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In This Issue

Feature Article

Reducing Inflammation through Micronutrient Therapy for Chronic Kidney Disease

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Introduction

Approximately 350,000 individuals in the U.S. diagnosed with chronic kidney disease (CKD) undergo therapeutic maintenance hemodialysis (MHD) on a regular basis. However, an astonishing 20% of this population dies each year as a result of associated cardiovascular disease (1). Uremia, along with the high prevalence of protein-energy malnutrition (PEM) and systemic inflammation are thought to be major contributors to the soaring cardiovascular mortality rate in CKD patients. This is attributed mainly to oxidative stress (2). Uremia also interrupts the delicate balance of pro-inflammatory and inhibitory cytokines, disturbing proper immune function. This contributes further to inflammatory complications, such as infection (3,4). Current research indicates malnutrition-inflammation atherosclerosis correction in CKD patients is complicated and intervention may require a multi-pronged approach. It is believed that improving nutrition status and reducing chronic inflammation may significantly improve cardiovascular morbidity and mortality rates in dialysis patients (2). This article will explore the use of micronutrient therapies to potentially regulate chronic inflammation and bolster the immune response in MHD patients.

Factors Leading to Micronutrient Losses

Pre-MHD patients are often malnourished and frequently suffer from micronutrient deficiencies as a result of reduced dietary intake, as well as modified dietary intake during renal failure progression. Once on dialysis, micronutrient losses occur during the actual MHD process, particularly water-soluble vitamins and potentially some trace minerals (5). Additionally, PEM contributes to high circulating concentrations of inflammatory proteins; promoting protein catabolism, muscle wasting, diminishing appetite, and ultimately, a vicious cycle of oxidative stress and inflammation (6).

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From the Editor's Desk

Rachael R. Majorowicz, RD, LD
Editor

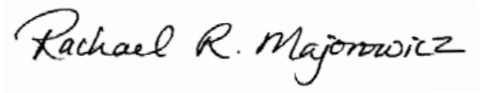
Despite the dismal state of the economy, RPG remains committed to provide positive experiences and needed resources for our membership. By continuing to help fund research, providing travel stipends for continuing education, sharing the resources available through the lending library, maintaining affordable member dues, constantly expanding/improving the web site, offering review courses for the Board Certified Specialist in Renal Nutrition, aka CSR (last offered at the 2009 NKF Clinical Meetings), and many more benefits—RPG remains ever focused on keeping your needs close-at-heart.

One of the most recent efforts by RPG is now available on the web site—the implementation of online CPEU recording. There is no more printing, folding, or mailing of CPE quizzes or wondering if your submission was ever received! The CPE inserts, quizzes, and certificates of completion are now available online in one, easy and convenient location. Kudos to RPG's Web Editor, Cathy Goeddeke-Merickel, MS, RD, LD, for all her time and dedication to bring this project to fulfillment.

But RPG is not immune from the changing economy and has also had to re-evaluate its budget. One result—the Spring 2010 Forum will be offered as an all-electronic publication. Additionally, in response to membership survey results, RPG will be providing one supplemental, electronic-only provider/patient education resource, which can be anticipated in spring or early summer 2009. These resources will arrive via e-blast and will remain available on the web site. Although paper copies will not be arriving in mailboxes, be assured that the Forum's editorial team is working to ensure that all RPG members are aware and have access to these electronic resources. If you have any questions or concerns, please feel free to contact any member of the editorial team (see page 27 for contact information).

Additionally, the Forum's editorial team strives to provide as many free CPEUs as possible in each issue. This 2009 Spring issue Feature article, "Reducing Inflammation through Micronutrient Therapy during Hemodialysis," provides an in-depth literature review outlining pertinent vitamins/minerals and suggestions for use against this invisible enemy to hemodialysis patients, offering 2 CPEUs. Notably, as we are accustomed to seeing in the nutrition world, it recommends the need for further research, which is an area that both RPG and CRN have advocated for—more dietitian-led and published research. The Advances in Practice article focuses on exactly that—the number of dietitians publishing research in select journals, barriers to conducting research, and concluding statements advocating for increased dietitian research, offering another CPEU. Also included is a weight management reprint, which provides internet resources to assist patients with weight loss. This may be especially helpful with pre-transplant patients striving to improve candidacy. But it certainly doesn't end there—the remainder of the Forum includes information on the Nutrition Care Process, as well as important updates and announcements.

Shortly after you receive this edition of the Forum also comes a change in the guard—please welcome the new renal leadership: Pat Williams, RD, LDN, incoming RPG chair and Karen Wiesen, MS, RD, incoming CRN chair. Lastly, as this is my final Forum issue as Editor, I pass the torch to Stacey C. Phillips, RD. I have cherished this experience as it has been a pleasure serving as your Editor, and I look forward to seeing where RPG and the Forum lead us in the future. ◆



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Oxidative Stress: Imbalanced Antioxidant - Reactive Oxygen Species Levels

Wratten, et al (2002), indicated that an imbalance of antioxidant defense in the body contributed to reactive oxygen species (ROS) production, resulting in oxidative stress (SOX), a pro-inflammatory condition. The researchers further indicated the process of MHD itself was a cause for metabolic disorders related to SOX. During MHD, ROS is activated by triggering an inflammatory response as cellular components are impaired, further reducing the antioxidant capacity. Chronic inflammation and continual formation of ROS is a major contributor to cardiovascular disease. Additionally, the use of synthetic dialysis membranes in the hemodialysis dialyzer, and toxins derived from the dialysate could trigger the immune-inflammatory response, continuing the chain-reaction of oxidation and magnifying SOX with subsequent MHD treatments (7).

Micronutrient antioxidants, such as vitamins C (VC) and E (VE), and trace minerals, selenium and zinc are mostly involved in scavenging free-radicals or by directly quenching the free-radical, by breaking the cascading oxidative reactions, reducing ROS concentrations, and repairing damaged cell membranes (8). An imbalance of free-radical scavenging antioxidants, such as VC and VE, through loss in MHD or via red blood cell (RBC) destruction can aggravate SOX.

Antioxidant Synergy: Recycling Activity of Vitamins C and E

Since the hemodialysis membrane is non-selective, water-soluble VC can be lost during MHD. Handelman (2007) indicated in a recent editorial that as much as several hundred milligrams of VC could be lost during a single session of MHD, resulting in VC deficiencies if not properly supplemented (9).

VC and VE function synergistically as antioxidants. Both VC and VE act by scavenging free-radicals often produced during lipid (especially, LDL) or RBC membrane oxidation. Typically, VE is the preferred chain-breaking antioxidant and acts by donating an electron, breaking the chain of LDL peroxidation. VC replenishes VE's oxidative activity and serves as a cofactor with various enzymes needed to suppress free-radical production. As a result, the immune response (cytokine production) is inhibited, reducing SOX activity.

RBC losses are common during MHD due to the stress of dialysis, and is one of the reasons CKD patients may be anemic. Supplementing with adequate VE helps to protect fragile RBC membranes with its free-radical quenching activity. VC combats epoietin hyporesponsiveness by assisting with iron absorption and promoting RBC synthesis along with hemoglobin production. VC is also essential in collagen synthesis and protects blood vessels from membrane impairment.

In a study done by Yang, et al (2006), the effects of VC infusion and a VE-coated dialyzer were tested on patients with MHD induced oxidative stress. Eighty end stage renal disease (ESRD) patients were randomly selected into either a control or one of four hemodialysis (HD) treatment groups: HD with VC infusion (VC); HD with VE-coated dialysis membrane (VE); HD with VC infusion + VE-coated membrane (VC+VE); and HD with neither VC, nor VE. Results of the study indicated that the VE-coated dialyzer effectively prevented RBCs from oxidative stress and had a partial effect in reducing ROS activity as a whole. However, VC infusions significantly diminished the MHD-induced SOX. This suggests a combination of VC infusion in the dialysate and a small amount of VE coated on the dialyzer could potentially reduce inflammation during MHD, and its antioxidant property could be recoverable (10).

Since a VE-coated dialyzer may not be readily available in a hemodialysis unit, supplementation with VE could potentially be beneficial. Therapeutic dosage between 300 to 700 IU/day is regarded as safe, and could prevent SOX-related complications (11).

European consensus indicates 50 mg/day of VC can be safely administered (12); however, since ascorbic acid could partially be broken down into oxalate, plasma oxalate levels should be monitored and VC dosage should be individualized (13).

Vitamin E and Selenium

Critically ill patients demonstrate systemic inflammation symptoms, frequently associated with low serum micronutrient levels as they are taken up in tissues and organs during protein synthesis and immune cell production (8). Selenium commonly functions with VE as an antioxidant especially during intradialysis iron infusion. Glutathione peroxidase (GSH-Px), a kidney-derived enzyme, acts as a free-radical protector within the cell cytosol and mitochondria, while VE maintains the cell membrane integrity (14).

Serum levels of GSH-Px have been shown to be deficient in patients undergoing renal replacement therapy in acute renal failure, and MHD in chronic kidney failure (15). Researchers have indicated SOX in uremic patients where selenium balances were disturbed and glutathione enzyme concentrations and activity were compromised (16). Conflicting studies suggest selenium may or may not necessarily be lost during dialysis (17,18), however poor dietary intake prior to MHD may strongly influence selenium deficiency. For this reason, CKD patients experiencing PEM warrant even closer monitoring of serum selenium levels. Uremic patients are highly susceptible to oxidative stress due in part to suppressed

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serum selenium levels. Both serum selenium levels and activity of the antioxidant enzyme was found to be depressed as kidney disease progressed to end stages, according to a 2004 study done by Zacchara, et al (19).

Serum selenium is most commonly found in the reduced state (GSH) to effectively serve as an antioxidant in GSH-Px reactions. In a recent study, selenium erythrocyte enzyme activity and serum GSH levels were observed in 29 hemodialysis patients against 20 control subjects for three months. Serum GSH levels and GSH-Px activity were found to be significantly lower in the hemodialysis patients compared to controls, indicating impaired antioxidant response (20).

Other metabolic alterations, such as selenium's role in the immune system, may also be compromised as a result of deficiency. Selenium has been found to potentially reduce carcinogenic effects after supplementing with moderate doses over a period of several years (21).

In healthy adults, DRI for selenium is 20-70 mcg/day, with dietary intakes of at least 40 mcg/day to maintain adequate GSH-Px activity. Although supplementation standards for CKD patients have not formally been established, MHD patients exhibiting selenium deficiency symptoms can be supplemented for 3-6 months, and monitored closely (22). Available renal multivitamin formulas including 70 mcg of selenium per tablet include Dialyvite 3000 and Renax, USA. Food sources of selenium are readily available; however, selenium content is not indicated on food labels. The daily value percent on the label is provided for one serving of the food and can be used as a guideline. A food containing 20% or more of the DV is high in selenium, 10% to 19% is considered good. Plant foods are major sources of selenium, but the amount is dependent upon the soil in which the plants are grown. Animal and seafood sources of selenium are derived from the plants the animals consume. In the U.S., Brazil nuts, meats and bread are good sources of selenium (14).

Zinc Supplementation and Immune Regulation and Response

Like selenium, zinc deficiencies can compromise the body's immune system, predisposing MHD patients to oxidative stress and inflammation (23). Zinc is an essential albumin-transported mineral found in practically every cell in the body. It is required for DNA synthesis, growth during pregnancy, childhood and adolescence, and catalyzes approximately 100 different enzyme activities in carbohydrate (and insulin) metabolism, alcohol metabolism, and lactic acid reduction (14). Although zinc deficiency is rare in western countries, food sources rich in zinc are often high in protein, which are limited in early stages of renal insufficiency and often avoided by patients during later CKD stages due to anorexia. Chronic uremic CKD patients commonly experience taste and smell dysfunction as a result of zinc deficiency, which amplifies anorexia and poor oral intake, intensifying PEM and chronic zinc insufficiency. Zinc absorption interactions can also occur in CKD patients on oral iron supplementation during erythropoietin therapy, or with use of calcium-based phosphate binders and corticosteroids. Chronic zinc deficiency manifests by increasing skin fragility, presenting peripheral neuropathy and compromising immune functions (24). Cell-mediated immunity has been shown to be suppressed in zinc deficiency, making CKD patients more susceptible to infections, intensifying malnutrition and inflammation, and increasing incidences of morbidity and mortality (25). In a recent randomized study, Jern, et al (2000), demonstrated that a daily 2.2 mg zinc sulfate supplementation can normalize serum zinc levels and reduce protein catabolism in MHD patients (26). Protein catabolism, commonly a result of cachexia in ESRD patients, has been found to promote inflammation, compromising the patient's immune system (14). Another randomized crossover study indicated 3 months of 50 mg of elemental zinc supplementation significantly increased serum zinc levels, normalized the protein catabolic rate, and improved serum cholesterol levels (27).

In healthy adults, DRI intakes of elemental zinc range from 8-15 mg/day. Again, since zinc supplementation standards have not been set, MHD patients experiencing zinc deficiency symptoms, and/or with chronic PEM should consider up to 50 mg/day of monitored zinc supplementation for 3 to 6 months until deficiency symptoms have subsided (22). Available renal multivitamin formulas with zinc include Dialyvite 5000 Rx, Dialyvite 3000 Rx, Dialyvite Rx + Zinc, Renax, Renax 5.5, Diatx Zn , NephPlex Rx, Dialyvite 800 + Zinc, and Renavit + Zinc.

Folic Acid, B12, and B6 – Controlling Uremia

Micronutrients vulnerable to loss during MHD and key in controlling uremia include specific B vitamins—folic acid, B_{12} and B_6. Kidney failure often results in abnormal homocysteine metabolism as a consequence of diminished glomerular filtration rate. Hyperhomocysteinemia, a uremic condition prevalent in MHD patients, activates inflammation and damages blood vessels contributing to the high incidences of cardiovascular disease in CKD patients (28).

In healthy individuals, adequate folic acid intake, along with sufficient vitamin B_{12} and vitamin B_6, is essential in maintaining normal homocysteine levels. Folic acid and vitamin B_{12} are required to convert homocysteine into methionine. With adequate levels of vitamin B_6, methionine can then be broken down into cysteine, which is then either reabsorbed for other metabolic needs or excreted in the urine (13).

