To Supplement or Not to Supplement: That Is the Bipolar Depression Question

By Jeffrey J. Rakofsky, MD

With the multitude of nutritional products available to patients via the Internet and health-food stores, psychiatrists need to be prepared to respond to questions from patients about the value of these supplements.

Many of our patients want to incorporate nutritional supplements into their pharmacologic regimen. They view psychotropics with skepticism and prefer natural products, which are more consistent with their values and beliefs toward life and health. For some, supplements represent a seemingly safe augmentation strategy. Others view nutritional supplements as a “natural” treatment option and hope such agents will replace their psychotropic regimen.

With the multitude of nutritional products available to patients via the Internet and health-food stores, psychiatrists need to be prepared to respond to questions from patients about the value of these supplements. With so few FDA-approved treatment options in bipolar depression, bipolar patients, in particular, are likely to ask whether these products will help eliminate their painful and recurring depressive symptoms.

Along with my co-author, Boadie W. Dunlop, MD, I recently reviewed the efficacy data of nutritional supplements for the treatment of bipolar depression. From the PubMed and Ovid MEDLINE databases, I identified all randomized clinical trials of nutritional supplements in bipolar depressed patients that met the following inclusion criteria: the subject sample included adult bipolar (I, II, or NOS) depressed or euthymic patients; were randomized controlled trials; reported changes in depressive symptoms or depressive episode recurrences; and were written in English. Studies that enrolled both non-bipolar and bipolar patients were included only if they reported the results for the bipolar patients separately. Supplements were organized into 3 categories: essential nutrients/minerals, non-essential nutrients, and combinations of nutritional products. The study design, and efficacy and adverse event data for each study were evaluated.

What the evidence showed

Among essential nutrients/minerals, omega-3-fatty acids had the strongest evidence of efficacy for bipolar depression, although some studies failed to find positive effects from this supplement. The interpretation of results from omega-3-fatty acid trials is complicated by the varying doses and ratios of eicosapentaenoic acid and docosahexaenoic acid—the 2 forms of omega-3-fatty acids used in trials of this supplement.

Weak evidence supported the efficacy of vitamin C, whereas no data supported the usefulness of folic acid and choline. However, folic acid’s role in prevention of birth defects, particularly among bipolar patients, is of great importance—regardless of its usefulness for bipolar disorder symptoms. Among the non-essential nutrients, the 2 studies of N-acetylcysteine produced unclear efficacy for treating acute depressive episodes relative to placebo. One study demonstrated its potential to improve depressive symptoms over time. The other, although nonsignificant, suggested it had a prophylactic effect against future depressive episodes.

Inositol is another nonessential nutrient for which the data were unclear. Although all but one of the studies of inositol failed to demonstrate efficacy, the negative studies were underpowered and indicated numerically positive effects. Cytidine was the least supported nonessential nutrient. Combination supplements (ie, 2 or more supplements taken as a single pill) come in a variety of OTC products, but very few have been the focus of controlled, clinical evaluations. We found no evidence of efficacy for citicoline in uncomplicated bipolar depression, although it may have value for comorbid substance abuse among bipolar patients. Finally, the combination of omega-3-fatty acids and cytidine demonstrated no evidence of efficacy.

Our review did not support routine use of nutritional supplements in the treatment or prophylaxis of bipolar depression. However, study design limitations for both the positive and negative studies reduced the confidence with which our conclusions could be drawn. For example, many of the acute...
treatment studies had a long duration that may have allowed patients to experience a natural recovery from their episode, unrelated to the study treatment. This would diminish any drug-placebo difference and lead to false-negative outcomes. Sample sizes were often small, which could lead to both false-positive and false-negative efficacy assessments. Baseline mood symptom severity and/or episode were often not reported, thus introducing a potentially significant uncontrolled confounder of outcomes. Some studies included patients in any mood pole of bipolar disorder, making it unclear which phase of the illness was most affected by the study compound.

For some supplements, particularly the omega-3-fatty acids, the unique taste may have unblinded the participants or raters, leading to symptom reporting or scoring based on the expectation of improvements, rather than actual improvements. Changes to adjunctive psychotropic medication doses were permitted in some studies, which made it unclear whether a reported benefit or lack of benefit for a supplement was influenced by such medication changes. Finally, some studies included patients with very low symptom severity, which made it difficult to demonstrate the supplement’s potential benefit because of a floor effect on potential improvement.

Patients with bipolar disorder who seek alternative treatments in the form of nutritional supplements will likely be disappointed by these findings. However, supplements can be expensive, and they are usually not covered by health care insurance policies. In addition, these products may present unknown physical harms, because the FDA holds them to a different standard of safety than psychotropic medications. Finally, those who stop psychotropics, believing that supplements are superior and safer, can experience a worsening symptom course.

Given these risks, better-designed studies must be conducted to determine whether nutritional supplements will help bipolar depression before we encourage widespread use of individual supplements. Despite these inconclusive findings, psychiatrists must remain open to the possibility that with further studies, we may eventually identify minerals and supplements that will benefit bipolar patients. Remember, lithium—the cornerstone of bipolar treatment for several decades—is also a mineral.

Disclosures:
Dr Rakofsky is Assistant Professor in the Mood and Anxiety Disorders Program at Emory University School of Medicine in Atlanta. He is also the Director of Medical Student Education in the Department of Psychiatry and Behavioral Sciences and trains psychiatry residents in outpatient psychopharmacology practice. His research interests include the treatment and neurobiology of bipolar depression.

References:


Source URL: http://www.psychiatrictimes.com/psychopharmacology/supplement-or-not-supplement-bipolar-depression-question

Links: