Title:
Depression and Vitamin D3 Supplementation in Women with Type 2 Diabetes

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Session Title:
Vitamin D and Its Impact Across the Lifespan
Slot:
F 12: Friday, 28 July 2017: 2:30 PM-3:45 PM
Scheduled Time:
2:50 PM

Keywords:
Depression, Type 2 Diabetes and Vitamin D

References:

Anglin R.S., Samaan Z., Walter S.D., McDonald S.D. (2013). Vitamin D deficiency and depression in adults: Systematic review and meta-analysis. *British Journal of Psychiatry*, 202, 100-107.

George P.S., Pearson E.R., Witham M.D. (2012). Effect of vitamin D supplementation on glycaemic control and insulin resistance: a systematic review and meta-analysis. *Diabetic Medicine*, 29: e142-e150.

Ju S-Y, Lee Y-J, Jeong S-N. (2013). Serum 25-hydroxyvitamin D levels and the risk of depression: A systematic review and meta-analysis. *The Journal of Nutrition, Health & Aging*, 17(5), 447-455.

Pan A., Lucas M., Sun Q., van Dam R.M., Franco O.H., Willett W.C., Manson J.E., Rexrode K.M., Ascherio A., Hu F.B. (2011). Increased mortality risk in women with depression and diabetes mellitus. *Archives General Psychiatry*, 68(1): 42-50.
Penckofer, S., Doyle, T., Byrn, M., Lustman, P. (2014). State of the science: Depression and type 2 diabetes. *Western Journal of Nursing Research*, 36(9): 1158-1182.

Shaffer J.A., Edmondson D., Wasson L.T., Falzon L., Homma K., Ezeokoli N., Li P., Davidson, K.W. (2014). Vitamin D supplementation for depressive symptoms: A systematic review and meta- analysis of randomized controlled trials. *Psychosomatic Medicine*, 76(3), 190-196.

Abstract Summary:
Presentation will address the evidence regarding the role that vitamin D may play in depression and its symptoms, in addition to its impact on glycemic control. Finally, an ongoing randomized clinical trial examining varying doses of vitamin D for treatment of women with both of these conditions will be discussed.

Learning Activity:

LEARNING OBJECTIVES	EXPANDED CONTENT OUTLINE
The learner will describe the evidence regarding low vitamin D levels on depression and diabetes.	Clinical trial evidence for using vitamin D supplementation to treat depression, to treat diabetes, and to treat both comorbid conditions will be presented.
The learner will understand the impact that depression has on diabetes outcomes.	Clinical trial evidence regarding the use of current depression treatments (medication, cognitive therapy, and alternative methods) in type 2 diabetes and their impact on diabetes outcomes will be addressed.

Abstract Text:

Purpose: Depression affects over 25% of women with type 2 diabetes (T2DM) and makes self-management challenging (Penckofer, Doyle, Byrn, Lustman, 2014). Having both T2DM and depression significantly increases mortality for women (Pan et al., 2011). Although antidepressants can effectively relieve depression and its related symptoms in persons with T2DM, side effects include weight gain and for some, difficulty with glycemic control.

Evidence indicates that low levels of vitamin D are associated with depressive symptoms and depression itself. A meta-analysis of cross-sectional and cohort studies examining levels of serum vitamin D measured as 25-hydroxyvitamin D [25 (OH) D], reported a significantly reduced risk for depression with a 10 ng/ml increase in 25 (OH) D levels (Ju, Lee, Jeong, 2013). Another meta-analysis reported that there was an increased risk for depression for the lowest as compared to the highest vitamin D categories for cohort studies when following nondepressed individuals until their first diagnosis of depression (Anglin, Samaan, Walter, McDonald, 2013). Studies examining the benefit of vitamin D supplementation on depression are currently in progress. One systematic review and meta-analysis using Cochran guidelines examined seven RCTs and found no effect on depressive symptoms following vitamin D supplementation; however, for persons who had significant depressive symptoms or depressive disorder, there was a moderate significant effect (Shaffer et al., 2014).

Persons with T2DM have lower levels of 25 (OH) D which may be due to obesity or diabetes itself. Cross sectional studies have examined whether vitamin D was associated with insulin action and secretion, but results were inconclusive. One systematic review and meta-analysis of 15 RCTS examined vitamin D supplementation on insulin resistance in patients with diabetes, impaired glucose tolerance and normal glucose tolerance. Small improvements in fasting glucose and insulin resistance, but no effect on HbA1c were found for those with T2DM (George, Pearson, Witham, 2012).

Currently, there are no studies examining vitamin D supplementation for persons with T2DM who have significant depressive symptoms. Thus, the purpose of this study is to determine the impact of vitamin D supplementation on depressive symptoms and diabetes outcomes.

Methods: These investigators are conducting a randomized clinical trial to determine whether vitamin D_3 supplementation impacts depressive symptoms (Center for Epidemiologic Studies, CES-D) and whether this improves diabetes self-management (Self-Care Inventory). In addition, the role of vitamin D on blood pressure control is being explored. Women must have T2DM, significant depressive symptoms (CESD > 16), and levels of 25 OH D < 32 ng/ml to enroll. Using a stratified block randomization (strata based on depression symptom severity) women are being assigned to either weekly vitamin D_3 supplementation (50,000 IUs) or a matching weekly placebo (5000 IU) for a period of six months. We

hypothesize that women receiving 50,000 IU vitamin D_3 supplementation will report fewer depressive symptoms, increased diabetes self- management mediated by depression improvement, and have a lower systolic BP compared to those taking placebo. Measurements of 25 (OH) D, glycemic control (HbA1c), and self-care are being collected at baseline, 3 and 6 months following supplementation.

Results: Thus far, we have phone screened over 1300 women, consented 227, and enrolled 111 participants. Among these participants, 108 have been randomized to treatment. The characteristics of those enrolled are consistent with those who have not enrolled due to exclusion criteria. The 111 women who have met inclusion criteria have the following mean characteristics: age of 51.12 (SD = 10.91), 9.23 years (SD = 6.93) with T2DM, HbA1c of 7.83% (SD = 1.87%), BMI of 38.37 (SD=8.12), and systolic and diastolic blood pressures of 132.73 (SD = 15.34) and 72.53 (SD = 9.22), respectively. The average CES-D is 29.32 (SD = 8.68), and there are 48 (43.2%) in low depression group (CESD < 26) and 63 (56.8%) in high depression group (CESD > 26) for treatment. At baseline, there was no difference in vitamin D levels for those in the low depression group (M = 20.71, SD = 7.13) and high depression group (M = 21.05, SD = 5.86; p = .78). Thus far, of the women who have started the study drug (n=108), we have 96% retention at 3 months and 92% retention at 6 months.

Conclusion: Since women with T2DM have low levels of vitamin D and high levels of depressive symptomology, vitamin D supplementation as a treatment option could have significant implications with minimal side effects. This trial is anticipated to conclude in October 2017, and report its findings shortly thereafter. Given that 1 in 10 Americans now take antidepressants which can have negative effects on weight and metabolic control, positive findings may have implications as a cost-effective therapy for preventing depressive symptoms and/or as an adjunctive treatment for depression in others.