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Table 1
Summary of Micronutrient Recommendations

Micronutrient	Therapeutic Dosage	Sources Include	Comments
Vitamin E	300 - 700 IU/day		Generally recognized as safe
Vitamin C	50 mg/day		Monitor plasma oxalate levels
Selenium	20-70 mcg/day	Dialyvite 3000 Rx Dialyvite 5000 Rx Renax Renax 5.5	70 mcg Se/tablet in these sources
Zinc	50 mg/day	Dialyvite Rx + Zinc Dialyvite 800 + Zinc Renavit + Zinc	Check for resolution of deficiency symptoms after three-six months
Folic Acid Vitamin B_6 Vitamin B_{12}	5 mg/day 50 mg/day 500 mcg/day	Dialyvite 5000 Rx Diatx Zn Folbee Plus	KDOQI Clinical Practice Guidelines Recommendations
Injectable Vitamin D	Individualized based on PTH, per NKF KDOQI recommendations	Calcitriol Doxicalciferol Paricalcitol	Follow NKF KDOQI goals to maintain PTH at 150-300 pg/mL

Renal vitamin information found at these sites accessed March 15, 2009: www.ritecare.com/prodsheets/asp/VTF-314002.asp, www.everettlabs.com/ever2/renax.asp, www.dialyvite.net/default.asp?edid=59, and www.folbeeplus.com.

In CKD patients, this normal process of homocysteine degradation is significantly impaired due to folic acid deficiencies, and potentially vitamin B_{12} and/or B_6 deficiencies. In a study conducted by Bernasconi, et al (2006), moderate and advanced stage renal failure subjects were given either 5 or 15 mg/day folic acid dosages. Results indicated both doses yielded a significant, yet similar reduction of plasma homocysteine levels, suggesting benefits for folic acid supplementation in MHD patients (29). Anemic MHD patients on erythropoietin therapy may require additional vitamin B_6 supplementation to alleviate hyperhomocysteinemia. In a 12-month cohort study including 37 patients on intermittent HD treatment, supplementation of 250 mg of B_6 was given three times per week along with 50 mg of folic acid, administered one time per week. The researchers found mean homocysteine levels significantly decreased in all of the patients. Twenty-nine out of the thirty-seven patients supplemented resulted in normal plasma homocysteine levels after the treatment, suggesting the combination of folic acid and B_6 provided an effective and safe means to normalize plasma homocysteine levels in chronic hemodialysis patients (30). Vitamin B_{12} was shown to decrease serum homocysteinemia by approximately 10% when 1 mg was administered on a monthly basis in ESRD patients (31). Incidentally, new research has indicated high doses of B-vitamins may not lower homocysteine levels, preventing CVD-related mortality in CKD patients. Between years 2001 and 2006, Jamison, et al, conducted a large randomized, double-blind, controlled trial on 2056 advanced CKD and ESRD patients with high homocysteine levels. The subjects were treated daily with either a placebo or with a supplement containing 40 mg folic acid, 100 mg vitamin B_6, and 2 mg of B_{12}. The subjects were followed quarterly for 3+ years. Results of the study indicated survival did not improve after several years of follow up, and there were no significant reductions in cardiovascular events (32). Such strong conflicting research recently published warrants further studies to determine long-term effectiveness of B-vitamin supplementation for CKD patients. However, due to diminished appetite and low dietary intake in these patients and in accordance with the KDOQI Clinical Practice Guidelines, it is prudent to recommend at least 5 mg of folic acid, 500 mcg of vitamin B_{12} and 50 mg vitamin B_6, to protect against cardiovascular disease induced by hyperhomocysteinemia, but also to elevate B-vitamin status in patients with poor dietary intake (33). Renal vitamins currently available with B-vitamins include Nephro-Vite, Nephrocaps, Dialyvite, Dialyvite 3000 Rx, Dialyvite 5000 Rx, Diatx Zn, and Folbee Plus.

Vitamin D

Uremic conditions often intensify endocrine dysfunction in CKD patients. In healthy individuals, optimal kidney function is essential to convert dietary vitamin D and vitamin D absorbed by the skin, into its active form, $1,25(OH)_2$-D_3, or calcitriol. Parathyroid hormone (PTH) and phosphorus also aid in calcitriol produc-

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tion. However, during renal failure, active vitamin D levels drop significantly. Consequently, phosphate levels become elevated and calcium levels drop, stimulating PTH to be released into the blood. High serum PTH levels stimulate calcium movement from the bones into the blood, reabsorption of calcium from kidneys, and accelerated absorption of calcium from the intestine; a condition known as hyperparathyroidism (13).

Reduced vitamin D synthesis also manifests itself as secondary hyperparathyroidism, a condition considered by researchers to be a "classical" cause of CVD-related mortalities in MHD patients (34). Research indicates that serum PTH level is correlated with the degree of secondary hyperparathyroidism. When PTH levels exceed 500 – 600 pg/mL, patients experience moderate to severe hyperparathyroidism. High levels of serum PTH along with low levels of calcitriol are associated with bone loss, cardiovascular disease, and increased mortality in patients with ESRD. In a 2005 large cohort study done by Teng, et al, researchers found that activated, injectable vitamin D (VD) (calcitriol or paricalcitol) increased patient survival. Between the beginning of 1996 and end of 1999, a total of 51,037 MHD patients received injectable VD while 13,864 did not. Survival rate of the treatment group was significantly higher than the control group, with approximately 75.6% of the treatment patients surviving throughout the three year period. Only 58.7% of the control group patients survived the three year period (35). According to the NKF KDOQI, initial dosing recommendations for injectable VD is dependent upon the type of VD sterol administered and the severity of secondary hyperparathyroidism and serum PTH levels. VD injection therapy should commence when PTH levels are greater that 300 pg/mL and should cease when PTH levels are less than 150 pg/mL (36).

Recently, researchers have begun to study the "non-classical" effects of VD, such as its antioxidant properties and immunocompetent properties. Studies with congestive heart failure patients with adequate serum VD levels have been shown to have reduced pro-inflammatory and enhanced inhibitory-cytokine activity versus VD deficient subjects (37). Research determining benefits of activated vitamin D as an antioxidant in MHD patients still needs to be conducted to determine appropriate therapy.

Conclusion

In uremic CKD patients, inflammation as a consequence of chronic oxidative stress is complex and often entangled with anorexia and PEM. Chronic inflammation commonly leads to further complications, frequently resulting in cardiovascular-related deaths prevalent in MHD patients. Although micronutrient therapies have been explored, recovering losses for various vitamins during hemodialysis along with micronutrient supplementation to reduce deficiencies from PEM can play a role in reducing oxidative stress. Antioxidant synergies between various micronutrients should be considered when supplementing; however, future studies need to be conducted to determine appropriate approaches and to set standards with goals of improving nutrition status and quality of life for those undergoing MHD. ◆

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"To give anything less than your best is to sacrifice the gift." Steve Prefontaine

Prevalence of Registered Dietitians Publishing in Select Nutrition Journals

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Introduction

The increased need for registered dietitians (RDs) to be actively involved in publishing research is a relevant topic of discussion among leaders in the dietetic profession. In particular, the importance of research stems from the increasing prevalence of evidence-based practice (EBP). Hence, research is needed to develop these standards, which can improve patient outcomes, increase the likelihood for insurance reimbursement for dietetic services, as well as facilitate multidisciplinary team interaction. Furthermore, research conducted by RDs is relevant as it adds to the credibility and respect for the dietetic profession.

According to a 1998 study by Eck et al, most nutrition research was published by physicians or individuals with a PhD who were not RDs (1). Eck et al found 61% of research articles reviewed were published by a non-dietitian as a primary author and 83% did not have an RD as a coauthor. Various studies have sought to identify the barriers that have prevented RDs from engaging in research. Slawson et al surveyed clinical RDs, RD managers, and dietetic interns and found lack of support from administration and lack of available time to be the most common reasons why RDs did not perform research despite an interest and recognized need (2). Furthermore, surveyed RDs acknowledged they felt they did not have the necessary skills to conduct research; however, they were interested in obtaining those skills (2). Byham-Gray et al found RDs' perceptions, attitudes, and knowledge of EBP, as well as education level, to be the strongest predictors of research involvement (3).

Several studies have sought solutions and have made recommendations in an attempt to increase the level of RD participation in research. Byham-Gray et al proposed the increased use of EBP in clinical care as well as promoting its use in didactic education to encourage research participation (3). Collaboration between an experienced researcher and an RD was the top response among two surveys completed by RDs on how they would like to become involved in research (1,2). Furthermore, the 2002 Commission on Accreditation for Dietetic Education standards now require dietetic internships to provide foundation knowledge in research, to include knowledge of research methodologies, needs assessments, outcome-based research, scientific method, and quality improvement methods as well as the demonstrated ability to interpret current research and statistics (4).

Benchmarking from Eck's 1998 article, we hypothesize that the number of RDs publishing in 3 select nutrition journals as primary author is now greater than 40% and publishing as a coauthor is greater than 17%. Therefore, the purpose of this study was to look at three select nutrition journals and measure the current publication rate of RDs (primary and co-authors), the authors' educational and professional credentials and their geographical location.

Methods

Articles published between 2004 and 2005 in the *Journal of the American Dietetic Association* (JADA), *Journal of Parenteral and Enteral Nutrition* (JPEN), and *Nutrition: The International Journal of Applied and Basic Nutritional Sciences* (Nutrition) were reviewed for this retrospective study. JADA was included as it is published by the American Dietetic Association, which is the largest professional association to represent registered dietitians. JPEN was selected because of its high impact factor, an indicator of how robust the journal is in terms of publications and citations. The higher the impact factor, the stronger the journal and clinical emphasis. Nutrition was included to allow for the assessment of RDs publishing research on an international level. Inclusion criteria for the journals included publication in 2004 and 2005, an impact factor of greater than 1.5 as of 2005, accessibility of full-text articles via the Internet, and availability of the education and professional credentials, as well as the geographical locations and type of facilities associated with the articles' author(s). In addition, articles reviewed for authorship were required to be greater than one page in length and included original research, review, and case studies. Articles that appeared to be editorials or abstracts that were one page or less were not included in this study.

Data Collection

The journal articles were accessed via the Internet using Virtual Private Networking, aka VPN, in the nutrition department at a major university. The first page of each article that met inclusion criteria was printed for authorship analysis.

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Table 1
Publishing Rate of RD Primary Authors in Three Select Nutrition Journals between 2004 and 2005

Journal	PA[a] an RD[b] Yes	PA an RD No	Total # of Articles
JADA[c]	182 (60%)*	122	304
JPEN[d]	12 (10%)	114	126
Nutrition[e]	18 (6%)	290	308

[a]PA=primary author, [b]RD=registered dietitian, [c]JADA=Journal of the American Dietetic Association, [d]JPEN=Journal of Parental and Enteral Nutrition, [e]Nutrition=Nutrition: The International Journal of Applied and Basic Nutritional Sciences, *p<0.001.

Statistical Analysis

Descriptive statistics, χ^2, and 1-way analysis of variance (ANOVA) were used to analyze the data. All data were analyzed using SPSS vs 14.0 (SPSS Inc., Chicago, IL, 2006) and $p<0.05$ was used to define significance.

Results

Forty-two percent of the total articles (n=738) reviewed were from Nutrition, 41% from JADA, and 17% from JPEN. An RD was the primary author of 28.7% of the articles, and 34.1% of the articles had an RD as a coauthor (Figure 1). JADA (182 out of 304) (60%) had significantly more RDs publishing as a primary author compared to JPEN (12 out of 126) (10%) and Nutrition (18 out of 308) (6%) ($p<0.001$) (Table 1). Additionally, the mean number of coauthors was significantly different between journals (JADA 1.8 ±1.2, JPEN 1.2±0.5, Nutrition 1.5±0.8) ($p<0.05$).

The majority of the RDs publishing research had advanced degrees. Ninety-three (44.1%) of the 212 primary authors had a PhD, 65 (30.8%) had an MS degree, and 10 (4.7%) had a DrPH degree. Comparatively, 185 (43%) of the 426 coauthors had a PhD, 90 (21%) had an MS degree, and 78 (18%) had a BS degree. The specialty credentials (such as Certified Specialist in Renal or Certified Nutrition Support Dietitian) of RDs publishing were not significantly different between primary and coauthors, as 91.9% of the primary authors and 92.9% of the coauthors did not have a professional credential in addition to RD. Among RDs with an additional professional credential, Fellow of the American Dietetic Association was the most common as 4.3% of the primary authors and 4.0% of the coauthors had this credential.

Within the United States, primary authors from California, Pennsylvania, and Tennessee published the most research with 13 (6.2%) authors from each of these states. Iowa, Ohio, and Texas each had 11 (5.2%), and Illinois had 9 (4.3%) primary authors. For coauthors publishing in the U.S., Pennsylvania had the greatest prevalence with 25 (5.9%) RDs, Minnesota had 23 (5.4%), and Massachusetts had 22 (5.2%) RDs.

Twenty primary authors were located outside the United States. Canada had 9 (4.3%), Europe had 6 (2.8%), Asia had 3 (1.4%), and South America had 2 (0.9%). Forty-eight coauthors outside the U.S. published articles with 27 (6.3%) of the coauthors from Canada, ten (2.3%) from Europe and six (1.4%) from South America. One hundred and sixty (75.8%) primary authors were affiliated with a university. Sixteen (7.6%) primary authors published their research while working at a community hospital and 12 (5.7%) from a university medical center. Two hundred seventy (63.4%) coauthors were affiliated with a university. Forty (9.4%) coauthors were based out of a community hospital and 32 (7.5%) were employed by a government agency.

Discussion

The results of this study indicate a paucity of research is being published in JADA, JPEN and Nutrition by RDs. In particular, the percentage of RDs publishing as primary authors is less than that of RDs publishing as coauthors. Hence, we must reject our hypothesis that the dietitian as a primary author is now greater than 40%; however, we can accept our hypothesis that RDs as coauthors are publishing greater than 17%. Moreover, RDs outside the United States published more research as a coauthor than primary author. From this finding stems the question as to why RDs are taking a supportive role rather than a lead role in conducting research. Eck et al and Slawson et al (1,2) found RDs' lack of time and research skills to be key deterrents to conducting research; therefore, assisting with a study in a minor role may seem more feasible and provides a less intimidating approach for RDs to participate in the research process.

