
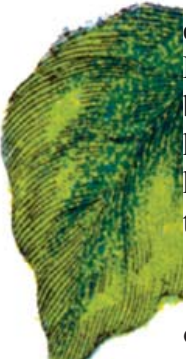


NEPHROLOGISTS HEAR ABOUT DIET & 39 DIETARY SUPPLEMENTS

At the American Society of Nephrology held in Philadelphia November 8 to 13, 2011, diet and dietary supplements were discussed for kidney disease patients. The take away message was that pomegranate juice can help manage high blood pressure and many kidney disease patients are taking dietary supplements that can be harmful.



Newswise, a journalists news feed organization, has tipped off those interested in medicine issues that Lilach Shema, PhD (Western Galilee Medical Center in Israel) and colleagues investigated the long-term effects of drinking pomegranate juice on heart disease risk factors—such as high cholesterol and blood pressure—in kidney disease patients. In 101 patients taking 3.5 ounces of pomegranate juice per week for a year, the pomegranate takers reduced blood pressure by 22% compared to 7.7% in those taking placebo. Also, another 12.2% of patients taking pomegranate juice had an increase in blood pressure, while 34.6% of the placebo group had increased in blood pressure. The same article said that cholesterol levels were healthier too, but did not explain. We will have to watch to see if the information is published so NML can report more.



Newswise also reported that another team led by Vanessa Grubbs, MD (University of California, San Francisco) looked at the use of dietary supplements among patients with chronic kidney disease (CKD). The National Kidney Foundation identifies 39 herbs that may be harmful to CKD patients, but no one knows how many of these patients take them. The herbs were not named, so we will have to watch to see if this is published, too.

This information was released a few days
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prior to the Philadelphia meeting and details are not available at NML's publication date on November 15. Contact : American Society of Nephrology -- Shari Leventhal, sleventhal@asn-online.org, 202-503-7804 or Adrienne Lea, alea@asn-online.org, 202-503-65


VITAMIN D IN CVD DEBATE CONTINUES

Readers who want to see how the debate continues between those on the Institute of Medicine (IoM) Committee that made the Vitamin D recommendations of 600 IU for persons up to 70 years of age and 800 IU for persons 71 years of age and older and the authors from the University of Queensland School of Medicine.

In an exchange of letters in the October 12, 2011 issue of *JAMA*; 2011; 306 (14) 1546-1547, Drs. O'Keefe, Lavie and Holick state that the Endocrine Society Clinical Practice Guidelines (*J. Clin Endocrinol Metab*, 2011;96(7): 1911-1930) recently suggested doses of 1000 to 2000 IU of Vitamin D to raise insufficient levels of Vitamin D to at least 30 ng/ml, which is well under any concern of toxicity. They suggest that while large trials are in progress for 5 or 6 years, that clinical prescribing be made on existing data. This means measuring levels of those at risk of deficiency, the elderly, those who live at high latitudes, people with darker skin, diabetes, obesity and minimal sun exposure. Screening may be warranted for people with liver or kidney disease, cystic fibrosis, primary hyperparathyroidism, sarcoidosis, inflammatory bowel disease, prior gastric bypass, osteoporosis, or osteopenia and those taking glucocorticoids or medications for human immunodeficiency virus infections or seizures.

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VITAMIN D DEBATE - Continued from p. 1...



Sue Shapses, Ph.D. (Rutgers) and JoAnn Manson, M.D., Dr.PH (Harvard Medical School) replied by letter in the same issue stating that the Endocrine Society Guidelines stated: “We do not recommend prescribing vitamin D supplementation beyond recommended daily needs for the purpose of preventing cardiovascular disease or death or improving quality of life.” They concluded that the Queensland doctors’ suggestions were puzzling. Then they admit that they stand by their report to IoM and will soon publish a response to the published guideline of the Endocrine Society. Shapses and Manson disagree that half of the population should be characterized as “at risk” of deficiency because 30 ng/ml has not been proven better than 20 ng/ml. They add that screening and prescribing Vitamin D is “unjustifiable health care cost of several billion dollars annually” and clinicians should not allow their “hope and enthusiasm for vitamin D to outpace the evidence.”

