Vitamins, Antidepressants and the Placebo Effect – How to Help Your Patients

Continuing Medical Education Poster
Nicko Inocencio

Objectives

Depression affects approximately 280 million people globally and increases risk for stroke, cardiovascular disease, hypertension, diabetes, and suicide. Due to the prevalence of depression and its adverse effects, this poster aims to identify risk factors, pathophysiology, and possible avenues for prevention and treatment using vitamins and minerals as relatively benign adjunctive therapy on top of the mainstay treatment of SSRIs/SNRIs +/- CBT.

Learning Outcomes:

- Identify the risk factors associated with depressive disorders.
- Understand the mechanisms by which vitamin D, magnesium, and vitamin B12 affect depressive symptoms.
- Develop a treatment plan using vitamin supplementation as adjunct therapy for patients with depressive disorders.

Introduction

- Affects 280 million globally
- Economic burden of $326.2 billion in the US alone
- Psychosocial risk factors: family history and major life events
- Neurobiological risk factors are less understood but may include:
    - Decreased serotonin
    - Inflammation
    - Buildup of homocysteine
    - Disruption of HPA axis
    - Elevated cortisol
- Pharmacotherapy primarily targets serotonin and norepinephrine but comes with numerous side effects
- **Vitamin D, magnesium, and Vitamin B12** are relatively benign, interact with the above risk factors, and may prove to be protective against depression

Mechanisms

Vitamin D

- Facilitates synthesis of serotonin
- Repression of reuptake and degradation of serotonin
- Inflammation modulation
- Protects against dopamine and serotonin depletion
- Regulates calcium homeostasis in neurotransmitter cellular signaling

Magnesium

- Inflammation modulation
- Reduces hyperactivation of the HPA axis via modulation of ACTH release and sensitivity

Vitamin B12

- Cofactor in the conversion of homocysteine to methionine, which is then converted to S-adenosylmethionine (SAMe) and then used to synthesize dopamine, norepinephrine, and serotonin

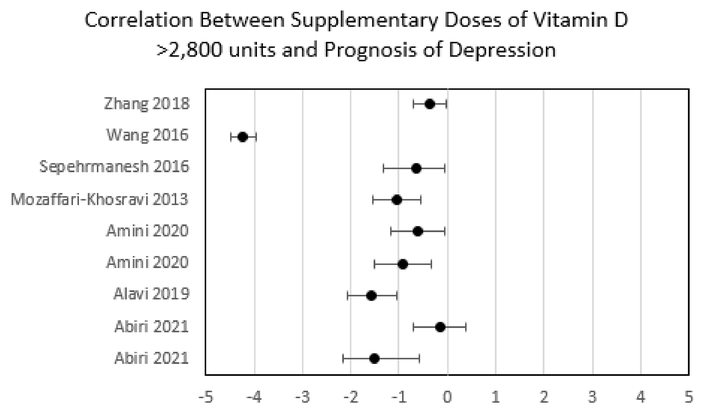

Fig. 1 above: Correlation between supplementary doses of vitamin D >2,800 units and prognosis of depression
Values <0 favor vitamin D supplementation while values > 0 favor placebo.

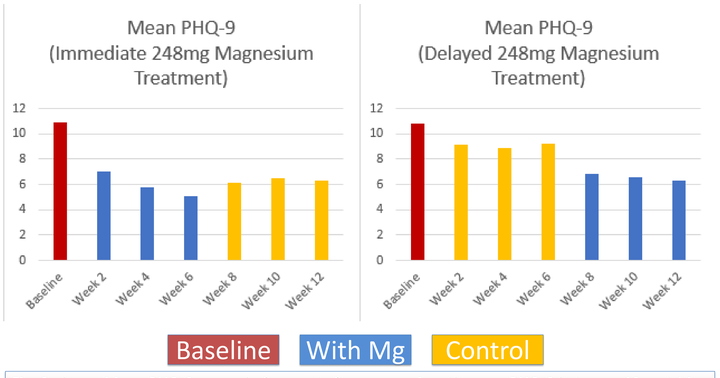

Fig. 2 above: Mean PHQ-9 scores before and after magnesium therapy. PHQ-9 between 10 and 14 signals moderate depression.

