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Is Vitamin D the New Antidepressant?

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Abstract
Depression is characterized by a depressed mood or loss of interest or pleasure in almost all daily activities for a period of at least two weeks. Depression is a common mental disorder, characterized by feeling blue, and disturbed appetite, sleeping disturbances, poor concentration and loss of interest in daily activities (WHO, 2011). There are many systematic reviews studies of Vitamin D and depression have formed reliable results and generally have had strong methodological. Recent findings from a randomized trial propose that high doses of supplemental Vitamin D may improve depressive symptoms. Overall, the summary estimates of all analyses propose a correlation between Vitamin D and depression. It point out that quality of evidence from each study is high. The observational studies to date offer some evidence for an association between Vitamin D deficiency and depression, but RCTs are immediately wanted to conclude whether Vitamin D can prevent and treat depression in longitudinal study.
Keywords: depression, Vitamin D deficiency, literature review

Introduction

Vitamin D is the fat soluble vitamin. It can either be formed in the skin by sun exposure or be achieved by the diet, Vitamin D, also identified as the sunshine vitamin; it is a steroid hormone precursor (Iqbal & Khanan, 2010). Vitamin D is transformed by the liver and kidneys into a hormone (Vieth, Kimball, & Walfish, 2012). Vitamin D hormone is significant for the absorption of calcium and plays a critical role in psychological health (Lašaite, Gailyte, Puzinas, Preikša, & Kazanavičius, 2011). Moreover Vitamin D receptors have been originated on cells positioned in the same places of the brain that are connected with depression (Nanri et al., 2009).

Humans obtain their Vitamin D in nature through skin contact to sunlight's ultraviolet B (UVB) rays (Berk et al., 2008). When the sun's UVB rays penetrate the skin, a complex chemical synthesis reaction starts, which transforms sunlight into the hormone Vitamin D. The amount of acquired sunlight exposure, depends on several factors; living place, skin color, time of exposure, and obesity (Bertone-Johnson et al., 2011). The word health organization (WHO) recommended the maximum amount of Vitamin D is 4000 IU (The word health organization [WHO], 2013; Vieth, Kimball, & Walfish, 2012).

The phrase for deficiency level of Vitamin D is hypovitaminosis, and is characterized by levels of the Vitamin D serum lower than less than 10 ng/ml (Iqbal & Khanan, 2010). Vitamin D deficiency is characterized by levels of Vitamin D serum less than 20 ng/mL (Iqbal & Khanan, 2010). Vitamin D receptors and enzymes exist in the brain, which links it reasonable for Vitamin D to be correlated to brain activity and depression (Nanri et al., 2009).

On the other hand, Vitamin D is a steroid hormone that acts critical physiological roles (Chan et al., 2011). Some of these actions, including an influence on mood health. As most Vitamin Deficiencies are uncommon and rare in developed countries, Vitamin D is the only one that remains prevalent (Baljit, Khamba, Aucoin, Tsirgielis, opeland, ermani, &Cameron, 2011).

Depression is a worldwide and global problem causing enormous morbidity for the individual and socioeconomic burdens for the community (Ganji, Milone, Cody, McCarty, & Wang, 2010). The World Health Organization estimated depression to be the fourth leading cause for diseases burden, and it is predicted to be the second leading cause by 2030 (WHO, 2013).

American psychological association (APA) defined the depression as persistently low mood and feelings of grief, helplessness, worthlessness, and hopelessness (APA, 2000). People experiencing depression may feel overwhelmed and exhausted, and discontinue participating in their routine activities (APA, 2000). Commonly, they may withdraw from family and friends. Patients may also have thoughts of death or suicide (APA, 2000).

The present study aims to explore and clarify the role of Vitamin D in the development of depression in several studies, and to investigate the association between the Vitamin D deficiency, and depression.

Review of Literature

Introduction

The purpose of this literature reviews to insight more information about the correlation between the Vitamin D deficiency and depression. There are a number of questions that derive based on other researches and reviews. The questions that can be answered and proved based on the accessible literature are: First of all, does Vitamin D

deficiency leads to the progression of depression? If this is the case, do depressive symptoms decrease after ingesting Vitamin D supplements?

Related Studies and Main Findings

Vitamin D is able to penetrate the blood-brain barrier and its receptors are located broadly throughout the brain including the cortex, cerebellum and limbic system (Lee et al., 2008). Insufficiency in Vitamin D cause to rise of parathyroid hormone which is correlated with depression. The depression tends to cure after handling of the hyperparathyroidism (Hoogendijk, Lips, Dik, Deeg, Beekman, &Penninx, 2009).

About 121 million people globally suffer from a depression, and an expected 850.000 people each year commit suicide while suffering from a depressive period (WHO, 2013; Grohol, 2013). There is a variation between a clinically classified major depression and depressive symptoms (Grant, 2011). Depressive symptoms can be determined with self-report questionnaires. A clinically classified major depression is determined by a professional (Grohol, 2013).