CLINICAL TRIALS NEEDED TO ASSESS RISK OF CVD FROM VITAMIN D DEFICIENCY

The title of this article is a paraphrase of the conclusions of three reviewers of Vitamin D studies at the University of Queensland School of Medicine in New Orleans, Louisiana. Lead author Carl J. Lavie, M.D., and co-authors John H. Lee, M.D. and Richard V. Milani, M.D. have cited 78 references covering the subtopics: ABCs of Vitamin D, Vitamin D and CV Risk Factors, Vitamin D Supplementation, Vitamin D and CV Disease: Is the Hype Merited? and Conclusions. The review contains 10 pages of well-written information about much of the Vitamin D research that has preceded submission for publication to the *J. Am. Coll. Cardiol.* 2011;58;1547-1556.

In their ABCs segment, they mention Vitamin

D2 and Vitamin D3, but not the new HyD product, which is just now being studied. Any serum level of 25-Hydroxyvitamin D, less than Sufficient or about 30 ng/ml is classified as three levels of deficiency. 40-50 mg/ml is “ideal” and over 150 mg/ml is in the toxicity range. The table in the review was adapted from Looker, AC, *et al* Vitamin D Status: United States, 2001-2006, *NCHS Data Brief* 2011;(59): 1-8. The same table points out that the Institute of Medicine (IOM) defines 20 – 50 ng/ml as Sufficient.

Under Vitamin D and CV Risk Factors, they mention research that indicated Vitamin D plays a role in determining risk for various cardiometabolic outcomes, “particularly metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM), and systemic hypertension.” [footnotes omitted] Epidemiological studies suggest that the rate of hypertension, T2DM, and coronary heart disease (CHD) increase in proportion to increasing distance from the equator, suggesting a potential link to the vitamin D mechanism. The article points out that chronic Vitamin D deficiency “causes” secondary hyperparathyroidism, which may mediate severe detrimental CV effects.

Low Vitamin D levels and increases in parathyroid hormone (PTH) levels increase the risk of inflammation. Administration of Vitamin D has been shown to down-regulate inflammatory biomarkers such as C-reactive protein.

Low Vitamin D levels are present in patients with mood disorders, including depression. But linking low levels, depression, and CV diseases seems “intriguing but speculative at best.”

The relationship of low Vitamin D levels, cardiovascular disease and mortality are being

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CLINICAL TRIALS - Continued from p. 2...

studies with varying results. Many studies suggest a CV risk with low levels, the data for routine supplementation are “sparse.”

Chronic kidney disease (CKD) patients have a markedly increased risk for CD disease and have more Vitamin D deficiencies. CKD patients getting hemodialysis and Vitamin D injections have survived longer, including those in a recent meta-analysis of 5 prospective studies.

Supplementation with Vitamin D is still controversial to some. IoM’s November 2010 recommendations for supplementation assumed minimal sun exposure and concluded that North Americans on average needed 400 IU of Vitamin D daily, and persons 71 or older need 800 IU per day. But the average American consumes only 230 IU per day. While IoM found evidence to support a role of Vitamin D in bone health, but did not believe that current evidence was sufficient for other health conditions, including the prevention and treatment of CV diseases.

Other experts say that 800 to 2000 IU per day may be needed and this is difficult to do without supplementation. The authors warn: “It should be recognized that an axiom of many essential nutrient, including in all likelihood Vitamin D, is that repleting a deficiency predictably confers powerful benefits, whereas supplementing a “normal” level to supraphysiologic ranges results in neutral to even potentially harmful effects.” FDA has noted a dose of 2000 IU daily is recognized as safe, but a recent review considered 10,000 IU per day was the safe upper limit.

Considering all of the information covered by the authors, they find a considerable debate continuing about the value of routine Vitamin D screening and supplementation for preventing

CV disease. They also conclude that “optimal levels of Vitamin D have not been established.” But these authors remain confident that the benefits of Vitamin D will outweigh the risks. They point out that a new 6,000 person clinical trial is comparing Vitamin D and Omega-3 oils in Boston that should provide important information.

VITAMIN D LEVELS HELP LUPUS


Another study from Paris, France, suggests that increasing Vitamin D (cholecalciferol) 100,000 IU per week for four weeks, then 100,000 IU per month for six months would raise 25(OH) D levels in two to six months to normal. This treatment increased the regulatory T cells and reduced the amount of T helper lymphocytes, previously shown to increase in SLE, together with other favorable changes, resulted in normalization of abnormal lymphocyte numbers.

