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Renal Nutrition Forum

A Peer Reviewed Publication of the Renal Dietitians Dietetic Practice Group

Volume 30 • Number 2

In This Issue

Vitamin A Deficiency in a Hemodialysis Patient – A Case Review

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This article has been approved for 2.0 CPE units. The online CPEU quiz and certificate of completion can be accessed in the Members Only section of the RPG web site via the *My CPEU* link. In addition, this CPE offering is available to current RPG members only and the expiration date is June 30, 2012.

Introduction

This article reviews the function of vitamin A and examines a case review of vitamin A deficiency in a hemodialysis patient, as well as his treatment and outcomes.

Background (1)

Vitamin A is a fat soluble vitamin and plays an essential role in vision, cellular differentiation, growth, immunity, bone development, and has antioxidant properties, among others. It is a collective term for several related, biologically active molecules called retinoids (preformed vitamin A)—retinol, retinal, retinyl esters, and retinoic acid—that comprise the active forms of vitamin A.

- Retinol is necessary for reproduction and is found in animal tissues as retinyl esters with long-chain fatty acids. Animal sources of vitamin A are found primarily in liver, eggs, and milk (see Table 1). Since animal or supplement sources of vitamin A are preformed, toxicity is more likely to occur (2).
- Retinal is an aldehyde derived from the oxidation of retinol. It is necessary for low-light or color vision.
- Retinoic acid is derived from the oxidation of retinal. It is necessary for cell maturation, differentiation and reproduction. It cannot be reduced in the body and therefore cannot give rise to either retinal or retinol (see Diagram 1).

Carotenoids, called provitamin A carotenoids, are plant-based precursors of vitamin A. Of the provitamin A carotenoids, beta-carotene is most efficiently made into retinol and thereby possesses the most provitamin A activity. Metabolism of provitamin A carotenoids into active vitamin A is highly regulated, so toxicity is unlikely from plant sources (2). One exception, is the overconsumption of beta carotene from supplements which acts as a pro-oxidant.

The recommended daily allowance (RDA) for vitamin A is provided as retinol activity equivalents A (RAE). One RAE = 1 mcg retinol = 3.3 International Units (IU) (2). The RDA's are divided into gender and age groups and are listed as micrograms of RAE's to account for the differing biological activities of provitamin A carotenoids and retinols (see Table 2) (3). Tolerable Upper Intake Levels (ULs) were established to prevent toxicity.

R P G

Renal Nutrition Forum is published quarterly (summer, fall, winter, spring) as a peer-reviewed publication of the Renal Dietitians Dietetic Practice Group of the American Dietetic Association.

Articles about successful programs, research interventions, evaluations and treatment strategies, educational materials, meeting announcements and information about educational programs are welcome and should be emailed to the editor by the next deadline.

Future Deadlines:
September 1, 2011
December 1, 2011
March 1, 2012
June 1, 2012

Please forward information to:
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From the Editor's Desk

Megan Sliwa, RD, LDN
Editor

When I was on the plane back from the National Kidney Foundation (NKF) Spring Clinical Meetings in Las Vegas, I was asked why I was in Vegas. After letting the person know the meeting that I was attending and introducing myself as a registered dietitian, the person with whom I was speaking went on to reveal that their brother was recently put on hemodialysis. In the discussion that followed, he shared that his brother attributed a good part of the treatment success to the counseling he received at the in-center dialysis clinic. As I look back on that conversation and the NKF Meeting, I am inspired by the energy of the attendees, their commitment to the research and the passion for increasing the quality of life for patients diagnosed with Chronic Kidney Disease (CKD). The role of the renal dietitian has such power to share their expertise, teach fellow clinicians as well as improve the health of their patients.

It is this commitment and dedication, along with their interest in sharing their knowledge and best practices that drives the contributions to the Renal Nutrition Forum. I encourage you to have a look at the Feature Article by Rachael R. Majorowicz, RD, LD, for an in-depth case study that reviews the function of vitamin A. This article also reports on the treatment course of a patient with a deficiency and provides 2.0 CPEU hours. Additionally, the Advances in Practice article by Amy Braglia Tarpey, MS, RD, CSR, CNSC, examines medical nutrition therapy for the CKD patient, its long-term benefits to the patient and overall reduction in health care costs, provides 1.5 CPEU hours. Another interesting article included in this issue is a reprint entitled Understanding Functional Foods Through the Eyes of the Consumers from the On the Cutting Edge Newsletter. It discusses effective communication as a critical element in realizing the benefits of functional foods.

With the demands of work and life, I know volunteer time is precious. Many thanks to all those that made this issue possible for your expertise and guidance; this would not have the quality it does without your contributions. This issue of the Forum will be my last as Editor as I transition into the role of Managing Editor and Sara Erickson, RD, CSR, LDN, CNSC will begin her term as Editor with the Summer 2011 issue. And… a big thank you to Stacey Phillips, RD, outgoing Managing Editor, for her three-year commitment and dedication to the Renal Nutrition Forum Editorial Board! I wish her luck in her new role on the Executive Committee as the incoming Treasurer.