Guowei, Mbuagbaw, and Zhang (2013) conducted a systematic review and meta-analysis of observational studies and randomized controlled trials. One case-control study, ten cross-sectional studies and three cohort studies with a total of 424 participants were analyzed, the authors presented arguments to emphasize that lower Vitamin D levels were found in people with depression compared with controls and there was an increased of depression for the lowest. The cohort studies noted a considerably increased risk ratio of depression for the lowest in vitamin.

The large cohort study pointed out that shortage in levels of Vitamin D were connected to the existence and severity of depressive disorder signifying that hypovitaminosis D correspond to an underlying biological susceptibility and vulnerability for depression (Chan et al., 2011). Milaneschi et al. (2010) additionally proved that hypovitaminosis D is common, particularly in the elderly. The authors emphasized that low levels of Vitamin D are correlated with poor mood.

Anglin et al. (2013) carried out systematic review. In ten cross-sectional studies, eight proved a significant and considerable association between low levels Vitamin D and depression and the authors emphasized the hypothesis that Vitamin D deficiency plays critical role in the pathogenesis of mood disorders or its potential as a therapeutic agent. It is well known that depressed individuals are more likely to be less physically active and as results have lower sun exposure.

May et al. (2010) in prospective study at 7358 participants stated that there are many causes of depression and they remarked that Vitamin D play significant role in mental health and in depression. Vitamin D acts on the areas of the brain those are associated to depression.

Shipowick et al. (2009) concluded that Vitamin D supplement is one of the most essential supplements were taken for depression. The researchers suggested that providing treatment for Vitamin D deficiency significantly diminishes women's depression in moderate and even severe cases. And further clarification the depressed women who contribute in the study received treatment for their Vitamin D deficiency without altering any of their antidepressant medication regimes or any other impactful factors in their environment. The researchers consequently confirmed that fixing the deficiency of vitamin D alone might have advantageous effects on depression (Shipowick et al., 2009).

Table 1: Summary Table

Authors & year of publication	objective	Design	N sample	Results	Level of evidence
Anglin, Samaan, Walter , & McDonald, 2013	To determine the relationship, if any, between Vitamin D deficiency and depression.	A systematic review and meta-analysis	424	Lower Vitamin D levels were found in people with depression compared with controls and there was an increased of depression for the lowest. The cohort studies showed a significantly increased hazard ratio of depression for the lowest in Vitamin D.	Level 1
Bertone-Johnson et al., 2011	To investigate the inverse linked between Vitamin D and depression.	cross-sectional prospective	81,18	Support of inverse association between Vitamin D and depression	Level 2
Chan et al., 2011	To clarify Significant inverse association between Vitamin D and depression.	cross-sectional prospective cohort	939	Significant inverse association between Vitamin D and depression	Level 4
Hoogendijk et al., 2008	To explore the relationship between depression and Vitamin D.	population based cohort	1,282	Association between depression and Vitamin D, adjusted for confounding variables	Level 4

Jorde et al., 2008	To determine the possible causal relation between Vitamin D and depression.	intervention	441	Possible causal relation between Vitamin D and depression	Level 2
May et al., 2010	To clarify the association of incidence of depression and Vitamin D levels.	prospective follow-up	7,358	Vitamin D levels are associated with incidence of depression	Level 2
Milaneschi et al., 2010	To examine if low Vitamin D is a risk factor for developing a depression in older people.	population based cohort	954	Low Vitamin D is a risk factor for developing a depression in older people	Level 4
Pan et al., 2009	To investigate the correlation between Vitamin D and depressive symptoms.	population based cross sectional	3,262	No association between Vitamin D and depressive symptoms	Level 2
Zhao et al., 2010	To explore the association between Vitamin D and depression .	cross-sectional population based	3,916	No significant association between Vitamin D and depression	Level 2
Hoogendijk et al ., 2009	To determine in a large population-based cohort whether there is an association between depression and altered 25(OH)D.	cohort study	1282	Depression severity was significantly associated with decreased serum 25(OH)D levels (*P*=.03) and increased serum PTH levels (*P*=.008).	Level 4
Guowei, Mbuagbaw, & Zhang, 2013	To evaluate the efficacy of oral Vitamin D supplementation in depression in adults with depressive symptoms/diagnosis or at risk of depression in RCTs.	randomized controlled trials (RCTs)	2510	The results of this systematic review will be helpful in clarifying the efficacy of Vitamin D supplementation and providing evidence to establish guidelines for implementation of Vitamin D for depression in general practice and other relevant settings.	Level 1
Berk et al., 2008	To explore Chart review studies patient psychiatric facility where serum 25-hydroxyvitamin D (25OHD) levels were routinely tested.	Cross-sectional	53	High rates of Vitamin D insufficiency in psychiatric inpatients.	Level 2
Nanri et al., 2009	To clarify the relationship between low 25OHDand depressive symptoms.	Cross-sectional	527	No significant difference in level of depressive symptoms between the two offices. Among participants in office B, prevalence of depressive symptoms decreased with increasing 25OHD; however, the results did not reach statistical significance.	Level 2
Lee, Tajar, O'Neill, 2010	To examine association between depressive symptoms, serum25OHD and PTH.	Cross-sectional	3151	Serum 25OHD was significantly lower in men with Beck Depression Inventory-II (BDI-II) scores # 14 (depressed men).	Level 2
Stewart& irani, 2010	To investigate the relationship between low serum 25OHD and depression in the elderly.	Cross-sectional	2070	Patients with <10ng/mL 25OHD had significantly higher frequency of depression than control than control.	Level 2