For RDs authoring research articles, certain nutrition journals had a higher RD publishing rate than others. Our study indicates JADA published a significantly greater number of articles with RDs as primary authors and coauthors compared to JPEN and Nutrition. This may be because RDs are submitting more articles to JADA, or JADA is more likely to accept articles authored by RDs. If it is indeed true that RDs are reluctant to submit articles to other nutrition journals, they may be limiting their credibility with other health professionals as their research is not reaching a varied yet relevant audience. If JPEN and Nutrition rarely accept articles authored by RDs, it would be of interest to the dietetic profession to determine why this is occurring and identify ways to overcome this hindrance.

Among RDs, our study found those with advanced academic

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degrees published the most research. While this finding might indicate RDs without advanced degrees are not involved in research, it is possible RDs are conducting research, but the results are not being published. Gardner et al found a significant relationship between clinical management RDs with advanced degrees and their increased involvement in outcomes-based research (5); however, the study also found nearly all research conducted by the RDs was not being published in peer-reviewed journals. Furthermore, our study indicates that professional dietetic credentials beyond that of RD are not needed to publish research, as almost all of the RD authors did not have additional specialty credentials related to dietetics.

Within the United States, our study found some states had a greater prevalence of RDs publishing research. This may be related to a greater number of universities located in these areas, as most research published by RDs was conducted in a university setting. In addition, these locations may be major health research hubs that provide an environment conducive to RDs' participation in research. Further research is warranted to determine the factors contributing to this occurrence, as the findings could be used to encourage RD participation in published research studies.

Although our numbers were very small in this area, outside the United States, our results provide a glimpse that RDs in westernized regions published the most research. These findings may be due to the prevalent use of modern, research-based medicine in these areas. However, as our study only included individuals with an RD credential, individuals who published research from countries that do not recognize or require the RD credential but work in a similar capacity were not accounted for; hence, the quantity of published research may be understated from these countries. This was a major limitation to the study.

Other studies have assessed the publishing rate among RDs as Eck et al (1), Slawson et al (2), and Gardner et al (5) examined the publishing rate and identified common barriers preventing participation in research by clinical RDs. Our study was different because we included all articles published by RDs, not just those working in a clinical setting. However, the study by Eck et al (1) was similar to ours as it also reviewed articles published in three research journals, two of which were used in this study. As we sought to examine publishing rates among international RDs, we included an international journal in place of a clinical journal used by Eck et al (1). The findings of all of these studies arrive at the same conclusion: RDs have been and continue to be underrepresented in the research process, both in conducting and publishing research.

Collaboration between an RD and an academic RD, or one with research experience, has been identified as a possible way to increase RDs' participation in research (1,2,5). In addition, Gardner et al recommends clinical RDs collaborate with other healthcare professionals to form interdisciplinary research teams (5). Not only is such a team more likely to gain hospital administrative support, but it will improve the respect and credibility of RDs with the other team members. Besides encouraging research among practicing RDs, it is important that didactic nutrition programs, at both the undergraduate and graduate level, provide students with the knowledge and skills needed to conduct research. Steiber and Barkoukis (6) and Hays et al (7) describe two academic programs that provide hands-on research experience to students and practicing RDs, most of whom work in a clinical setting. An RD and student are paired together, after which they complete a research project under the guidance of the class instructor. Not only is such an opportunity likely to empower current RDs to conduct research, but it can promote research as part of the standard scope of practice for future RDs.

Conclusions and Applications

The dietetic profession would reap a tremendous benefit from RDs' increased participation in conducting and publishing research. In addition to developing standards for EBP, involvement in research will enhance RDs' recognition in the health care environment as credible and valued health care providers. Currently, it appears that the best way to improve RDs' participation in research is through collaboration with an experienced research RD or with a multidisciplinary team of health care providers. ◆

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ZEMPLAR is indicated for the prevention and treatment of secondary hyperparathyroidism (SHPT) associated with chronic kidney disease (CKD) stage 3 and 4 (ZEMPLAR Capsules) and stage 5 (ZEMPLAR Injection)[1,2]

HELP FIGHT A COMPLICATION OF CKD

Important Safety Information[1,2]

- ZEMPLAR Capsules and Injection are contraindicated in patients with evidence of vitamin D toxicity, hypercalcemia, or hypersensitivity to any product ingredient.
- Excessive administration of vitamin D compounds can cause over suppression of parathyroid hormone (PTH), hypercalcemia, hypercalciuria, hyperphosphatemia, and adynamic bone disease. High intake of calcium and phosphate concomitant with vitamin D compounds may lead to similar abnormalities, and patient monitoring and individualized dose titration is required. Progressive hypercalcemia due to overdosage of vitamin D may require emergency medical attention. Acute hypercalcemia may exacerbate tendencies for cardiac arrhythmias and seizures and may potentiate the action of digitalis. Use caution when digitalis compounds are prescribed concomitantly with ZEMPLAR. Chronic hypercalcemia can lead to vascular and soft-tissue calcifications. Chronic administration of ZEMPLAR Injection may place patients at risk for hypercalcemia, elevated Ca x P product, and metastatic calcification.
- ZEMPLAR is partially metabolized by CYP3A. Care should be taken while dosing ZEMPLAR with ketoconazole and other strong cytochrome P450 3A inhibitors including atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin or voriconazole.
- During ZEMPLAR Capsules therapy withhold pharmacologic doses of vitamin D compounds. PTH, calcium and phosphorus levels should be monitored at least every 2 weeks for 3 months after initiation or following dose adjustments, then monthly for 3 months, and every 3 months thereafter. Patient monitoring and individualized dose titration are required to maintain physiologic targets and optimum reduction/levels of PTH. The dose of ZEMPLAR Capsules should be reduced or interrupted if hypercalcemia or elevated Ca x P is observed.
- During ZEMPLAR Injection therapy withhold phosphate or vitamin D related compounds. PTH should be monitored at least every 3 months and more frequently at initiation and dosage changes. Calcium and phosphorus should be measured at least monthly and more frequently at initiation or following dosage changes. If clinically significant hypercalcemia develops or an elevated Ca x P product greater than 75 mg^2/dL^2 is noted, the dose should be immediately reduced or interrupted.
- Patients should be informed to adhere to their diet and phosphorus restriction, to take prescribed phosphate binders, and should be knowledgeable about the symptoms of hypercalcemia. While taking ZEMPLAR Capsules patients should be informed to comply with dosage instructions.
- Adverse events reported by at least 5% and at a frequency of at least twice that of placebo were allergic reaction, rash, arthritis, and vertigo for the ZEMPLAR Capsules Stage 3 and 4 treated patients and chills, fever, sepsis, gastrointestinal bleeding, vomiting, edema, light-headedness, and pneumonia for the ZEMPLAR Injection Stage 5 treated patients.

Please see brief summary of Prescribing Information for ZEMPLAR Injection and ZEMPLAR Capsules on following pages.

References: 1. ZEMPLAR (paricalcitol) Capsules [package insert]. North Chicago, IL; Abbott Laboratories. **2.** ZEMPLAR (paricalcitol) Injection [package insert]. Lake Forest, IL; Abbott Laboratories.

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INDICATIONS AND USAGE

Zemplar Capsules are indicated for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease (CKD) Stage 3 and 4.

CONTRAINDICATIONS

Zemplar Capsules should not be given to patients with evidence of vitamin D toxicity, hypercalcemia, or hypersensitivity to any ingredient in this product (see **WARNINGS**).

WARNINGS

Excessive administration of vitamin D compounds, including Zemplar Capsules, can cause over suppression of PTH, hypercalcemia, hypercalciuria, hyperphosphatemia, and adynamic bone disease. Progressive hypercalcemia due to overdosage of vitamin D and its metabolites may be so severe as to require emergency attention. Acute hypercalcemia may exacerbate tendencies for cardiac arrhythmias and seizures and may potentiate the action of digitalis. Chronic hypercalcemia can lead to generalized vascular calcification and other soft-tissue calcification. High intake of calcium and phosphate concomitant with vitamin D compounds may lead to similar abnormalities and patient monitoring and individualized dose titration is required.

Pharmacologic doses of vitamin D and its derivatives should be withheld during Zemplar treatment to avoid hypercalcemia.

PRECAUTIONS

General

Digitalis toxicity is potentiated by hypercalcemia of any cause, so caution should be applied when digitalis compounds are prescribed concomitantly with Zemplar Capsules.

Information for Patients

The patient or guardian should be informed about compliance with dosage instructions, adherence to instructions about diet and phosphorus restriction, and avoidance of the use of unapproved nonprescription drugs. Phosphate-binding agents may be needed to control serum phosphorus levels in patients, but excessive use of aluminum containing compounds should be avoided. Patients also should be informed about the symptoms of elevated calcium (see **ADVERSE REACTIONS**).

Laboratory Tests

During the initial dosing or following any dose adjustment of medication, serum calcium, serum phosphorus, and serum or plasma iPTH should be monitored at least every two weeks for 3 months after initiation of Zemplar therapy or following dose-adjustments in Zemplar therapy, then monthly for 3 months, and every 3 months thereafter.

Drug Interactions

Paricalcitol is not expected to inhibit the clearance of drugs metabolized by cytochrome P450 enzymes CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1 or CYP3A nor induce the clearance of drugs metabolized by CYP2B6, CYP2C9 or CYP3A.

A multiple dose drug-drug interaction study demonstrated that ketoconazole approximately doubled paricalcitol $AUC_{0-\infty}$. Since paricalcitol is partially metabolized by CYP3A and ketoconazole is known to be a strong inhibitor of cytochrome P450 3A enzyme, care should be taken while dosing paricalcitol with ketoconazole and other strong P450 3A inhibitors including atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin or voriconazole. Dose adjustment of Zemplar Capsules may be required, and iPTH and serum calcium concentrations should be closely monitored if a patient initiates or discontinues therapy with a strong CYP3A4 inhibitor such as ketoconazole.

Drugs that impair intestinal absorption of fat-soluble vitamins, such as cholestyramine, may interfere with the absorption of Zemplar Capsules.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 104-week carcinogenicity study in CD-1 mice, an increased incidence of uterine leiomyoma and leiomyosarcoma was observed at subcutaneous doses of 1, 3, 10 mcg/kg given three times weekly (2 to 15 times the AUC at a human dose of 14 mcg, equivalent to 0.24 mcg/kg based on AUC). The incidence rate of uterine leiomyoma was significantly different than the control group at the highest dose of 10 mcg/kg. In a 104-week carcinogenicity study in rats, there was an increased incidence of benign adrenal pheochromocytoma at subcutaneous doses of 0.15, 0.5, 1.5 mcg/kg (< 1 to 7 times the exposure following a human dose of 14 mcg, equivalent to 0.24 mcg/kg based on AUC). The increased incidence of pheochromocytomas in rats may be related to the alteration of calcium homeostasis by paricalcitol. Paricalcitol did not exhibit genetic toxicity *in vitro* with or without metabolic activation in the microbial mutagenesis assay (Ames Assay), mouse lymphoma mutagenesis assay (L5178Y), or a human lymphocyte cell chromosomal aberration assay. There was also no evidence of genetic toxicity in an *in vivo* mouse micronucleus assay. Paricalcitol had no effect on fertility (male or female) in rats at intravenous doses up to 20 mcg/kg/dose (equivalent to 13 times a human dose of 14 mcg based on surface area, mcg/m^2).

Pregnancy

Pregnancy category C

Paricalcitol has been shown to cause minimal decreases in fetal viability (5%) when administered daily to rabbits at a dose 0.5 times a human dose of 14 mcg or 0.24 mcg/kg (based on body surface area, mcg/m^2), and when administered to rats at a dose two times the 0.24 mcg/kg human dose (based on body surface area, mcg/m^2). At the highest dose tested, 20 mcg/kg administered three times per week in rats (13 times the 14 mcg human dose based on surface area, mcg/m^2), there was a significant increase in the mortality of newborn rats at doses that were maternally toxic and are known to produce hypercalcemia in rats. No other effects on offspring development were observed. Paricalcitol was not teratogenic at the doses tested.

Paricalcitol (20 mcg/kg) has been shown to cross the placental barrier in rats.

There are no adequate and well-controlled clinical studies in pregnant women. Zemplar Capsules should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Nursing Mothers

Studies in rats have shown that paricalcitol is present in the milk. It is not known whether paricalcitol is excreted in human milk. In the nursing patient, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Geriatric Use

Of the total number (n = 220) of patients in clinical studies of Zemplar Capsules, 49% were 65 and over, while 17% were 75 and over. No overall differences in safety and effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Pediatric Use

Safety and efficacy of Zemplar Capsules in pediatric patients have not been established.

ADVERSE REACTIONS

The safety of Zemplar Capsules has been evaluated in three 24-week (approximately six-month), double-blind, placebo-controlled, multicenter clinical studies involving 220 CKD Stage 3 and 4 patients. Six percent (6%) of Zemplar Capsules treated patients and 4% of placebo treated patients discontinued from clinical studies due to an adverse event. All reported adverse events occurring in at least 2% in either treatment group are presented in Table 3.