Benjamin Terrier, MD; Patrice Cacoub, MD, PhD; and Nathalie Costedoat-Chalumeau, MD, PhD; from the Internal Medicine Department of the Pitié-Salpêtrière Hospital in Paris, France — studied 24 people in this study. Dr. Terrier presented the results at the American College of Rheumatology Annual Scientific meeting in Chicago on November 6.

[Note – The September issue of *NML* (Supplement) contained a summary of four other studies about SLE to demonstrate how much is known in the medical literature about this disease. Still needed are large, multiple million dollar studies to prove all of the points being made and to satisfy regulatory schemes of the FDA. If these are successful, then patients may get some relief. – Ed.]



VITAMIN E AND THE RISK OF PROSTATE CANCER



In a follow-up to the Selenium and Vitamin E Cancer Prevention Trial (SELECT) the long term use of selenium and Vitamin E was examined. The original trial was conducted from August 2001 to June 2004. After conclusion of data collection in July 2011, the group of 34,533 men had an increase in prostate cancer if they took 400 IU of (all rac- α -tocopheryl acetate) Vitamin E.

There were four groups: 8752 received 200 μ g of L-selenomethionine; 8737 received Vitamin E (400 IU/d of all rac- α -tocopheryl acetate), 8702 received both agents, and 8696 received placebos.

529 men developed prostate cancer in the placebo group, 620 men in the Vitamin E group developed prostate cancer, as did 575 in the selenium group. Compared with placebo, the absolute increase in risk of prostate cancer per 1000 person-years was 1.6 for vitamin E, 0.8 for selenium, and 0.4 for the combination.

Eric A. Klein, MD and 20 others conducted the study at: Department of Urology, Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, Ohio (Dr Klein); Cancer Therapy and Research Center, University of Texas Health Science Center, San Antonio (Dr Thompson); SWOG Statistical Center, Fred Hutchinson Cancer Research Center, Seattle, Washington (Drs Tangen and Crowley and Mss Goodman and Darke); Department of Pathology, University of Colorado Health Science Center, Aurora (Dr Lucia); Division of Cancer Prevention, National Cancer Institute, Bethesda, Maryland (Drs Minasian, Ford, and Parnes); Veterans Epidemiology Research and Information Center, VA Boston Healthcare System, and the Brigham and Women's Hospital, Division of Aging, Boston, Massachusetts (Dr Gaziano); Department of Thoracic/Head and Neck Medical Oncology, Division of Cancer

Medicine, MD Anderson Cancer Center/University of Texas, Houston (Drs Karp and Lippman); Department of Urology, Mayo Clinic, Rochester, Minnesota (Dr Lieber); Department of Urology, Duke University Medical Center, Durham, North Carolina (Dr Walther); Department of Urology, Sunnybrook Medical Center, North York, Ontario, Canada (Dr Klotz); Department of Surgery, Moores Cancer Center, University of California San Diego, La Jolla (Dr Parsons); London Health Sciences Center, London, Surgical Oncology, Ontario, Canada (Dr Chin); Swedish Medical Center Cancer Institute, Medical Oncology, Seattle, Washington (Dr Goodman); University of California at Irvine, Department of Medicine, Orange (Dr Meyskens); and University of Michigan, Division of Hematology/Oncology, Ann Arbor (Dr Baker). Dr Karp's previous affiliation was Beth Israel Deaconess Medical Center, Medical Oncology, Boston, Massachusetts.

Trial Registration www.Clinicaltrials.gov Identifier: NCT00006392. This study was published in *JAMA*, 2011;306(14):1549-1556. doi: 10.1001/jama.2011.1437

VITAMIN D AND MULTIPLE SCLEROSIS

In a recent article by Andrew J. Solomon in *Neurology* it is reported that Vitamin D appears to act as a hormone on a number of different systems in the human body. One role where vitamin D seems to be important is the immune system. Solomon describes an Australian study using Vitamin D2, plant derived, instead of animal derived Vitamin D3. He lists 8 references of recent research. This 23 patient study ended with the conclusion that high dose Vitamin D2 did not provide an advantage for relapsing-remitting multiple sclerosis. The high dose was 6000 IUs and the regular dose was 1000 IUs. The patients took the Vitamin D2 for six months. Solomon, *Neurology*, DOI 10.1212/WNL.0b013e318237c282 and see Stein MS, Liu Y, Gray OM, *et al*, A randomized trial of high-dose vitamin D2 in relapsing-remitting multiple sclerosis, *Neurology* 2011; 77: 1611-1618.