Summary of Review

The purpose of literature review was to explore if the Vitamin D is a new antidepressant. The results illustrate correlation between Vitamin D deficiency and the presence of mood disorders. Vitamin D supplementation might also be helpful in the treatment of mood disorders and to ameliorate depression symptoms.

In summation, three cross-sectional studies (Pan et al., 2009; Zhao et al., 2010) concluded no significant association between Vitamin D and depression. The five prospective cohort studies confirmed a significant and considerable relationship between Vitamin D and the development of depression (Bertone-

Johnsonet et al., 2011; Chan et al., 2011; Hoogendijk et al., 2008; Jorde et al., 2008; May et al., 2010; Milaneschi et al., 2010).

The Contrary Evidences

Iqbal and Khanan (2010) carried out two studies in Pakistan, the authors showed a incidence of 70% and 97% Vitamin D deficiency in healthy asymptomatic . Two cross sectional studies conducted in Karachi and Lahore on clinical populations exclusive of psychiatric patients, confirmed a 92% and 81% occurrence of Vitamin D deficiency correspondingly .Vitamin D deficiency has been initiate to be connected with major mental disorders such as depression, schizophrenia, and alcoholism but the plausibility is not well-known yet. However, relationship is not identical with causation (Jorde et al., 2008).

There is at present inadequate evidence to argue powerfully for Vitamin D supplementation in patients with depression, but such a strategy is worthy of consideration in depressed patients whose lifestyle and geographical residence may point out a risk of Vitamin D deficiency (Pan et al., 2009; Zhao et al., 2010).

The Corroborative Evidences

The efficacy of Vitamin D supplementation in depression has raised lots of concern. Vitamin D can cross the blood–brain barrier. Because of the widespread presence of Vitamin D receptor in areas of the brain including the hippocampus which is associated with the development of depression, it could be speculated that there is a clinical effect of Vitamin D on depression (Sanders al., 2011).

A randomized controlled trial was conducted by Vieth, Kimball, and Walfish (2012) advocated the view that participants with low Vitamin D levels had notably higher depression scores than participants with high Vitamin D levels ($P < .05$).

Strength and Weakness Points

The strength of this review is novel and innovative design. Most reviews examine the association between two variables, and control for others. In this review the information was gathered and put together about three variables and finally the influence of two other variables was also integrated. Furthermore the present paper comprehends contemporary studies from 2008- 2013 which comprises an original and unique topic.

The weakness of the review that the variations in measurement of depression influence the comparison of the results from the different articles. The following table summarizes the strengths and weaknesses.

Table 2: Analysis and Critique

Weaknesses	Strengths
1. Methodology of some studies cross-sectional design which means low response rate, and can't draw cause and effect relationship. 2. Focusing on single area. 3. No clear theoretical or conceptual framework was used. 4. Data collection tools (assessment tools) were not tested in terms of reliability and validity. 5. The lack of matched groups of appropriate control subjects makes it impossible to draw cause-effect conclusions. 6. Comparison between key studies, or important gaps in the literature was not identified. 7. Reliability of the instrument evaluated in a separate study was not depending on the current research sample itself.	1. Experimental design that fit the research hypothesis. 2. The dependent and independent variables operationally and conceptually defined 3. Using parametric test to examine significance effect of independent variable on dependent variable was presented in figures. 4. Good background information. 5. The study included in developed countries. 6. Control group, interventions, and frequency of measurement clearly identified. 7. Large sample size. 8. The inferential statistics using multi-test for analysis described clearly and thoroughly enough to be understood by reader, and presented in text, tables, and figures. 9. Recording thread was controlled by two investigators regularly visited the study wards on randomly selected dates.

Summary and Conclusion

Depression is characterized by a depressed mood or loss of interest or pleasure in almost all daily activities for a period of at least two weeks. Depression is a common mental disorder, characterized by feeling blue, and disturbed appetite, sleeping disturbances, poor concentration and loss of interest in daily activities (WHO, 2011). There are many systematic reviews studies of Vitamin D and depression have formed reliable results and generally have had strong methodological. Recent findings from a randomized trial propose that high doses of

supplemental Vitamin D may improve depressive symptoms.

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