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VITAMIN D3

This is really a hormone and one of the eight predictive biomarkers with some 73% of Americans insufficient or deficient. Besides absorption of calcium and phosphorous from the small intestine, this vitamin is involved in the modulation of more than 1,000 genes and plays a seminal role in the three top killers: cancer, cardiovascular disease and Alzheimer's. There are two forms: vitamin D2 (the less potent plant-based ergo-calciferol) and actual vitamin D3 (i.e., fish liver cholecalciferol). Vitamin D3 converts into 1,25-hydroxy-cholciferol (calcitriol), the most potent endogenous steroid hormone. The most abundant source of vitamin D is sunlight.

The OWNS board reminds optometrists to proactively achieve a vitamin D status between 50ng/ml and 80ng/ ml in our patients by calculating the required dose of D3 based on lab results. This is crucial for patients facing recalcitrant uveitis/retinitis, multiple sclerosis, herpes simplex and zoster reactivation, decreasing neovascularization in macular degeneration and patients with or at risk for diabetes and multiple systemic cancers. Vitamin D repletion typically decreases excessive anti Vitamin D repletion typically decreases excessive anti-Vitamin D repletion typically decreases excessive anti- VEGF treatments in housebound elderly patients. Vitamin D status also plays a role in systolic blood pressure, and the degree of arteriolar sclerotic retinopathy, arcus senilis and cardiovascular plaque.

Pearls:

• 25-hydroxy OH vitamin D serum liver reserve status varies by ethnicity, which is why it is critical to do this lab test or order a home finger blood spot test (see www. vitamindcouncil.org for testing kits) to calculate the proper dose. Unfortunately, the 25-OH D blood test is not yet part of routine blood screening but one's status correlates with morbidity and mortality.

• Vitamin D status is lower in people with higher melanin counts (i.e., darker skin) due to the pigment's interference with sunlight absorption. Deficiency is also common in older people, those living in northern latitudes and patients prescribed chronic use of proton pump inhibitors.

VITAMIN E ISOMERS

This nutrient is composed of eight isomers: four tocopherols and four tocotrienols (alpha, beta, gamma, delta). Only one isomer of vitamin E (alpha tocopherol) was employed in the AREDS1 and ARED2 studies, an obvious criticism. Vitamin E tocotrienols are potent antioxidants in competition with the tocopherols. The best sources of gamma and delta tocotrienol (ideal for protection against cardiovascular disease, cancer and diabetes) derive from annatto beans. Tocotrienols increase tear production, retard cataract formation and reduce propensity for diabetic retinopathy and angiogenesis.

Pearl:

• A 2005 study in JAMA suggested that excessive (400 IU) vitamin E can be deadly! However, a closer look shows that the isolated finding applied only to an older cohort of patients (over age 70) with a long history of heart disease, stroke or diabetes, who were also taking a combination of medications, including ACE inhibitors, calcium channel blockers, anti-platelet agents and lipid-lowering agents during the course of the study. A significant number of subjects were also cigarette smokers.

LUTEIN AND ZEAXANTHIN

While most of the research investigating the role of lutein and zeaxanthin in preventing AMD has focused on these carotenoids alone, lutein and zeaxanthin may also improve responses to standard treatments to wet AMD. For example, a recent two-year, randomized trial found oral supplementation with zeaxanthin in addition to triple therapy (photodynamic therapy plus intravitreal administration of bevacizumab and dexamethasone) led to improved visual function, with 27% of eyes gaining ≥15 letters compared with 9% in eyes treated with triple therapy without zeaxanthin. Adding oral zeaxanthin also led to a 74% reduced incidence of subsequent neovascular AMD in fellow eyes compared with eyes treated with triple therapy without zeaxanthin.9 Supplementation may also lengthen the time between treatment cycles.10

• Augmenting our dietary intake of carotenoids with supplements can add another layer of protection, particularly for at-risk patients. The indications for such interventions should be at the fingertips of every optometrist. According to Dr. Richer, patients already at an increased risk of AMD should consider both nutrition and supplementation with 4mg to 10mg of zeaxanthin and 6mg to 20mg of lutein. The exact amount needed for 'repigmentation' of the fovea will depend upon various patient characteristics such as gender, omega-3 index and baseline MPOD.32-33 Patients taking warfarin are ideal candidates for carotenoid supplementation.

MESO-ZEAXANTHIN: WHERE DO WE GO FROM HERE?

We would argue that the fovea is the most valuable real estate in the eye. With its tightly packed cones and two major retinal carotenoids (zeaxanthin and meso-zeaxanthin), it is critical for hyperacute visual acuity and color vision. Unfortunately, the fovea is also the most vulnerable area for occult subretinal neovascular membrane formation in AMD. Though we disagree with the claim that supplementing with lutein, zeaxanthin and meso-zeaxanthin on a long-term basis is superior to supplementing with just lutein and zeaxanthin, we are encouraged by research on the short-term use of zeaxanthin and meso-zeaxanthin for late-stage AMD. Let's start with the CREST2 trial, which evaluated the impact of supplementation with lutein, zeaxanthin and meso-zeaxanthin in early AMD.8 The two-year, randomized, double-blind, controlled study compared a 25mg zinc/ AREDS2 formulation vs. 25mg zinc/AREDS2 plus 10mg of meso-zeaxanthin in minimal-risk AMD patients. The primary outcome measure was letter contrast sensitivity (CS) at six cycles per degree. CREST 2 showed no difference in this primary outcome (p=0.88). Global improvement in CS and secondary measures of visual function were virtually identical with or without the addition of 10mg mesozeaxanthin. Of concern, the meso-zeaxanthin-enhanced formulation dramatically diminished serum zeaxanthin levels (p=0.005). This is troubling because dietary lutein and zeaxanthin have emerged as crucial brain nutrients. More work needs to be done to address the issue of carotenoid competition. In another questionable finding for meso-zeaxanthin, a team of researchers looking at retinal proteins and carotenoids demonstrated that the isomerase enzyme RPE65 was responsible for converting lutein to meso-zeaxanthin in vertebrates.9,10 This essentially implied that retinal mesozeaxanthin was readily available to those supplementing with lutein.11 On a more positive note, two other published clinical studies investigating supplementation of zeaxanthin, and anecdotally meso-zeaxanthin, on approximately 700 patients resulted in fewer anti-vascular endothelial growth factor (VEGF) injections.12-14 This reduced AMD progression in the fellow eye by 75%.12,