drug. Most occurred in patients with multiple co-morbidities who were in advanced stages of their hematological disorders.

Before beginning therapy with Exjade, all patients should have their serum creatinine assessed in duplicate to establish a baseline level, and then creatinine should be monitored monthly during treatment. Patients who may be at increased risk of complications should be monitored weekly during the first month of Exjade therapy or when the treatment is modified, and then monthly thereafter. These high-risk patients include the elderly, people with pre-existing renal disease or other co-morbid conditions, and those receiving drugs that can depress renal function.

There have also been reports of cytopenias in patients on Exjade, some of them fatal. The relationship between the drug and these effects is uncertain, since most of the patients had pre-existing hematological disorders that themselves are associated with bone marrow failure. Blood counts should be monitored regularly and treatment interrupted in patients who develop unexplained cytopenia.

Additional Information:

FDA MedWatch Safety Alert. Exjade (deferasirox) Tablets For Oral Suspension. May 22, 2007. <http://www.fda.gov/medwatch/safety/2007/safety07.htm#Exjade>



USP Chapter 797 updates should be available soon!



Patients who cannot tolerate Exjade may return to Desferal therapy

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Xolair: Updates on Recent Warnings

Revised Prescribing Information for Xolair

Genentech is informing health care professionals and asthmatic patients that the prescribing information for *Xolair* (omalizumab) injection has been revised to include a new Boxed Warning and also updated Warnings, Precautions, and Adverse Reactions sections describing the risk for anaphylaxis (which can be delayed for 24 hours or more) when taking this medication. A new Medication Guide has also been developed and will be provided to patients with each *Xolair* prescription. The FDA advisory states that *Xolair* should only be administered to patients in a health care setting under direct medical supervision and that patients should be observed for a specified amount of time after each *Xolair* injection for signs and symptoms of anaphylaxis. The package insert is available at: <http://www.gene.com/gene/products/information/pdf/xolair-prescribing.pdf>

Dangerous Drug Interaction: Cipro and Zanaflex

Acorda Therapeutics recently alerted healthcare professionals about new contraindications for Zanaflex (tizanidine), a drug used to treat spasticity.

New labeling says that this drug should not be used concomitantly with either of two CYP1A2 inhibitors: fluvoxamine, which is used to treat depression and anxiety disorders, or the antibiotic ciprofloxacin. Taking either of these drugs together with tizanidine can cause dangerously elevated serum levels of tizanidine, which can lead to side effects such as severe hypotension and sedation.

The company says that other CYP1A2 inhibitors may also lead to substantial increases in tizanidine blood concentrations, although there have been no clinical studies to substantiate this. Therefore, using tizanidine with other CYP1A2 inhibitors should ordinarily be avoided. These drugs include zileuton, other fluoroquinolones, antiarrhythmics, H-2 blockers, oral contraceptives, acyclovir and ticlopidine.

Additional Information:

FDA MedWatch Safety Alert. Zanaflex (tizanidine hydrochloride) Tablets and Capsules. April 11, 2007.

<http://www.fda.gov/medwatch/safety/2007/safety07.htm#Zanaflex>

New Autoimmune Disease Vaccine in Clinical Trials

Investigators recently completed the first human clinical trial of a DNA vaccine for Multiple Sclerosis (MS). It appeared to produce beneficial brain and immune system changes in patients with moderate MS, without making the disease worse.

DNA vaccines have been researched for almost 20 years. DNA vaccines for cancer and infectious diseases have usually been developed to activate the immune system. The goal for that research was to mobilize the immune system to fight the disease. In most cases, results of past clinical trials of DNA vaccines have been disappointing. In contrast, the BHT-3009 (Bayhill Therapeutics, Palo Alto, California) vaccine was designed to down-regulate or alter an ongoing immune response. This is because MS is a disease where the immune system is overactive.

The clinical trial was conducted in 4 centers in the U.S. and Canada, and included only 30 patients. The patients had relapsing-remitting or secondary progressive MS, and were not taking any other disease-modifying agents. BHT-3009 was administered by IM injection at weeks 1, 3, 5, and 9. Three different dose strengths were used: 0.5 mg, 1.5 mg, and 3 mg per dose.

The researchers are currently conducting a randomized, placebo-controlled clinical trial of BHT-3009 in 290 MS patients. Results from this subsequent study should be available later this year.



*DNA Vaccine shows
promise in MS
patients*