Table 3. Treatment - Emergent Adverse Events by Body System Occurring in ≥ 2% of Subjects in the Zemplar-Treated Group of Three, Double-Blind, Placebo-Controlled, Phase 3, CKD Stage 3 and 4 Studies; All Treated Patients

	Number (%) of Subjects			
Body System[a] COSTART V Term	**Zemplar Capsules (n = 107)**		**Placebo (n = 113)**	
Overall	**88**	**(82%)**	**86**	**(76%)**
Body as a Whole	**49**	**(46%)**	**40**	**(35%)**
Accidental Injury	10	(9%)	8	(7%)
Pain	8	(7%)	7	(6%)
Viral Infection	8	(7%)	8	(7%)
Allergic Reaction	6	(6%)	2	(2%)
Headache	5	(5%)	5	(4%)
Abdominal Pain	4	(4%)	2	(2%)
Back Pain	4	(4%)	1	(1%)
Infection	4	(4%)	4	(4%)
Asthena	3	(3%)	2	(2%)
Chest Pain	3	(3%)	1	(1%)
Fever	3	(3%)	1	(1%)
Infection Fungal	3	(3%)	0	(0%)
Cyst	2	(2%)	0	(0%)
Flu Syndrome	2	(2%)	1	(1%)
Infection Bacterial	2	(2%)	1	(1%)
Cardiovascular	**27**	**(25%)**	**19**	**(17%)**
Hypertension	7	(7%)	4	(4%)
Hypotension	5	(5%)	3	(3%)
Syncope	3	(3%)	1	(1%)
Cardiomyopathy	2	(2%)	0	(0%)
Congestive Heart Failure	2	(2%)	5	(4%)
Myocardial Infarct	2	(2%)	0	(0%)
Postural Hypotension	2	(2%)	0	(0%)
Digestive	**29**	**(27%)**	**31**	**(27%)**
Diarrhea	7	(7%)	5	(4%)
Nausea	6	(6%)	4	(4%)
Vomiting	6	(6%)	5	(4%)
Constipation	4	(4%)	4	(4%)
Gastroenteritis	3	(3%)	3	(3%)
Dyspepsia	2	(2%)	2	(2%)
Gastritis	2	(2%)	4	(4%)
Rectal Disorder	2	(2%)	0	(0%)
Hemic and Lymphatic System	**4**	**(4%)**	**10**	**(9%)**
Hypervolemia	2	(2%)	4	(4%)
Ecchymosis	2	(2%)	4	(4%)
Metabolic and Nutritional Disorders	**24**	**(22%)**	**34**	**(30%)**
Edema	7	(7%)	5	(4%)
Uremia	7	(7%)	9	(8%)
Gout	4	(4%)	6	(5%)
Dehydration	3	(3%)	1	(1%)
Acidosis	2	(2%)	1	(1%)
Hyperkalemia	2	(2%)	3	(3%)
Hyperphosphatemia	2	(2%)	4	(4%)
Hypoglycemia	2	(2%)	4	(4%)
Hypokalemia	2	(2%)	1	(1%)
Musculoskeletal	**12**	**(11%)**	**9**	**(8%)**
Arthritis	5	(5%)	1	(1%)
Leg Cramps	3	(3%)	0	(0%)
Myalgia	2	(2%)	5	(4%)
Nervous	**18**	**(17%)**	**12**	**(11%)**
Dizziness	5	(5%)	5	(4%)
Vertigo	5	(5%)	0	(0%)
Depression	3	(3%)	0	(0%)
Insomnia	2	(2%)	2	(2%)
Neuropathy	2	(2%)	1	(1%)
Respiratory	**26**	**(24%)**	**25**	**(22%)**
Pharyngitis	11	(10%)	12	(11%)
Rhinitis	5	(5%)	4	(4%)
Bronchitis	3	(3%)	1	(1%)
Cough Increased	3	(3%)	2	(2%)
Sinusitis	3	(3%)	1	(1%)
Epistaxis	2	(2%)	1	(1%)
Pneumonia	2	(2%)	0	(0%)
Skin and Appendages	**17**	**(16%)**	**10**	**(9%)**
Rash	6	(6%)	3	(3%)
Pruritus	3	(3%)	3	(3%)
Skin Ulcer	3	(3%)	0	(0%)
Skin Hypertrophy	2	(2%)	0	(0%)
Vesiculobullous Rash	2	(2%)	1	(1%)
Special Senses	**9**	**(8%)**	**11**	**(10%)**
Amblyopia	2	(2%)	0	(0%)
Retinal Disorder	2	(2%)	0	(0%)
Urogenital System	**10**	**(9%)**	**10**	**(9%)**
Urinary Tract Infection	3	(3%)	1	(1%)
Kidney Function Abnormal	2	(2%)	1	(1%)

a. Includes all patients with events in that body system.

Potential adverse effects of Zemplar Capsules are, in general, similar to those encountered with excessive vitamin D intake. The early and late signs and symptoms of hypercalcemia associated with vitamin D overdoses include:

Early: Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, and metallic taste.

Late: Anorexia, weight loss, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated BUN, hypercholesterolemia, elevated AST and ALT, ectopic calcification, hypertension, cardiac arrhythmias, somnolence, death, and, rarely, overt psychosis.

OVERDOSAGE

Excessive administration of Zemplar Capsules can cause hypercalcemia, hypercalciuria, and hyperphosphatemia, and over suppression of PTH (see **WARNINGS**).

Treatment of Overdosage

The treatment of acute overdosage of Zemplar Capsules should consist of general supportive measures. If drug ingestion is discovered within a relatively short time, induction of emesis or gastric lavage may be of benefit in preventing further absorption. If the drug has passed through the stomach, the administration of mineral oil may promote its fecal elimination. Serial serum electrolyte determinations (especially calcium), rate of urinary calcium excretion, and assessment of electrocardiographic abnormalities due to hypercalcemia should be obtained. Such monitoring is critical in patients receiving digitalis. Discontinuation of supplemental calcium and institution of a low-calcium diet are also indicated in accidental overdosage. Due to the relatively short duration of the pharmacological action of paricalcitol, further measures are probably unnecessary. If persistent and markedly elevated serum calcium levels occur, there are a variety of therapeutic alternatives that may be considered depending on the patient's underlying condition. These include the use of drugs such as phosphates and corticosteroids, as well as measures to induce an appropriate forced diuresis.

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PROFESSIONAL BRIEF SUMMARY
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Zemplar®

(paricalcitol) Injection

Fliptop Vial

℞ only

INDICATIONS AND USAGE

Zemplar is indicated for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5.

CONTRAINDICATIONS

Zemplar should not be given to patients with evidence of vitamin D toxicity, hypercalcemia, or hypersensitivity to any ingredient in this product (see **WARNINGS**).

WARNINGS

Acute overdose of Zemplar may cause hypercalcemia, and require emergency attention. During dose adjustment, serum calcium and phosphorus levels should be monitored closely (e.g., twice weekly). If clinically significant hypercalcemia develops, the dose should be reduced or interrupted. Chronic administration of Zemplar may place patients at risk of hypercalcemia, elevated Ca x P product, and metastatic calcification.

Treatment of patients with clinically significant hypercalcemia consists of immediate dose reduction or interruption of Zemplar therapy and includes a low calcium diet, withdrawal of calcium supplements, patient mobilization, attention to fluid and electrolyte imbalances, assessment of electrocardiographic abnormalities (critical in patients receiving digitalis), hemodialysis or peritoneal dialysis against a calcium-free dialysate, as warranted. Serum calcium levels should be monitored frequently until normocalcemia ensues.

Phosphate or vitamin D-related compounds should not be taken concomitantly with Zemplar.

PRECAUTIONS

General

Digitalis toxicity is potentiated by hypercalcemia of any cause, so caution should be applied when digitalis compounds are prescribed concomitantly with Zemplar. Adynamic bone lesions may develop if PTH levels are suppressed to abnormal levels.

Information for the Patient

The patient should be instructed that, to ensure effectiveness of Zemplar therapy, it is important to adhere to a dietary regimen of calcium supplementation and phosphorus restriction. Appropriate types of phosphate-binding compounds may be needed to control serum phosphorus levels in patients with chronic kidney disease (CKD) Stage 5, but excessive use of aluminum containing compounds should be avoided. Patients should also be carefully informed about the symptoms of elevated calcium (see **ADVERSE REACTIONS**).

Laboratory Tests

During the initial phase of medication, serum calcium and phosphorus should be determined frequently (e.g., twice weekly). Once dosage has been established, serum calcium and phosphorus should be measured at least monthly. Measurements of serum or plasma PTH are recommended every 3 months. An intact PTH (iPTH) assay is recommended for reliable detection of biologically active PTH in patients with CKD Stage 5. During dose adjustment of Zemplar, laboratory tests may be required more frequently.

Drug Interactions

Paricalcitol is not expected to inhibit the clearance of drugs metabolized by cytochrome P450 enzymes CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A nor induce the clearance of drug metabolized by CYP2B6, CYP2C9 or CYP3A.

Specific interaction studies were not performed with Zemplar Injection.

A multiple dose drug-drug interaction study with ketoconazole and paricalcitol capsule demonstrated that ketoconazole approximately doubled paricalcitol $AUC_{0-\infty}$. Since paricalcitol is partially metabolized by CYP3A and ketoconazole is known to be a strong inhibitor of cytochrome P450 3A enzyme, care should be taken while dosing paricalcitol with ketoconazole and other strong P450 3A inhibitors including atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin or voriconazole.

Digitalis toxicity is potentiated by hypercalcemia of any cause, so caution should be applied when digitalis compounds are prescribed concomitantly with Zemplar.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 104-week carcinogenicity study in CD-1 mice, an increased incidence of uterine leiomyoma and leiomyosarcoma was observed at subcutaneous doses of 1, 3, 10 mcg/kg (2 to 15 times the AUC at a human dose of 14 mcg, equivalent to 0.24 mcg/kg based on AUC). The incidence rate of uterine leiomyoma was significantly different than the control group at the highest dose of 10 mcg/kg.

In a 104-week carcinogenicity study in rats, there was an increased incidence of benign adrenal pheochromocytoma at subcutaneous doses of 0.15, 0.5, 1.5 mcg/kg (<1 to 7 times the exposure following a human dose of 14 mcg, equivalent to 0.24 mcg/kg based on AUC). The increased incidence of pheochromocytomas in rats may be related to the alteration of calcium homeostasis by paricalcitol.

Paricalcitol did not exhibit genetic toxicity *in vitro* with or without metabolic activation in the microbial mutagenesis assay (Ames Assay), mouse lymphoma mutagenesis assay (L5178Y), or a human lymphocyte cell chromosomal aberration assay. There was also no evidence of genetic toxicity in an *in vivo* mouse micronucleus assay. Zemplar had no effect on fertility (male or female) in rats at intravenous doses up to 20 mcg/kg/dose [equivalent to 13 times the highest recommended human dose (0.24 mcg/kg) based on surface area, mg/m^2].

Pregnancy

Pregnancy Category C.

Paricalcitol has been shown to cause minimal decreases in fetal viability (5%) when administered daily to rabbits at a dose 0.5 times the 0.24 mcg/kg human dose (based on surface area, mg/m^2) and when administered to rats at a dose 2 times the 0.24 mcg/kg human dose (based on plasma levels of exposure). At the highest dose tested (20 mcg/kg 3 times per week in rats, 13 times the 0.24 mcg/kg human dose based on surface area), there was a significant increase of the mortality of newborn rats at doses that were maternally toxic (hypercalcemia). No other effects on offspring development were observed. Paricalcitol was not teratogenic at the doses tested.

There are no adequate and well-controlled studies in pregnant women. Zemplar should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Nursing Mothers

Studies in rats have shown that paricalcitol is present in the milk. It is not known whether paricalcitol is excreted in human milk. In the nursing patient, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

The safety and effectiveness of Zemplar were examined in a 12-week randomized, double-blind, placebo-controlled study of 29 pediatric patients, aged 5-19 years, with end-stage renal disease on hemodialysis and nearly all had received some form of vitamin D prior to the study. Seventy-six percent of the patients were male, 52% were Caucasian and 45% were African-American. The initial dose of Zemplar was 0.04 mcg/kg 3 times per week, based on baseline iPTH level of less than 500 pg/mL, or 0.08 mcg/kg 3 times a week based on baseline iPTH level of ≥ 500 pg/mL, respectively. The dose of Zemplar was adjusted in 0.04 mcg/kg increments based on the levels of serum iPTH, calcium, and Ca x P. The mean baseline levels of iPTH were 841 pg/mL for the 15 Zemplar-treated patients and 740 pg/mL for the 14 placebo-treated subjects. The mean dose of Zemplar administered was 4.6 mcg (range: 0.8 mcg – 9.6 mcg). Ten of the 15 (67%) Zemplar-treated patients and 2 of the 14 (14%) placebo-treated patients completed the trial. Ten of the placebo patients (71%) were discontinued due to excessive elevations in iPTH levels as defined by 2 consecutive iPTH levels > 700 pg/mL and greater than baseline after 4 weeks of treatment.

In the primary efficacy analysis, 9 of 15 (60%) subjects in the Zemplar group had 2 consecutive 30% decreases from baseline iPTH compared with 3 of 14 (21%) patients in the placebo group (95% CI for the difference between groups –1%, 63%). Twenty-three percent of Zemplar vs. 31% of placebo patients had at least one serum calcium level > 10.3 mg/dL, and 40% vs. 14% of Zemplar vs. placebo subjects had at least one Ca x P ion product > 72 $(mg/dL)^2$. The overall percentage of serum calcium measurements > 10.3 mg/dL was 7% in the Zemplar group and 7% in the placebo group; the overall percentage of patients with Ca x P product > 72 $(mg/dL)^2$ was 8% in the Zemplar group and 7% in the placebo group. No subjects in either the Zemplar group or placebo group developed hypercalcemia (defined as at least one calcium value > 11.2 mg/dL) during the study.

Geriatric Use

Of the 40 patients receiving Zemplar in the three phase 3 placebo-controlled CKD Stage 5 studies, 10 patients were 65 years or over. In these studies, no overall differences in efficacy or safety were observed between patients 65 years or older and younger patients.

ADVERSE REACTIONS

Zemplar has been evaluated for safety in clinical studies in 454 CKD Stage 5 patients. In four, placebo-controlled, double-blind, multicenter studies, discontinuation of therapy due to any adverse event occurred in 6.5% of 62 patients treated with Zemplar (dosage titrated as tolerated) and 2.0% of 51 patients treated with placebo for 1 to 3 months. Adverse events occurring with greater frequency in the Zemplar group at a frequency of 2% or greater, regardless of causality, are presented in the following table:

Adverse Event Incidence Rates For All Treated Patients In All Placebo-Controlled Studies

Adverse Event	Zemplar (n=62) %	Placebo (n=51) %
Overall	71	78
Body as a Whole		
Chills	5	0
Feeling unwell	3	0
Fever	5	2
Flu	5	4
Sepsis	5	2
Cardiovascular		
Palpitation	3	0
Digestive System		
Dry mouth	3	2
Gastrointestinal bleeding	5	2
Nausea	13	8
Vomiting	8	4
Metabolic and Nutritional Disorders		
Edema	7	0
Nervous System		
Light-headedness	5	2
Respiratory System		
Pneumonia	5	0

A patient who reported the same medical term more than once was counted only once for that medical term.

Safety parameters (changes in mean Ca, P, Ca x P) in an open-label safety study up to 13 months in duration support the long-term safety of Zemplar in this patient population.

Potential adverse events of Zemplar Injection are, in general, similar to those encountered with excessive vitamin D intake. Signs and symptoms of vitamin D intoxication associated with hypercalcemia include:

Early

Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, and metallic taste.