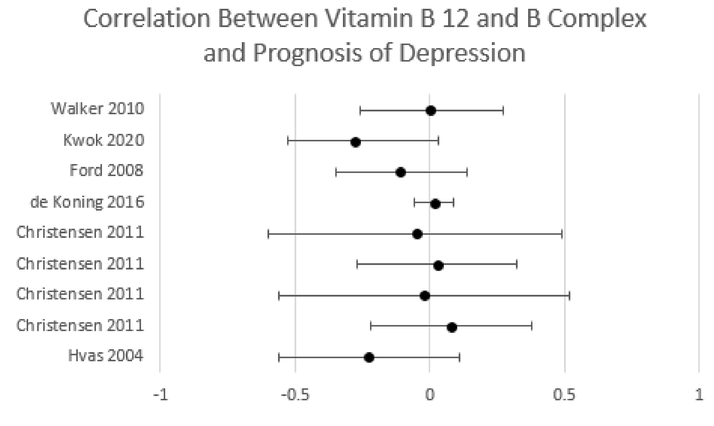

Fig. 3 above: Correlation between vitamin B12 and B complex and prognosis of depression.
Values <0 favor Vitamin B supplementation while values >0 favor placebo.

Data interpretation and Recommendations

The data suggests there is a positive correlation between vitamin D supplementation and prognosis of depression and lower mean PHQ-9 scores in patients receiving magnesium supplementation. Conversely, the data does not show a positive correlation between vitamin B12 or B complex and prognosis of depression. With those points in mind along with studies showing the efficacy of PHQ-9 in screening, diagnosis, and monitoring of symptoms, the following recommendations can be made:

- **Vitamin D**: 2,800 units daily for at least 8 weeks, then follow with 1,25-dihydroxyvitamin D assay aiming for > 30 ng/mL
- **Magnesium**: 248mg of elemental magnesium daily
- **Vitamin B12**: Only for patients at risk for developing depression or incidentally found to be deficient
- Monitor depressive symptoms with **PHQ-9** every visit and adjust therapy as needed

Above recommendations are in addition to SSRI/SNRI +/- CBT. Vitamin supplementation should not be used as monotherapy

CME Questions

1. Which is **not** a mechanism by which vitamin D affects the physiologic processes leading to the development of depression?
    a) Reducing hyperactivation of the HPA axis
    b) Repression of both the uptake and degradation of serotonin
    c) Regulation of calcium homeostasis in neurotransmitter cell signaling
    d) Inflammation modulation
2. Which of the following vitamins is more useful as a **preventative** therapy for depressive disorders?
    a) Vitamin D
    b) Magnesium
    c) Vitamin B12
    d) Calcium
3. Which of the following is used to follow a patient's clinical progress with regards to depressive symptoms?
    a)1,25-dihydroxyvitamin D assay
    b) GAD-7
    c) PHQ-9
    d) CGI-SCH

a, c, c

References:

1. Sangle P, Sandhu O, Aftab Z, Anthony AT, Khan S. Vitamin B12 Supplementation: Preventing Onset and Improving Prognosis of Depression. *Cureus*. 2020;12(10):e11169. Published 2020 Oct 26. doi:10.7759/cureus.11169
2. Tarleton EK, Littenberg B, MacLean CD, Kennedy AG, Daley C. Role of magnesium supplementation in the treatment of depression: A randomized clinical trial. PLoS One. 2017;12(6):e0180067. Published 2017 Jun 27. doi:10.1371/journal.pone.0180067
3. Xie F, Huang T, Lou D, et al. Effect of vitamin D supplementation on the incidence and prognosis of depression: An updated meta-analysis based on randomized controlled trials. Front Public Health. 2022;10:903547. Published 2022 Aug 1. doi:10.3389/fpubh.2022.903547
4. 1.Duffy FF, Chung H, Trivedi M, Rae DS, Regier DA, Katzelnick DJ. Systematic Use of Patient-Rated Depression Severity Monitoring: Is It Helpful and Feasible in Clinical Psychiatry? Psychiatric Services. 2008;59(10):1148-1154. doi:https://doi.org/10.1176/ps.2008.59.10.1148