My goal is for you to enjoy and learn from this issue of the Forum. The editorial team welcomes your comments and suggestions for future issues as well. And if you've recently attended an interesting seminar or read a compelling article, it is likely that fellow members of the RPG would agree… consider sharing it as an original article submission to the RNF Editorial staff. ◆

Happy Spring!

Erratum
from Winter 2011 Forum:

Please accept our apologies, in the print version of the Renal Nutrition Forum, Vol. 30, No. 1 on page 1, the CPEU expiration date for the Feature Article entitled 'Maintenance Hemodialysis Patient is Improved with Intradialytic Parenteral Nutrition (IDPN): A Case Study' is listed incorrectly as 'April 15, 2011' and should read 'April 15, 2012'. Please note that the pdf version of the issue and the article on www.renalnutrition.org have been corrected.

Vitamin A Metabolism (1)

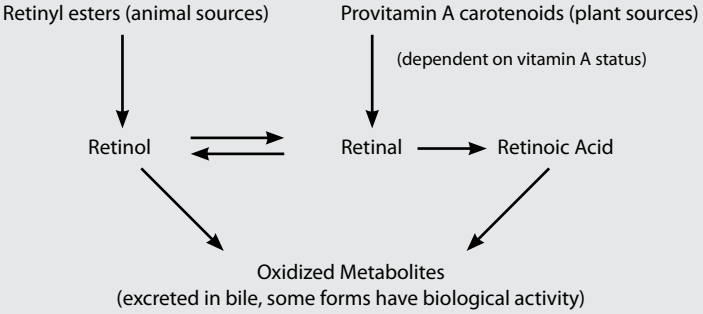
After some digestion in the stomach, retinol is esterified and packaged with chylomicrons in the small intestine, while some carotenoids are metabolized to retinoids and then esterified. Retinoic acid, on the other hand, enters the portal vein and tightly binds to albumin. Pancreatic and intestinal hydrolases act on the retinyl esters, freeing carotenoids and retinols to remain solubilized in micelle solutions. These are absorbed in the duodenum and jejunum, incorporated into chylomicrons, and transported to extrahepatic tissues. Those not taken up into tissues are then transported to the liver for storage or further metabolism. Roughly 50-85% of the total body retinol is stored in the liver (2).

Table 1
Food Sources of Vitamin A (3)

Animal Sources	Vitamin A (IU)*
Liver, beef, cooked (3 oz)	27,185
Milk, fortified skim (1 cup)	500
Cheese, cheddar (1 oz)	284
Milk, whole (1 cup)	249
Egg, fried (1 large)	362
Plant Sources	**Vitamin A (IU)**
Carrots, boiled (1/2 cup)	13,418
Spinach, frozen, boiled (1/2 cup)	11,458
Kale, frozen, boiled (1/2 cup)	9,558
Carrots, 1 raw (7 ½ inches)	8,666
Cantaloupe (1 cup)	5,411
Spinach, raw (1 cup)	2,813
Apricots, raw (1 cup)	3,178
Peach, 1 medium	319

*IU = International Units.

Diagram 1
Vitamin A Conversions



Note: conversion from retinol to retinal is reversible whereas the pathway from retinal to retinoic acid is not.

Table 2
RDAs and ULs for Vitamin A* (3)

Age (years)	Children (mcg RAE)	Males (mcg RAE)	Females (mcg RAE)	ULs
1-3	300 (1,000 IU)	n/a	n/a	600 (2,000 IU)
4-8	400 (1,320 IU)	n/a	n/a	900 (3,000 IU)
9-13	600 (2,000 IU)	n/a	n/a	1,700 (5,610 IU)
14-18	n/a	900 (3,000 IU)	700 (2,310 IU)	2,800 (9,240 IU)
19+	n/a	900 (3,000 IU)	700 (2,310 IU)	3,000 (10,000 IU)

* RDA's for pregnancy and lactation and Adequate Intakes for infants are found at http://ods.od.nih.gov/factsheets/vitamina

Within cells, retinol binds to cellular retinol-binding protein (RBP), which may function to regulate cellular levels of free retinol and to direct the vitamin to specific metabolic enzymes. Within the blood, retinol transport requires RBP, transthyretin (TTR, formerly known as prealbumin), and thyroxine. These carrier proteins circulate retinol to the tissues, with a half-life ≤ 15 hours. Once retinol has been deposited, the carrier proteins are filtered in the glomeruli and absorbed in the proximal tubules, making the kidneys indispensable to the process.

Vitamin A Deficiency

Vitamin A deficiency is uncommon in developed countries. Those at risk include preschool children eating inadequate fruit or vegetable intake, the urban poor, the elderly, or those with liver failure. Additionally, individuals with fat malabsorption, such as Crohn's disease, chronic diarrhea, celiac disease, and other disorders, have a higher risk of vitamin A deficiency.