Late

Anorexia, weight loss, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated BUN, hypercholesterolemia, elevated AST and ALT, ectopic calcification, hypertension, cardiac arrhythmias, somnolence, death, and rarely, overt psychosis.

Adverse events during post-marketing experience: Taste perversion, such as metallic taste, and allergic reactions, such as rash, urticaria, pruritus, facial and oral edema rarely have been reported.

OVERDOSAGE

Overdosage of Zemplar may lead to hypercalcemia, hypercalciuria, hyperphosphatemia, and over suppression of PTH. (see **WARNINGS**).

Treatment of Overdosage and Hypercalcemia

The treatment of acute overdosage should consist of general supportive measures. Serial serum electrolyte determinations (especially calcium), rate of urinary calcium excretion, and assessment of electrocardiographic abnormalities due to hypercalcemia should be obtained. Such monitoring is critical in patients receiving digitalis. Discontinuation of supplemental calcium and institution of a low calcium diet are also indicated in acute overdosage.

General treatment of hypercalcemia due to overdosage consists of immediate suspension of Zemplar therapy, institution of a low calcium diet, and withdrawal of calcium supplements. Serum calcium levels should be determined at least weekly until normocalcemia ensues. When serum calcium levels have returned to within normal limits, Zemplar may be reinitiated at a lower dose. If persistent and markedly elevated serum calcium levels occur, there are a variety of therapeutic alternatives that may be considered. These include the use of drugs such as phosphates and corticosteroids as well as measures to induce diuresis. Also, one may consider dialysis against a calcium-free dialysate.

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Online Weight Management

The Spectrum, E-Tools and Integration into Practice

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Abstract

Global usage of the Internet has exploded, accompanied by a corresponding increase in online weight management web sites that feature electronic tools including nutrition trackers, web logs, weight and activity calculators, and more. Online weight management web sites are also incorporating best practice designs, such as digitized programs based on social cognitive theory. This article reviews the current landscape of fee-based or free online weight management web sites. It also provides registered dietitians with strategies to integrate these programs into their practice as well as the short- and long-term weight and health goals and outcomes of their clients.

Introduction

When I began working for eDiets in January 2000, there were just a few online weight management web sites. Eight years later, in March 2008, a web search on "diet" matched 311 million web sites. Ironically, the epidemics of obesity and type 2 diabetes mellitus are linked to the increased time spent in sedentary behaviors (1,2) and it may seem counterintuitive for clinicians to encourage more sedentary behavior with the use of online weight management programs. However, people are accessing information online in unprecedented numbers, especially in North America (3). Research shows that online weight management programs that emphasize changes in food intake and physical activity and use cognitive and behavior strategies with personalized feedback and support help people lose weight and maintain the weight loss (4). This article reviews the features that make online weight management effective and discusses ways in which clinicians can integrate these resources into their practices.

The Spectrum of Offerings

A wide spectrum of online weight management web sites exist today. A sampling of these is provided in Table 1 with their names, web addresses, key features, and costs. Many self-help web sites offer similar unique electronic tools (e-tools) as described below. Some of these are free to users and others are fee-based. Other programs are made available by commercial ventures, for example web sites that promote a product or brand.

Description of Electronic Tools

Behavior Modification e-Tools — E-tools in the area of modifying behaviors for weight management include goal setting, self-monitoring, problem solving, and relapse prevention (5-7). Some programs have adapted motivational interviewing techniques (by gathering data from online questionnaires) to assess barriers to change (8). For example, on Diet.com, new subscribers complete a comprehensive "personality profile" designed by Robert Kushner, MD, to assess the dominant "eating, exercise and coping" patterns of the dieter (my eating pattern is "steady snacker"—my coping is "self-scrutinizer"). The user receives a phased plan and is emailed weekly content that addresses his or her unique profile and stage of change. On WebMD.com/diet, users complete an online questionnaire that assesses eating patterns and food frequency, and receive menus that reflect modifications to each meal—then their overall menu becomes lower in calories, and individuals hopefully move toward their weight goal. On ChangeOne.com, each week users are asked to "overhaul" their meals and snacks, and the virtual dietitian identifies small, achievable modifications over a 12-week period. On Slim-Fast.com, users are prompted to set reasonable diet and fitness goals, and receive regular emails urging them to monitor their weight regularly and stay active. Similarly, SparkPeople.com prompts new users to opt in for and follow a phased program with behavioral lessons; they receive recommendations to join support "SparkTeams" based on their profile information.

Food and Nutrition e-Tools—CalorieKing.com offers a "drag and drop" tracker that was developed in partnership with the Joslin Diabetes Center. Users download a free food database "toolbar" for quick access to nutrition information on specific foods. Users then log that item into their daily food record, or may save the food, add the food to another meal, and then "click" to learn what happens to all the nutrients if they cut their portion, or if they choose a different food instead. Diet.com offers a free cell phone text message service to access menu item nutrition information at the point of purchase. Some programs offer predetermined meal plans, others allow users to "build their own" meals, "save favorites" and learn how to lower calories by modifying menus and recipes.

Fitness e-Tools—Users can receive a prescribed activity schedule, "see" exercise demonstrations and learn proper form and technique. Personalized programs reflect the users' level of fitness

➞

and even their equipment. Users can participate in a program using gym or home equipment, sign up for a challenge group, and log in regularly to participate. Exercise trackers are useful self-help tools to set goals and monitor progress.

Online Diabetes Management—People with diabetes may use programs specifically designed to educate and improve their condition while losing weight. New registrants for ChangingDiabetes-us.com, a program sponsored by Novo-Nordisk Pharmaceuticals, complete a profile that defines their diabetes care plan, and are pointed to the site's web tools to help them manage their diabetes, including calorie-appropriate meal plans and fitness recommendations. The program provides a priorities tool to define positive lifestyle changes, and the program and content are provided by certified diabetes educators and fitness and medical experts. Commercial sites offered by companies to promote a product or brand to people with diabetes are available. For example, Glucerna's web site DiabetesControlforLife.com provides users who sign up 24 weeks of targeted emails and content addressing self-assessment, nutrition and diabetes information and relapse prevention. LifeScan's web site OneTouchGold.com provides diabetes support plus menus, fitness planners and trackers. A registered dietitian/certified diabetes educator conducts monthly live lessons and chats for eDiets.com Living with Diabetes meal plan. Online weight management programs are available for Spanish-speaking clients. MiDieta.com is a Spanish language weight management program, and also offers a premium phone service and access to Spanish-speaking dietitians. ChangingDiabetes.com, WeightWatchers.com and Slim-Fast.com also have Spanish language programs with menus, fitness and diabetes information.

Integration into Practice

Before recommending an online web site, the clinician should determine their clients' needs and desires regarding type of program, features and costs. For example, do clients need a comprehensive program with structured lessons and feedback, or are they already on the way toward a healthy lifestyle; can they use some interesting tools for nutrition education, meal planning and fitness recommendations in a self-help program? A client in the action stage of change may benefit from tracking meals to reinforce healthy behaviors. Clinicians may ask their clients to record their intake and activities, email their records, or bring them to their next meeting. For a client who may need structure and support, VTrim.com (uvm.edu/vtrim) is a program that has demonstrated that an online, therapist-led, structured behavioral weight loss web site produced greater weight loss than a self-help commercial web site (9). Participants commit to a six-month program, with 24 weekly behavioral modification lessons; they are asked to track their meals and activities daily, and they receive personalized feedback from the expert facilitator and participate in small, 20-participant weekly online meetings facilitated by the group's expert leader. Another program that offers "one-to-one" counseling is Fit4D.com, which is created to help people using insulin to increase their fitness and balance health. Coaches (including nurses, exercise physiologists, registered dietitians, and certified personal trainers with extensive diabetes experience and accreditations (including certified diabetes educators) and clients communicate via the Internet and other mobile technologies including phone.

Clinicians may use the Internet to enhance and complement their own practice, taking advantage of the online weight management technologies rather than directing clients to a self-help program. On the Health Insurance Portability and Accountability Act (HIPAA)-compliant NutrihandPro.com, experts can correspond, review and analyze their clients' meals, fitness and medical data. They can also modify their programs according to their schedule and that of their clients', as well as create auto-generated menus and activities.

Self-help or Structured Programs

"Self-help" means that the program provides the information and the users utilize pieces and functions according to their schedule. Most of the online weight management web sites are "self-help." Structured programs provide online meetings individually or with a group at predetermined times. Studies confirm that participants given a structured online behavioral treatment program with consistent contact and individualized feedback had better weight loss results than those going it strictly alone (10-13). Logging on frequently, journaling weight, food and fitness regularly, participating in discussions, as well as receiving targeted email counseling, improves results. Programs offer different levels of support, ranging from expert articles to message boards, to live chat via the Internet, phone, or web camera. While convenience, anonymity and accessibility are desirable attributes of online programs, such programs are only as good as the user's frequency; online programs offer entertaining and informative quizzes, videos, podcasts and blogs to encourage increased participation (14).

Take a Tour

Before referring clients to online programs, choose a few programs of interest and then take a tour to explore their use and features. Also encourage clients to use this feature if they are choosing a program. An option to learn more about (some) online weight loss programs is to log on to www.bestdietforme.com which recommends programs based on food preferences, diet and activity history, and budget concerns.

Table 1
Spectrum, Features and Costs of a Cadre of Online Weight Management Programs

WEB SITE	PROGRAM FEATURES	COST AS OF MARCH 2008
Self-help: User options for tools, programs and support. All recommended programs include nutrition & activities trackers, logs, graphs, and reports.		
FitDay: www.fitday.com	• Long-term diet analyses	Free
MyFoodDiary: www.myfooddiary.com	• Recipe builder to save favorites	$9/month
MyPyramid: www.mypyramid.gov	• Links to nutrition information	Free
Calories-Count: www.caloriescount.com	• Meal plans, fitness plans, recipes, community boards	$25 for 3 months/$45 lifetime
CalorieCountPlus (From About.com): www.caloriecount.about.com	• Individual foods are letter 'rated' and program suggests foods to improve diet	Free
ChangeOne from Reader's Digest: www.changeone.com	• Change one meal per week for four weeks to improve total nutritional profile	$15 per month
eDiets: www.ediets.com	• All of the above plus live RD support (CDE for diabetes program)	$54/3 months minimum
MyDiet (MiDieta): www.midieta.com	• All of the above • Completely translated into Spanish • 'Gold' plan includes live RD support (Spanish language dietitian)	$35/3 months or $54 3 months and weekly phone consult
In addition to food and activity trackers, these self-help sites offer peer community, plus behavioral modification/lesson plans; targeted email		
CalorieKing: www.calorieking.com	• 'University' program • Superior nutrition tracker	$7 month/$45 year
SparkPeople: www.sparkpeople.com	• Targeted emails to engage member through changes	Free
Diet.com: www.diet.com	• Personality quiz determines type of menu recommendations and content	$64 for 3 months
WebMD Weight Loss Clinic: www.weightloss.webmd.com	• Diet assessment tool: menus reflect proposed food improvements	$22 per month
Weightwatchers: www.weightwatchers.com	• Choose points or core program online	$65/3 for months
Men's Health Personal Trainer: www.menshealthtrainer.com	• Dynamic program adjusts fuel to accommodate fitness activities	$45.50 for 3 months
Corporate diet programs with meal items		
Slim-Fast: www.slim-fast.com	• User has option to use meal replacements or substitute	All offer free e-tools (BMI & activities calculators; link to food intake database. Add costs for meals and/or meal replacements
Jenny Craig: www.jennycraig.com	• E-tools enhance face-to-face and phone consults with trained experts	
Condition specific: diabetes & other		
Fitness4Diabetics: www.fit4d.com	• A variety of program options include professional personal coaching • Goal is to balance insulin, food intake, BG levels and exercise activity.	Costs depend on group or personalized and customized programs, approx. $75-150/month
Diabetes Control for Life from Abbott Labs: http://diabetescontrolforlife.com/	• Targeted email addresses behavioral change • Live support from RD, includes Glucerna meal replacement products	Free
Changing Diabetes: Diabetes Care Plan (from NovoNordisk) www.changingdiabetes-us.com	• Self-directed program • Learn to manage diabetes through increased knowledge and behavior modification • Has Spanish-language version	Free
Davita Diet Helper (from Davita Dialysis): www.davita.com	• Enter nutrition prescription (sodium, potassium, protein)	Free
Other Web-based programs		
Vtrim: www.uvm.edu/~vtrim	• Structured plan with real-time expert-led online weekly meetings + behavioral modification lessons & e-tools	$595/6 months
Nutrihand Pro: www.nutrihand.com	• HIPAA-protected platform for expert and client • e-tools and tracking, reports and fitness	$99/year for 100 clients

Conclusion

Online weight management web sites available today offer sophisticated e-tools. Clinicians should explore the features of various web sites and then based on clients' needs and desires; they can recommend optimal web sites. Clinicians can recommend preferred web sites to clients based on their weight management needs as well as the clinician's desire to work with their clients online, or be engaged independently. Online weight management web sites offer clinicians additional tools and avenues to enhance their practice and help their clients manage their weight and prevent disease. ◆

TelePractice

The American Dietetic Association (ADA) advises that standardized definitions for telehealth, telepractice or telemedicine have not been adopted, and that each state regulatory board determines practice regulations. For example, in Florida, rule 64B8-44.007 states that the initial nutrition assessment by a licensed nutritionist must be face-to-face, but subsequently the nutritionist can communicate via telephone, Internet, fax, etc., with exceptions for some federally funded programs. Consult ADA's web site to review state licensure laws to determine whether and how the practice of nutrition is defined in your state, and decide whether your services fall within the definition; you may consider licensure in other states. You may also contact the applicable licensure board for clarification if needed.
www.eatright.org/ada/files/Telehealth_FAQsf07.pdf
www.eatright.org/ada/files/STATE_LICENSURE_SUMMARY_7_07_PDF.pdf.

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Adding Sensipar® now?
Good thinking.

81%
of dialysis patients achieved PTH treatment goal when starting Sensipar® at
iPTH 300–500 pg/mL[1]

Waiting until now?
Think again.

22%
of dialysis patients achieved PTH treatment goal when starting Sensipar® at
iPTH > 800 pg/mL[1]

Think ahead.

