

## **Vitamin D Deficiency Linked to Diabetic Retinopathy**

*By: Miriam E Tucker, Medscape Nurses*

Diabetic retinopathy may be yet another ill effect associated with vitamin D deficiency, a new metaanalysis and systematic review suggests. The findings were presented May 27, 2016 here at the American Association of Clinical Endocrinologists 2016 Annual Meeting by Anawin Sanguaneko, MD, a second year resident in the department of internal medicine, Bassett Medical Center, Cooperstown, New York.

"Patients with diabetes and low vitamin D levels may develop earlier or more severe diabetic retinopathy," Dr Sanguaneko told Medscape Medical News in an interview.

The mechanism could be twofold, he said. Studies suggest that vitamin D might improve insulin secretion in type 2 diabetes and may also directly reduce vascular endothelial growth factors. (Thus, deficiency would have the opposite effects.) Animal studies have demonstrated vitamin D receptors in the retina, and when given vitamin D, vascularization was reduced in animal models.

"But in humans, there are very few studies that assess how vitamin D supplementation affects diabetic retinopathy," Dr Sanguaneko commented. And such research would be needed before vitamin D supplementation could be recommended as an intervention to prevent diabetic retinopathy, he explained during a press briefing, adding that he plans to start such a study soon.

Asked to comment, W Reid Litchfield, MD, an endocrinologist in private practice in Henderson, Nevada, and an AACE board member, called the study "hypothesis generating" but cautioned that the location of the individual trials would have a major effect on the outcome, given that people living in more northern climates naturally have lower vitamin D levels. Indeed, a UK cross sectional study that was too recent to be included in this review found no association between vitamin D deficiency and diabetic retinopathy or maculopathy.

But the principal investigator of that study, Rayaz A Malik, MD of the University of Manchester, United Kingdom, told Medscape Medical News that he doesn't think the current data challenge

his group's findings. "To be honest, I was surprised that we didn't find an association, but I think the major reason was that vitamin D deficiency was highly prevalent in our population — everyone had low levels, as the population was in Manchester, and most patients do not receive treatment for vitamin D deficiency....Overall, even if our study was to be included in the metaanalysis, I don't think it would have changed the results."

And there has been prior research showing a link between another microvascular complication of diabetes, painful peripheral neuropathy, and significantly reduced vitamin D levels. In addition, a recent paper — on which Dr Malik was senior author — showed a single intramuscular dose of 600,000 IU of vitamin D was associated with a significant decrease in the symptoms of painful diabetic neuropathy in more than 100 patients (BMJ Open Diabetes Res Care. 2016;4:e000148).

### **Vitamin D Deficiency Linked to all Types of Diabetic Retinopathy**

Dr Sanguaneko and colleagues searched the literature published through July 2015 (Dr Malik's paper was published in Vitamin D Deficiency Linked to Diabetic Retinopathy Miriam E Tucker 5/31/2016 [www.medscape.com/viewarticle/863974\\_print](http://www.medscape.com/viewarticle/863974_print) [http://www.medscape.com/viewarticle/863974\\_print](http://www.medscape.com/viewarticle/863974_print) 2/2 January 2016) and extracted data from 13 studies involving 9350 participants with diabetes who had undergone assessment for both diabetic retinopathy and vitamin D deficiency. All of the studies were observational (either case control or cohort). For any diabetic retinopathy, the odds ratio (OR) between those with and without vitamin D deficiency was 1.391 (P = .011). For nonproliferative diabetic retinopathy, the OR was 1.209 (P = .001), and for proliferative retinopathy 1.315 (P < .001). For all the studies combined, the odds ratio was 1.267 (P < .001). Moreover, patients with diabetic retinopathy had significantly lower serum 25hydroxyvitamin D levels, with an overall mean difference of 2.22 ng/mL (P < .001).

"Food for Thought" Dr Malik told Medscape Medical News, "I am pleasantly surprised by this analysis, as it provides support for a large amount of basic experimental and other clinical data. We really need an adequately powered trial to see whether correcting vitamin D deficiency will improve outcomes." And Dr Litchfield noted, "Vitamin D is involved in many different areas of human physiology and [may contribute to] everything from infection to cancer to now maybe the complications of diabetes."

"It's conceivable that having inadequate vitamin D lowers your threshold for developing these complications....The question is whether there's a direct causative effect or it simply lowers the threshold for underlying disorders to create their complications. We don't know," he added.

He praised Dr Sanguaneko's plan to pursue a randomized clinical trial investigating the effect of vitamin D supplementation on diabetic retinopathy as well as a variety of other conditions, including macular degeneration, vitiligo, obstructive sleep apnea, and sepsis.

"I think his study has created new questions...and he's going to design more powerful clinical trials," Dr Litchfield said, adding that in the meantime "It may be premature to issue new recommendations on these things, but it's definitely food for thought."

Dr Sanguaneko and Dr Malik have no relevant financial relationships. Dr Litchfield is a speaker for Novo Nordisk. For more diabetes and endocrinology news, follow us on Twitter and on Facebook. Endocr Pract. 2016;22 (Supp 2); Abstract 309 Medscape Medical News © 2016 WebMD, LLC Send comments and news tips to [news@medscape.net](mailto:news@medscape.net). Cite this article: Vitamin D Deficiency Linked to Diabetic Retinopathy. Medscape. May 28, 2016.

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