A diagnosis of vitamin A deficiency is generally made by clinical findings but can be supported by serum retinol levels < 20 mcg/L or the ratio of retinol:RBP < 0.8 (2). Serum retinol levels may underestimate vitamin A stores in the setting of severe protein-calorie malnutrition since dietary protein, energy, and zinc are necessary for synthesis of RBP (2). Additionally, serum retinol

levels may be low if infection is present due to decreases in the negative acute phase proteins, such as RBP (2). Notably, vitamin A deficiency decreases the mobilization of iron from stores, leading to microcytic anemia.

Vitamin A Toxicity (1)

In comparison, vitamin A toxicity, or hypervitaminosis A, can result from acute or chronic supplementation. Acute symptoms in adults, possibly resulting from even one large dose of >660,000 IU, can include: nausea, vomiting, headache, blurred vision, and dizziness. Chronic toxicity may result from sustained intake of as little as 3-4 times the RDA. Symptoms include: bone or muscle pain, anorexia, dry/itchy skin, or hair loss. Excess vitamin A can also interfere with vitamin K absorption. Unfortunately, serum levels of retinol are not helpful in diagnosing vitamin A toxicity because most vitamin A is stored in the liver (2).

Vitamin A in Chronic Kidney Disease

In the chronic kidney disease (CKD) population, serum levels of vitamin A and RBP typically run higher than the general population (4) and can remain elevated for two years post-transplant (5,6). Additionally, patients with bilateral nephrectomies may have serum retinol levels elevated above that of hemodialysis (HD) patients (7). Elevated values may result from reduced ability of the kidneys to filter or absorb carrier proteins, as well as impaired conversion of retinol to retinoic acid (4). Additionally, Chen et al. reported elevated vitamin A levels associated with elevated creatinine, cautioning against vitamin A supplementation in the general population, but especially those with chronic renal insufficiency (8).

Vitamin A deficiency is uncommon in the CKD population since dialysis does not interfere with vitamin A status (5,9). Therefore, supplementation of vitamin A is not recommended in CKD (5,6) unless malabsorption is present (5). Notably, although HD does not decrease vitamin A levels, carotenoids have been shown to decline with dialysis (7). Symptoms of vitamin A deficiency in patients with CKD include scalded-appearing skin, hyperkeratosed hair follicles, Bitot's spots in the sclera of eyes, and dry eyes. Each can be monitored with use of the subjective global assessment (SGA) (10). Certainly, any acute changes in vision would be suspicious as well.

A recent study has shown, though, that low levels of vitamin A are an independent predictor of cardiovascular mortality in HD patients (11). Although this study could not identify if the increase in mortality was a result of reduced nutritional intake or vitamin A's role in immunity, there was speculation that the reduced ratio of retinol:RBP may affect the bioavailability of retinol within cells (11).

Conversely, Kalantar & Kopple reported elevated calcium and alkaline phosphatase levels in patients with CKD with intake of only 7,500-15,000 IU/day of vitamin A (7). Therefore, they recommend limiting food and supplemental sources of vitamin A to the RDA for patients with CKD (7). Vitamin A toxicity may also manifest as dark margins along the gums or may be associated with anemia (5,6,7,10).

Vitamin A toxicity could change cell membranes and transportation of ions, such as calcium, disrupting the normal intracellular groupings (12). Conversely, despite the elevated serum vitamin A values in HD patients, Aguilera et al. speculated that physiological or intracellular signs of hypovitaminosis A exist possibly due to a change in vitamin A receptors or the vitamin:carrier complex, leading to lower bioavailability and reduced retinol intracellularly (13). Thereby, the risk of vitamin A toxicity may be greatly reduced in the HD population. Additionally, they pondered whether more accurate vitamin A results could be obtained by checking vitamin:carrier-complex levels, rather than serum vitamin A levels (13).

Case Review—Patient M

Patient M is a 60 year old male who has been on in-center hemodialysis since 54 years of age in November 2004. His CKD is due to chronic interstitial nephritis. He also has a medical history of coronary artery disease, hypertension, debilitating gout, Crohn's disease resulting in colectomy in 1979 and small bowel resections with an ileostomy in 1990. Until the initiation of dialysis, he worked full-time as a chef.

Beginning in January 2005, he reported seeing black spots when standing too quickly or when getting up at night to go to the bathroom. At that time, it was attributed to dehydration and low blood pressure, resulting in an increase in his dialysis dry weight. By early February, he experienced "loss of vision in twilight hours" and difficulty distinguishing objects in low light. His vitamin A levels were checked and were normal at 398 mcg/L (see Table 3), so he was referred to Neurology and Ophthalmology.

By mid-March, his vision continued to deteriorate despite follow-up with a second ophthalmologist and a consult in neuro-ophthalmology with no conclusive diagnosis. Numerous medications were discontinued or substituted and he purchased new glasses, without improvement. Within the next two weeks, he could no longer drive at night. He was also having difficulty at work and, without improvement, would need to consider disability.

A recheck of the patient's vitamin A on April 1st, 2005 was low at 272 mcg/L and was associated with his night-blindness,