Sensipar® simultaneously lowers[2]
PTH · Ca · P · Ca x P

Sensipar®
(cinacalcet) Tablets
30mg · 60mg · 90mg

Sensipar® is indicated for the treatment of secondary hyperparathyroidism (HPT) in patients with chronic kidney disease (CKD) on dialysis.

Important Safety Information

Significant reductions in calcium may lower the threshold for seizures. Secondary hyperparathyroidism (HPT) patients, particularly those with a history of seizure disorder, should be carefully monitored for the occurrence of low serum calcium or symptoms of hypocalcemia.

In Sensipar® postmarketing use, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia were reported in patients with impaired cardiac function. The causal relationship to Sensipar® therapy could not be completely excluded and may be mediated by reductions in serum calcium levels.

Sensipar® lowers serum calcium; therefore, it is important that patients have a serum calcium ≥ 8.4 mg/dL when initiating therapy.

Adynamic bone disease may develop if intact parathyroid hormone (iPTH) levels are suppressed below 100 pg/mL.

Patients with moderate to severe hepatic impairment should be monitored throughout treatment with Sensipar®, as cinacalcet exposure assessed by area under the curve (AUC) was higher than in patients with normal hepatic function.

Serum calcium and serum phosphorus should be measured within 1 week and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar®. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months.

The most commonly reported side effects were nausea, vomiting, and diarrhea.

References: 1. Moe SM, Chertow GM, Coburn JW, et al. Achieving NKF-K/DOQI™ bone metabolism and disease treatment goals with cinacalcet HCl. *Kidney Int*. 2005;67:760-771. **2.** Sensipar® (cinacalcet) prescribing information, Amgen.

Please see brief summary of prescribing information on next page.

Brief Summary

See package insert for full prescribing information

SENSIPAR® (cinacalcet) Tablets

INDICATIONS AND USAGE

Sensipar® is indicated for the treatment of secondary hyperparathyroidism in patients with Chronic Kidney Disease on dialysis.

CONTRAINDICATIONS

Sensipar® is contraindicated in patients with hypersensitivity to any component(s) of this product.

WARNINGS

Seizures: In three clinical studies of CKD patients on dialysis, 5% of the patients in both the Sensipar® and placebo groups reported a history of seizure disorder at baseline. During the trials, seizures (primarily generalized or tonic-clonic) were observed in 1.4% (9/656) of Sensipar®-treated patients and 0.4% (2/470) of placebo-treated patients. Five of the nine Sensipar®-treated patients had a history of a seizure disorder and two were receiving anti-seizure medication at the time of their seizure. Both placebo-treated patients had a history of seizure disorder and were receiving anti-seizure medication at the time of their seizure. While the basis for the reported difference in seizure rate is not clear, the threshold for seizures is lowered by significant reductions in serum calcium levels. Therefore, serum calcium levels should be closely monitored in patients receiving Sensipar®, particularly in patients with a history of a seizure disorder (see PRECAUTIONS, Hypocalcemia).

Hypotension and/or Worsening Heart Failure: In postmarketing safety surveillance, isolated, idiosyncratic cases of hypotension and/or worsening heart failure have been reported in patients with impaired cardiac function, in which a causal relationship to Sensipar® could not be completely excluded and may be mediated by reductions in serum calcium levels. Clinical trial data showed hypotension occurred in 7% of Sensipar®-treated patients, 12% of placebo-treated patients, and heart failure occurred in 2% of patients receiving Sensipar® or placebo.

PRECAUTIONS

General

Hypocalcemia: Sensipar® lowers serum calcium, and therefore patients should be carefully monitored for the occurrence of hypocalcemia. Potential manifestations of hypocalcemia include paresthesias, myalgias, cramping, tetany, and convulsions. Sensipar® treatment should not be initiated if serum calcium is less than the lower limit of the normal range (8.4 mg/dL). Serum calcium should be measured within 1 week after initiation or dose adjustment of Sensipar®. Once the maintenance dose has been established, serum calcium should be measured approximately monthly (see DOSAGE AND ADMINISTRATION). If serum calcium falls below 8.4 mg/dL but remains above 7.5 mg/dL, or if symptoms of hypocalcemia occur, calcium-containing phosphate binders and/or vitamin D sterols can be used to raise serum calcium. If serum calcium falls below 7.5 mg/dL, or if symptoms of hypocalcemia persist and the dose of vitamin D cannot be increased, withhold administration of Sensipar® until serum calcium levels reach 8.0 mg/dL, and/or symptoms of hypocalcemia have resolved. Treatment should be re-initiated using the next lowest dose of Sensipar® (see DOSAGE AND ADMINISTRATION). In the 26-week studies of patients with CKD on dialysis, 66% of patients receiving Sensipar® compared with 25% of patients receiving placebo developed at least one serum calcium value < 8.4 mg/dL. Less than 1% of patients in each group permanently discontinued study drug due to hypocalcemia. Sensipar® is not indicated for CKD patients not on dialysis. In CKD patients with secondary HPT not on dialysis, the long-term safety and efficacy of Sensipar® have not been established. Clinical studies indicate that Sensipar®-treated CKD patients not on dialysis have an increased risk for hypocalcemia compared to Sensipar®-treated CKD patients on dialysis, which may be due to lower baseline calcium levels. In a phase 3 study of 32 weeks duration and including 404 subjects (302 cinacalcet, 102 placebo), in which the median dose for cinacalcet was 60 mg at the completion of the study, 80% of Sensipar®-treated patients experienced at least one serum calcium value < 8.4 mg/dL compared to 5% of patients receiving placebo. **Adynamic Bone Disease:** Adynamic bone disease may develop if iPTH levels are suppressed below 100 pg/mL. One clinical study evaluated bone histomorphometry in patients treated with Sensipar® for one year. Three patients with mild hyperparathyroid bone disease at the beginning of the study developed adynamic bone disease during treatment with Sensipar®. Two of these patients had iPTH levels below 100 pg/mL at multiple time points during the study. In the three 6-month, phase 3 studies conducted in CKD patients on dialysis, 11% of patients treated with Sensipar® had mean iPTH values below 100 pg/mL during the efficacy-assessment phase. If iPTH levels decrease below the NKF-K/DOQI recommended target range (150-300 pg/mL)[1] in patients treated with Sensipar®, the dose of Sensipar® and/or vitamin D sterols should be reduced or therapy discontinued. **Hepatic Insufficiency:** Cinacalcet exposure as assessed by $AUC_{(0\text{-inf})}$ in patients with moderate and severe hepatic impairment (as indicated by the Child-Pugh method) were 2.4 and 4.2 times higher, respectively, than that in normals. Patients with moderate and severe hepatic impairment should be monitored throughout treatment with Sensipar® (see CLINICAL PHARMACOLOGY, Pharmacokinetics and DOSAGE AND ADMINISTRATION). **Information for Patients:** It is recommended that Sensipar® be taken with food or shortly after a meal. Tablets should be taken whole and should not be divided. **Laboratory Tests:** ***Patients with CKD on Dialysis with Secondary Hyperparathyroidism:*** Serum calcium and serum phosphorus should be measured within 1 week and iPTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar®. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months (see DOSAGE AND ADMINISTRATION). All iPTH measurements during the Sensipar® trials were obtained using the Nichols IRMA. In patients with end-stage renal disease, testosterone levels are often below the normal range. In a placebo-controlled trial in patients with CKD on dialysis, there were reductions in total and free testosterone in male patients following six months of treatment with Sensipar®. Levels of total testosterone decreased by a median of 15.8% in the Sensipar®-treated patients and by 0.6% in the placebo-treated patients. Levels of free testosterone decreased by a median of 31.3% in the Sensipar®-treated patients and by 16.3% in the placebo-treated patients. The clinical significance of these reductions in serum testosterone is unknown. **Drug Interactions and/or Drug/Laboratory Test Interactions:** See CLINICAL PHARMACOLOGY, Pharmacokinetics and Drug Interactions. Effect of Sensipar® on other drugs: Drugs metabolized by cytochrome P450 2D6 (CYP2D6): Sensipar® is a strong in vitro, as well as in vivo, inhibitor of CYP2D6. Therefore, dose adjustments of concomitant medications that are predominantly metabolized by CYP2D6 and have a narrow therapeutic index (e.g., flecainide, vinblastine, thioridazine and most tricyclic antidepressants) may be required. Desipramine: Concurrent administration of cinacalcet (90 mg) with desipramine (50 mg) increased the exposure of desipramine by 3.6 fold in CYP2D6 extensive metabolizers. Amitriptyline: Concurrent administration of 25 mg or 100 mg cinacalcet with 50 mg amitriptyline increased amitriptyline exposure and nortriptyline (active metabolite) exposure by approximately 20% in CYP2D6 extensive metabolizers. Midazolam: There were no significant differences in the pharmacokinetics of midazolam, a CYP3A4 and CYP3A5 substrate, in subjects receiving 90 mg cinacalcet once daily for 5 days and a single dose of 2 mg midazolam on day 5 as compared to those of subjects receiving 2 mg midazolam alone. This suggests that cinacalcet would not affect the pharmacokinetics of drugs predominantly metabolized by CYP3A4 and CYP3A5. Effect of other drugs on Sensipar®: Sensipar® is metabolized by multiple cytochrome P450 enzymes, primarily CYP3A4, CYP2D6, and CYP1A2. Ketoconazole: Sensipar® is metabolized in part by CYP3A4. Co-administration of ketoconazole, a strong inhibitor of CYP3A4, increased cinacalcet exposure following a single 90 mg dose of Sensipar® by 2.3 fold. Dose adjustment of Sensipar® may be required and PTH and serum calcium concentrations should be closely monitored if a patient initiates or discontinues therapy with a strong CYP3A4 inhibitor (e.g., ketoconazole, erythromycin, itraconazole; see DOSAGE AND ADMINISTRATION). **Carcinogenesis, Mutagenesis, and Impairment of Fertility: Carcinogenicity:** Standard lifetime dietary carcinogenicity bioassays were conducted in mice and rats. Mice were given dietary doses of 15, 50, 125 mg/kg/day in males and 30, 70, 200 mg/kg/day in females (exposures up to 2 times those resulting with a human oral dose of 180 mg/day based on AUC comparison). Rats were given dietary doses of 5, 15, 35 mg/kg/day in males and 5, 20, 35 mg/kg/day in females (exposures up to 2 times those resulting with a human oral dose of 180 mg/day based on AUC comparison). No increased incidence of tumors was observed following treatment with cinacalcet. **Mutagenicity:** Cinacalcet was not genotoxic in the Ames bacterial mutagenicity assay or in the Chinese Hamster Ovary (CHO) cell HGPRT forward mutation assay and CHO cell chromosomal aberration assay, with and without metabolic activation or in the in vivo mouse micronucleus assay. **Impairment of Fertility:** Female rats were given oral gavage doses of 5, 25, 75 mg/kg/day beginning 2 weeks before mating and continuing through gestation day 7. Male rats were given oral doses 4 weeks prior to mating, during mating (3 weeks) and 2 weeks post-mating. No effects were observed in male or female fertility at 5 and 25 mg/kg/day (exposures up to 3 times those resulting with a human oral dose of 180 mg/day based on AUC comparison). At 75 mg/kg/day, there were slight adverse effects (slight decreases in body weight and food consumption) in males and females. **Pregnancy Category C:** In pregnant female rats given oral gavage doses of 2, 25, 50 mg/kg/day during gestation no teratogenicity was observed at doses up to 50 mg/kg/day (exposure 4 times those resulting with a human oral dose of 180 mg/day based on AUC comparison). Decreased fetal body weights were observed at all doses (less than 1 to 4 times a human oral dose of 180 mg/day based on AUC comparison) in conjunction with maternal toxicity (decreased food consumption and body weight gain). In pregnant female rabbits given oral gavage doses of 2, 12, 25 mg/kg/day during gestation no adverse fetal effects were observed (exposures less than with a human oral dose of 180 mg/day based on AUC comparisons). Reductions in maternal food consumption and body weight gain were seen at doses of 12 and 25 mg/kg/day. In pregnant rats given oral gavage doses of 5, 15, 25 mg/kg/day during gestation through lactation no adverse fetal or pup (post-weaning) effects were observed at 5 mg/kg/day (exposures less than with a human therapeutic dose of 180 mg/day based on AUC comparisons). Higher doses of 15 and 25 mg/kg/day (exposures 2-3 times a human oral dose of 180 mg/day based on AUC comparisons) were accompanied by maternal signs of hypocalcemia (periparturient mortality and early postnatal pup loss), and reductions in postnatal maternal and pup body-weight gain. Sensipar® has been shown to cross the placental barrier in rabbits. There are no adequate and well-controlled studies in pregnant women. Sensipar® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Lactating Women:** Studies in rats have shown that Sensipar® is excreted in the milk with a high milk-to-plasma ratio. It is not known whether this drug is excreted in human milk. Considering these data in rats and because many drugs are excreted in human milk and because of the potential for clinically significant adverse reactions in infants from Sensipar®, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the lactating woman. **Pediatric Use:** The safety and efficacy of Sensipar® in pediatric patients have not been established. **Geriatric Use:** Of the 1136 patients enrolled in the Sensipar® phase 3 clinical program, 26% were ≥ 65 years old, and 9% were ≥ 75 years old. No differences in the safety and efficacy of Sensipar® were observed in patients greater or less than 65 years of age (see DOSAGE AND ADMINISTRATION, Geriatric Patients).

ADVERSE EVENTS

Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease on Dialysis: In 3 double-blind placebo-controlled clinical trials, 1126 CKD patients on dialysis received study drug (656 Sensipar®, 470 placebo) for up to 6 months. The most frequently reported adverse events (incidence of at least 5% in the Sensipar® group and greater than placebo) are provided in Table 1. The most frequently reported events in the Sensipar® group were nausea, vomiting, and diarrhea.

Table 1. Adverse Event Incidence (≥ 5%) in Patients On Dialysis

Event*:	Placebo n=470 (%)	Sensipar® n=656 (%)	Event*:	Placebo n=470 (%)	Sensipar® n=656 (%)
Nausea	19	31	Hypertension	5	7
Vomiting	15	27	Asthenia	4	7
Diarrhea	20	21	Anorexia	4	6
Myalgia	14	15	Pain Chest, Non-Cardiac	4	6
Dizziness	8	10	Access Infection	4	5

*Included are events that were reported at a greater incidence in the Sensipar® group than in the placebo group.

The incidence of serious adverse events (29% vs. 31%) was similar in the Sensipar® and placebo groups, respectively. **12-Month Experience with Sensipar®:** Two hundred and sixty-six patients from 2 phase 3 studies continued to receive Sensipar® or placebo treatment in a 6-month double-blind extension study (12-month total treatment duration). The incidence and nature of adverse events in this study were similar in the two treatment groups, and comparable to those observed in the phase 3 studies. **Postmarketing Experience with Sensipar®:** Rash, hypersensitivity, diarrhea and myalgia have been identified as adverse reactions during post-approval use of Sensipar®. Isolated, idiosyncratic cases of hypotension and/or worsening heart failure have been reported in Sensipar®-treated patients with impaired cardiac function in postmarketing safety surveillance. Because these reactions 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 drug exposure. **Laboratory values**: Serum calcium levels should be closely monitored in patients receiving Sensipar® (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

OVERDOSAGE

Doses titrated up to 300 mg once daily have been safely administered to patients on dialysis. Overdosage of Sensipar® may lead to hypocalcemia. In the event of overdosage, patients should be monitored for signs and symptoms of hypocalcemia and appropriate measures taken to correct serum calcium levels (see PRECAUTIONS). Since Sensipar® is highly protein bound, hemodialysis is not an effective treatment for overdosage of Sensipar®.

DOSAGE AND ADMINISTRATION

Sensipar® tablets should be taken whole and should not be divided. Sensipar® should be taken with food or shortly after a meal. Dosage must be individualized. ***Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease on Dialysis:*** The recommended starting oral dose of Sensipar® is 30 mg once daily. Serum calcium and serum phosphorus should be measured within 1 week and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar®. Sensipar® should be titrated no more frequently than every 2 to 4 weeks through sequential doses of 60, 90, 120, and 180 mg once daily to target iPTH consistent with the NKF-K/DOQI recommendation for CKD patients on dialysis of 150-300 pg/mL. PTH levels should be assessed no earlier than 12 hours after dosing with Sensipar®. Sensipar® can be used alone or in combination with vitamin D sterols and/or phosphate binders. During dose titration, serum calcium levels should be monitored frequently and if levels decrease below the normal range, appropriate steps should be taken to increase serum calcium levels, such as by providing supplemental calcium, initiating or increasing the dose of calcium-based phosphate binder, initiating or increasing the dose of vitamin D sterols, or temporarily withholding treatment with Sensipar® (see PRECAUTIONS). **Special Populations: Geriatric patients:** Age does not alter the pharmacokinetics of Sensipar®; no dosage adjustment is required for geriatric patients. **Patients with renal impairment:** Renal impairment does not alter the pharmacokinetics of Sensipar®; no dosage adjustment is necessary for renal impairment. **Patients with hepatic impairment**: Cinacalcet exposures, as assessed by $AUC_{(0\text{-inf})}$, in patients with moderate and severe hepatic impairment (as indicated by the Child-Pugh method) were 2.4 and 4.2 times higher, respectively, than in normals. In patients with moderate and severe hepatic impairment, PTH and serum calcium concentrations should be closely monitored throughout treatment with Sensipar® (see CLINICAL PHARMACOLOGY, Pharmacokinetics and PRECAUTIONS). **Drug Interactions:** Sensipar® is metabolized in part by the enzyme CYP3A4. Co-administration of ketoconazole, a strong inhibitor of CYP3A4, caused an approximate 2-fold increase in cinacalcet exposure. Dose adjustment of Sensipar® may be required and PTH and serum calcium concentrations should be closely monitored if a patient initiates or discontinues therapy with a strong CYP3A4 inhibitor (e.g., ketoconazole, erythromycin, itraconazole; see CLINICAL PHARMACOLOGY, Pharmacokinetics and PRECAUTIONS).

Storage: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). [See USP controlled room temperature]. Rx Only: This product, or its use, may be covered by one or more US Patents including US Patent Nos. 6313146, 6211244, 6031003 and 6011068, in addition to others, including patents pending.

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A Renal Nutrition Forum Series with Practice-Based Examples of the Nutrition Care Process (NCP): Where Does Nutrition Diagnosis Fit in the New Conditions for Coverage?

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Introduction

In recent months, dietitians employed in end-stage renal disease (ESRD) facilities have been implementing new forms, new procedures, and new timetables to comply with mandates in the Conditions for Coverage (CfCs) which became effective on October 14, 2008 (1). These preparations, aided by the release of Interpretive Guidelines (IGs) by the Centers for Medicare and Medicaid Services (CMS), were developed to support surveyors as they apply the new CfCs (2).

Perhaps the two sections in the new rules of greatest interest to nephrology dietitians are §494.80 and §494.90. These describe requirements for assessment and for interdisciplinary plans of care for ESRD patients. For example, §494.80 establishes the mandate for patient assessment in ESRD facilities. The IGs are explicit about the general categories of patient care that must be assessed. These include but are not limited to medical history, dialysis adequacy, blood pressure and fluid management, anemia management, renal bone disease, nutritional status, and psychosocial needs. Tag number V509 in the IGs specifies what to include in a nutrition assessment. Other tags describe assessment topics that may also be addressed by the nephrology dietitian depending on the practice setting, such as renal bone disease and anemia management.

Later in §494.90, the CfC rules state that an individualized plan of care (POC) must be developed for each patient by the ESRD facility's interdisciplinary team (IDT). IG Tags V540-V559 explain how each POC should be developed and implemented, with Tag V545 being specific to nutritional issues. Once again other categories of data in the POC, such as adequacy, may also be addressed by the facility's dietitian as part of the team working together to plan and implement an individualized POC.

Where is the Nutrition Diagnosis?

Since the regulations mandate an assessment and POC but do not specify "diagnosis" as a step in this process, diagnosis has not been included in some forms and procedures at ESRD facilities. This leaves many nutrition practitioners feeling a gap in planning and documenting individualized nutrition care. Table 1 traces the steps of the NCP and their comparable components in the CfCs. Diagnosis represents an essential step between assessing patients and planning care (that is, planning interventions and identifying outcomes by progress toward an intervention that is measured).

The NCP includes 4 steps: assessment, diagnosis, intervention (this step includes a care plan), and monitoring and evaluation (3). Nutrition diagnosis, defined as the identification and labeling of a nutritional problem that a dietetics practitioner is responsible for treating, creates an important link between assessment and intervention.

Case Study—Background Information

The patient described in Table 2 is a 53-year-old female, a new in-center hemodialysis (HD) patient. Although she carries the diagnosis of Diabetes Mellitus Type 2 (DM2), she is not on any medications for blood glucose management and does not seem to be monitoring glucose levels at home. She has had only a quick nutrition education session with a dietitian during a hospitalization immediately before starting HD. It was at that time that she first met a nephrologist as well.

At the end of the assessment, the IDT determined this patient to be stable, in keeping with the IG definition (2). Thus her first re-assessment will be in 3 months, again in accordance with the IGs.

Next Step: Nutrition Diagnosis

The information presented in Table 2 would be used to complete the nutrition portions of the ESRD facility's interdisciplinary assessment document. The next logical step in nutrition care involves establishing the nutrition diagnosis(es).
It may be appropriate to identify more than one nutrition diagnosis for a patient as long as the POC will address all that are identified. The 3-month time frame before re-assessment for this stable new HD patient certainly allows time to address more than one diagnosis. Some of the thinking in establishing the diagnoses that are included here was:

- Education about the important components of a healthy and safe eating plan for patients with ESRD is always a high priority with new HD patients;
- During the initial interview, the dietitian identified a lack of

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Table 1
Comparison of NCP and CfC Mandates

NCP Steps (3)	Counterparts in CfCs (1) with Supporting IG Tags Noted (2)
Assessment	§494.80 describes requirements for patient assessment. IG Tags V500-V515 describe information to be included in assessments (V509 is specific to nutrition; topics discussed in other tags, such as factors associated with renal bone disease, also relate to nutrition and may be completely or partially addressed by the nephrology dietitian in accordance with accepted practice patterns at a given ESRD facility).
Diagnosis	Not mandated, but should be included as it is Step 2 in the NCP.
Intervention/POC	§494.90 states that the IDT must develop and implement a comprehensive POC that describes services needed (interventions) and outcomes (monitoring and evaluation step of NCP). IG Tag V545 sets expectations for an outcome-oriented POC related to nutritional status.
Monitoring and Evaluation	

self-monitoring skills and inability to name her meds for DM2, both potentially serious problems, especially given the objective data of her very high glucose; and

- The use of regular multivitamin supplements is unsafe over the long term, particularly with the multiple doses in the case study. This patient is very committed to her supplements, so this issue was not addressed at her first session with the dietitian. But this is an important problem to address before the re-assessment.

The diagnosis labels used in Table 3 are taken from the standardized language (SL) in the International Dietetics and Nutrition Terminology Reference Manual (3). The nutrition diagnoses have been incorporated in PES statements. There is no requirement to use the standardized terms, but there are strong advantages in doing so. SL makes it much easier to audit nutrition care and to study frequency of certain diagnoses, interventions and outcomes; it also supports data mining to allow analyses which may help to quantify nutrition care and to validate the positive impact of certain interventions for particular diagnoses. Practice-based research into relationships between certain nutrition diagnoses, interventions and outcomes can be much stronger when a common language is used.

Next Step: Plan of Care

Following the assessment, the CfCs call for an individualized POC which includes services needed (same thing as interventions) and outcomes (which are the focus of the NCPs monitoring and evaluation stage). Table 3 presents a POC, which is preceded by the nutrition diagnoses, for the case study.

One advantage of PES statements is that they point the way forward to the appropriate intervention. Most often the intervention will be directed towards the etiology. In the first diagnosis in Table 3, for instance, the etiology "lack of in-depth education on appropriate food choices" takes the clinician to an intervention of comprehensive nutrition education. Other times an intervention may be aimed at reducing signs and symptoms. This is the case in the second diagnosis. The dietitian determined that the patient's failure to monitor blood glucose control was a symptom of poor self-management; and comprehensive education about self-monitoring seems like a reasonable service to address this problem. The intervention terms are taken from the SL of the NCP (3).

The final step in the NCP is to identify outcomes that will support monitoring and evaluation. The outcome criteria that are listed in Table 3 are taken from new terms for monitoring and evaluation which were introduced in the 2nd Edition of the IDNT Reference Manual (3).

Ultimately the cycle repeats, beginning with a re-assessment and continuing through the remaining 3 steps of the NCP. This long-term relationship with the patients we serve is one of the major attractions to those of us in nephrology nutrition.

Summary

Many of us who have been in the dietetics for a while were not taught diagnosis as a fundamental clinical skill; as a matter of fact, some of us have heard dietitians say that diagnosis is not within our scope of practice. If this ever was true, it is certainly not true now. Dietitians are uniquely skilled to diagnose problems in the nutrition well-being of our patients.

The NCP model was published to describe a framework for

Table 2
Case Study—Data for Assessment of New In-Center HD Patient

53 yr old female with ESRD due to DM2.

CLINICAL DATA: Co-morbidities—Hypertension, hyperlipidemia, reactive airway disease, left ventricular hypertrophy, congestive heart failure.
Newly diagnosed with ESRD—first in-center dialysis 1 week prior to this interview.
HD prescription: 3x/wk on Optiflux 180NRE dialyzer, 240 minutes, 3K* and 2.5 Ca* baths.
Prescribed meds with nutrition significance: Erythropoietin (20,000 units IV per HD session), Tums 500 (2 per meal). Cannot recall her meds for DM2 at this initial interview.
Over-the-counter meds: Centrum Silver multivitamin (2/day), One-A-Day multivitamin (2/day), Slo-Fe (1/day), 1000 IU cholecalciferol (1/day).
FOOD AND NUTRITION HISTORY: Good appetite. Denies history of pica, denies specific cultural preferences. Lives alone, rarely eats out, eats most meals alone. Takes 3 meals/day with 1-2 snacks. Dietary protein appears adequate in 24-hour food recall. Describes brief nutrition education with hospital dietitian, including handouts on renal diabetic diet. Attended diabetes classes years ago upon DM2 diagnosis. Avoids sweets. States she tries to follow diabetic diet but her "sugars are all over the place and no one has ever been able to help me control them better….nothing has ever worked."
ANTHROPOMETRICS: Height 167.6 cm, target weight 74.5 kg. Weight after last HD = 73.9 kg (target weight being challenged), Body Mass Index (using 73.9 kg) = 26.2. No weight change in last 3 months. Interdialytic weight gains: 1 – 2 kg.
PHYSICAL EXAM: No gastrointestinal complaints. Appears pale. No edema. Skin warm, no evident ulcers or sores.

BIOCHEMS	Results	Lab Norm	BIOCHEMS	Results	Lab Norm
Potassium	6.0 mEq/L	3.5-5.5	Phosphorus	5.9 mEq/L	3.5-5.5
CO2	24.0 mmol/L	22-30	Corrected Calcium x Phosphorus	51.5	≤ 55
BUN	48 mg/dL	60-100	iPTH*	206 ng/L	150-300
Creatinine	6.8 mg/dL	0.7-1.5†	Kt/V*	2.04	>1.2
Albumin	3.8 g/dL	goal ≥4.0	URR*	83.3%	>65
Glucose	259 mg/dL (non-fasting)	70-110	Cholesterol	124 mg/dL (non-fasting)	<200
Calcium	9.0 mg/dL	8.4-10.2	Triglycerides (TG)	385 mg/dL	35-135
Adj. Calcium	9.2 mg/dL	8.4-10.2	Hemoglobin (HGB)	10.9 g/dL	11-12

Last hemolgobin A1c= not known
†Not adjusted for ESRD
*K=potassium; Ca=calcium; iPTH=intact parathyroid hormone; Kt/V=a measure of dialysis adequacy; URR=urea reduction ratio
(see reference 4 for further information about some anthropometric and biochemical terms and K/DOQI standards in the case study)

delivery of nutrition care to broad groups. The second step in the NCP model, diagnosis, represents a major step in critical thinking about the care of the individual. In a 2006 New England Journal of Medicine (NEJM) article, Bowen describes how diagnostic reasoning skills can grow and develop (6). It is important to include diagnosis in policies and procedures for nutrition care of ESRD patients so that nutrition diagnosis will remain central in the practice of nephrology nutrition. ◆

Table 3
Nutrition Diagnosis and POC

DIAGNOSES (Problem—Etiology—Signs and Symptoms or PES)

1. **Problem (or Diagnosis):** Nutrition-related knowledge deficit related to
   Etiology: lack of in-depth education on appropriate food choices as evidenced by
   Signs and symptoms: high potassium and phosphorus foods in 24-hour diet recall.
2. **Problem (or Diagnosis):** Self-monitoring deficit related to
   Etiology: feeling overwhelmed by progression of kidney disease as evidenced by
   Signs and symptoms: patient not checking capillary blood glucose (CBGs) and patient unaware of medications for DM2.
3. **Problem (or Diagnosis):** Excess vitamin and mineral intake related to
   Etiology: patient unaware of special needs in ESRD, as evidenced by
   Signs and symptoms: taking double doses of 2 different multivitamins.

INTERVENTIONS/POC

Nutrition Prescription: 2200 kcal/day (30 kcal/kg), 90-95 g protein (1.2-1.3 g/kg), 2 g sodium, 2 g potassium, 1200 mg phosphorus, consistent CHO (5-6 carbs/meal with 15 g CHO per carb serving) (4)

1. **Goal:** Improved compliance with guidelines for dietary control of potassium and phosphorus to maintain serum levels within goal.
   Intervention: Comprehensive nutrition education regarding advanced topic.
2. **Goal:** Improved compliance with self-management of blood glucose.
   Intervention: Comprehensive nutrition education regarding advanced topic.
   Intervention: Nutrition-related medication management.
3. **Goal:** Patient will take a multivitamin that is safe and appropriate in ESRD.
   Intervention: Nutrition-related medication management.

MONITORING AND EVALUATION

Outcome Indicator	Criteria
1. Potassium and phosphorus intake	1. Will limit high potassium foods to 1 serving/day and will limit dairy to 1 serving/day. Serum potassium and phosphorus will be within goal next month (see Table 2 for target ranges).
2a. Preprandial capillary blood glucose	2a. Will record CBGs at least 1-2 times a day, before and 2 hours after meals, by the next monthly labs.
2b. Medication use	2b. Will consult with primary care provider about blood glucose management medications.
3. Vitamin and mineral intake	3. Will replace current multivitamins with a renal-specific multivitamin within the 2-4 weeks.

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WANT TO GET INVOLVED?
Let us know!

Contact: Danielle Frazer, RD @ rd813303@gmail.com.

Member Spotlight

Sandra McDonald-Hangach, RD, CSR
Recipient of an RPG educational stipend for the 2008 American Dietetic Association's Food & Nutrition Conference & Expo in Chicago, IL.
Renal Dietitian
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I recently attended the American Dietetic Association's Food & Nutrition Conference & Expo in Chicago. I went to sessions on various topics and was also able to take advantage of walking the expo floor to learn about new products, gather educational handouts, and collect samples for patient prizes.

Since the majority of my patient population is African American, one of the lectures I decided to attend was presented by Claudia Sealey-Potts PhD, RD, LD and Jo Ann Pegues, RD, MPA, titled, "African Americans' Dietary Lifestyles: Health Implications, Community Interventions and Outcomes." The presenters discussed the cultural food heritage of African Americans, typical African American intake, barriers to adequate nutrition and community efforts to promote a healthy lifestyle within this population.

Dietary habits of African Americans have been documented in several studies over the years. Overall results show low consumption of fruit, vegetables and whole grains and moderate intake of milk and meat. Intake of fat, salt and sugar tend to be above recommended dietary guidelines. Foods commonly consumed by African Americans are pork, wheat flour, cabbage, sweet potatoes and sugar.

Barriers such as financial constraints, inability to afford healthcare, limited education, lack of exercise and motivation to make dietary changes—all affect food choices. African Americans have a higher prevalence of cardiovascular disease, cancer, hypertension, diabetes and obesity than Caucasians. Studies have shown that intensive health and lifestyle treatment that are culturally sensitive can reduce disease progression in African Americans.

Ms. Pegues, an employee of the Center for African American Health in Denver, CO., discussed the health problems and challenges of African Americans and how community intervention programs have helped to overcome some of these barriers. The Center provides community programs that promote an active and healthy lifestyle to reduce serious health barriers that affect African Americans. Annually, the Center for African American Health conducts a health and lifestyle survey with Faith and Health Ministries within the metro Denver area. The results of the survey are then used to determine programs most crucial in reducing health disparities facing African Americans.

Diabetes self-management classes are a specific program that has developed from the outreach. Basic nutrition and cooking classes are taught. Participants learn about different foods and seasonings, such as chicken broth and herbs, to use with their traditional cultural dishes, along with simple kitchen skills such as measuring and preparing foods more effectively. Instructors also exercise with participants to stress the importance of physical activity. The classes provide a clear and encouraging message with an active and understandable format.

The two speakers provided valuable insight into the history of the African American diet. They discussed how health can be affected by many negative disparities, but how community intervention can help improve outcomes. As an RD, I hope to use the presented information in my own practice to identify health and lifestyle needs of my clients. ◆

If you would like to apply for an educational stipend, visit our web site.

In the members area, click on Awards/Stipends or go to
www.renalnutrition.org/members_only/awards.php

Renal Dietitians Chair Message

Pamela S. Kent, MS, RD, CSR, LD
RPG Chair

As I complete my term as Chair of the American Dietetic Association Renal Dietitians Dietetic Practice Group (RPG), the practice group is 2295 members strong, an increase of almost 5% this past year. Membership is the lifeblood of any association and members are RPG's greatest resources. The efforts of RPG could not have been accomplished without the dedication and hard work of all the volunteers, whom I would like to personally thank. Additionally, despite the current economic conditions, RPG has been proud to maintain our dues at $25.00 for the past seven years while still implementing enhanced benefits tailored to meet members' evolving needs.

This past year, RPG aligned with ADA's Organizational Identity on all print and electronic media. The new logo incorporates colors of healthy foods like leafy green, apple red and plum, along with the strong, positive phrase that has long been associated with ADA: "Eat Right." The Evidence Analysis Library (EAL) is another excellent free member benefit. The original evidence-based guideline on chronic kidney disease (CKD) was published in 2001 and revision is currently underway. In 2008, two evidence-based questions on fish oils, physical activity and CKD were posted online. If you haven't already explored the EAL, please check out www.adaevidencelibrary.com. Another helpful resource for the renal dietitian is the release of the Emergency Preparedness Task Force report, which was posted in May 2008 and can be found at www.eatright.org/cps/rde/xchg/ada/hs.xsl/nutrition_17403_ENU_HTML.htm.

In addition, CRN and RPG have collaborated on the development of Standards of Practice and Standards of Professional Performance for RDs in Nephrology Care, which will be published in the near future. Both organizations are also partnering on the revision of the 2nd edition of *A Clinical Guide to Nutrition Care in Kidney Disease.*

Your RPG leadership responded to your needs expressed in the 2008 Membership Survey, resulting in two, one-day seminars. The ever popular Board Certified Specialist in Renal Nutrition (CSR) review course was held at the 2009 NKF Clinical Meetings and a Medical Nutrition Therapy workshop was held at FNCE '08. A total of 10.5 free CPEUs were offered via the quarterly publication of the *Renal Nutrition Forum.* If you can't locate a hard copy of the Forum, check out www.renalnutrition.org for current and archived Forum issues. RPG has also added a new, exciting and time-saving member service to the web site: online completion and recording of CPEUs!

As we embark on a new era with the 44th U.S. President and the 111th U.S. Congress, Public Policy and Reimbursement initiatives remain critical. Mary Hagar, PhD, RD, FADA and Karen Basinger, MS, RD, LD have done a phenomenal job at representing RPG at the Centers for Medicaid & Medicare and the National Kidney Disease Education Program meetings. "Never has there been a greater need for ADA members to be active in support of an agenda that sees optimal health for Americans through food and nutrition investments. And despite the economy, there are multiple reasons to be optimistic that we can and will make progress on issues that affect you as dietitians and citizens," said Tracy Wilczek, MS, RD, LD, incoming chair of ADA's Legislative and Public Policy Committee. ADA's policy agenda for 2009 will be under the umbrella of work associated with health care reform. To stay well positioned, RPG must continue grassroots efforts across the nation. This past February, the 2009 Public Policy Workshop was provided in an electronic format to engage 3700 ADA members who participated in this free workshop. The workshop empowered RDs with the tools to be the nation's food and nutrition leaders.

It has been my pleasure and honor to serve as your Chair this past year. It has been a great experience to meet many of you and work with exceptional dietitians in our association. RPG will remain strong with the forward thinking leadership from our 2009-2010 Chair, Pat Williams, RD, LDN, and her experienced Executive Committee. As Johann Wolfgang von Goethe once said, "Knowing is not enough; we must apply. Willing is not enough; we must do." The opportunity is now and you can make a difference. Remember to renew your RPG membership for 2009-2010. ◆

RPG Member Benefits

- Receive the quarterly *Renal Nutrition Forum*
- Access to the Members' Only area of the RPG Web Site
- Access to the Lending Library (viewable under "Member Resources" on the RPG web site)
- Member stipends, awards, and scholarships
- Patient education resources (free or for purchase)
- And many more!

CRN Chairperson Message

Maria Karalis, MBA, RD, LDN
CRN Chair

"The achievements of an organization are the results of the combined effort of each individual." - Vincent Lombardi

Over the past few years, I believe that the CRN Executive Committee has made some significant strides in advancing the agenda of the CRN. We did this in a "divide and conquer strategy," and by leveraging each other's strengths. We re-examined our five year strategic goals and discovered we were mostly on track. We also realized the need to increase our focus in chronic kidney disease (CKD) patient education and awareness of medical nutrition therapy, areas we will surely focus on as the CKD population continues to grow. A *complete* listing of our activities can be found at www.kidney.org.

Highlights of Our Progress:

Legislation

- Responded to *draft* Conditions of Coverage (CfCs) and Interpretive Guidance prior to their final release.
- Provided membership support when the final CfCs were released by hosting a CRN Webinar the fall of 2008 and distributed a FAQ document specific to RDs and nutrition implications of these new rules.
- Participated on ANNA/NKF Taskforce for the development of a multidisciplinary patient assessment form or CIPA.
- With ADA/RPG, we filed a response to FDA to "Advance Notice for Proposed Rulemaking on Food Labeling" under Food Labeling: Revision of Reference Values and Mandatory Nutrients with recommendation to change labeling to add potassium and calcium on Nutrition Facts Panel.

Promoting Quality Nutrition Care

- The 4th Edition of the Pocket Guide is slated for release in spring 2009, under the leadership of Linda McCann, RD, CSR, LD. This "dietitians' bible" will be available for no additional charge to all CRN members.
- Last fall, we appointed Dr. Jerrilyn Burrowes, PhD, RD, CDN as Deputy Editor of the *Journal of Renal Nutrition*. Dr. Burrowes' term will begin officially with the January 2010 issue. We are excited to have Dr. Burrowes as the next Co-Editor-in-Chief.
- Standards of Practice (SOP) and Standards of Professional Performance (SOPP) for Registered Dietitians in Nephrology Care remain under development. This has been a joint project in collaboration with the American Dietetic Association Renal Practice Group (ADA-RPG). The SOP and SOPP will be published later in 2009.
- CRN continues collaboration with ADA-RPG to promote the Nutrition Care Process and nutrition diagnostic terminology. Special thanks to Maureen McCarthy, MPH, RD, CSR, LD, for leading these efforts.
- Under the leadership of Ann Beemer Cotton, MS, RD, CRN members continue to make regular contributions to the *Nephrology Nursing Journal* "Issues in Renal Nutrition" column.
- CRN and NKF Patient and Family Council sent a letter to the Office of Inspector General to support Fresenius' Advisory Opinion Request No.R638 to provide oral supplements to patients during dialysis.

Research

- Continue to fund the research grant program and announced targeted research or a call for proposals for determination of a predictive equation to estimate energy requirements in the HD population.
- Research Steering Committee organized and met for the first time at CM08. This group will help CRN identify best demonstrated practices as well as barriers to research and develop membership resources to overcome those barriers.

My term as Chair has been a fulfilling journey and one that I will never forget. I'd like to personally thank the 2007 and 2008 Executive Committee for their support, passion and commitment to this organization. The gavel now passes to Karen Wiesen, MS, RD. Karen is a great leader with sound judgment and wisdom and someone who "makes things happen." I look forward to the future of CRN under her leadership. ◆

2008-2009 RPG Executive Committee

Mission: Renal dietitians dietetic practice group is leading the future of dietetics by promoting and supporting its members working in nephrology nutrition.
Vision: RPG members are a valued source of expertise in nephrology nutrition.

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RNF Guidelines for Authors

Article length: Article length is determined by the Editor for each specific issue. The feature article (including abstract) is approximately 3000 words (not including tables/graphs). Other articles are usually 1000-1500 words; member highlights and reports are approximately 400-500 words.

Text format: Times New Roman font, 12 point, double space.

Tables/illustrations: Tables should be self-explanatory. All diagrams, charts and figures should be camera-ready. Each should be accompanied by a title and brief caption that clearly explains the table, chart, diagram, figure, illustration, etc.

References: References should be cited in the text in consecutive order parenthetically. At the end of the text, each reference should be listed in order of citation. The format should be the same as the *Journal of the American Dietetic Association.*

Reference citation examples:
Article in periodical:
Knower WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Eng J Med*. 2002;346:393–403.
Book:
Institute of Medicine. *Dietary Reference Intakes: Applications for Dietary Assessment*. Washington, D.C.: National Academy Press; 2001.
Chapter in a book:
Walsh J. Which insulin to use and how to start. In: *Using Insulin*. San Diego, Calif.: Torry Pines Press; 2003.
Web site:
Medscape drug info. Available at www.medscape.com/druginfo. Accessed Feb. 3, 2004.
Author information: List author with first name, middle initial (if any), last name, professional suffix and affiliation below the title of the article. Also include the primary author's complete contact information including affiliation, phone, fax and email address.

All submissions for publication should be submitted to the editor as an email attachment (MS word file). The feature articles from the Renal Nutrition Forum will be posted on the Members Only Section of the RPG website (password protected). Thus, please include a brief abstract along with feature article submissions.

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a dietetic practice group of the
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