What term do you prefer when talking about the use of nutrients in psychiatry?

I generally prefer the term “integrative,” though I believe the term “complementary and alternative medicine (CAM)” is more recognizable to healthcare providers and the public in general. Thus, I often use the term “CAM.” Complementary approaches generally refer to those that would not be considered mainstream or conventional but would be consistent with general concepts of Western medicine. Alternative approaches are usually considered outside traditional Western conceptual frameworks.

However, what is considered conventional is often subjective and dynamic, with changes over time. Therefore, the terms do not really give us a category that is very meaningful. We might find different modalities lumped together that may not be related, which makes it more difficult to study treatments in a systematic way.

I prefer “integrative” because it captures in a clinical way what we really want to convey, which is hopefully evidence-based, clinically important strategies that use whatever safe and effective treatments we can offer in a way that would be individualized for patients’ needs and preferences. The term means integrating whatever is considered conventional and mainstream with whatever is currently considered CAM. The spirit of the term really captures an openness to any treatment that would be evidence based and reasonable in a clinical context.

Why do mainstream medical journals rarely publish positive clinical-based studies that show therapeutic outcomes with some of these alternative or integrative approaches?

Many mainstream journals are very rigorous, excellent journals. They have a respected peer review process and can only accept a small number of papers. Very often, the amount of funding that is put into an area will affect the size and the quality of studies that are conducted. In an area where there is not a lot of funding available, studies are more likely to be seen as preliminary in nature. They are less likely to be adequately powered. I think in CAM or integrative medicine studies, we often have small studies that are deemed preliminary in nature, that might suggest future studies but may not be definitive. I think this is true across numerous treatments that have been studied.

In addition, many CAM study findings are inconsistent. Some studies may show positive results and some may not. Sometimes there is a lack of enthusiasm when the studies show inconclusive findings taken together as a group. I think that is true with most modalities. We have inconsistent findings across studies even with our best-studied antidepressants.

Not to generalize the mainstream medical journals, but I think many leaders in the field of psychiatry and many peer reviewers do have biases. Sometimes they are pro-complementary and alternative medicine, but very often they are against. I think that it is probably at the level of the individual.
What interested you in omega-3 fatty acids?

I had a great clinical research experience as a resident working with Andrew Stoll, MD, in the area of omega-3 fatty acids for bipolar disorder. I was really struck at that time by how deeply affected patients are by side effects from medications. I was intrigued by looking at something that would, for example, actually offer health benefits rather than increase cardiovascular risk. I saw how interested patients were in something that was being offered in a non-conventional way.

Other than the initial reports Stoll produced, what is the overall status of clinical studies with omega-3 fatty acids?

There have been quite a number since then. Stoll and colleagues published the first treatment study in mood disorders using omega-3 fatty acids, which was in bipolar disorder. Since then, there have been numerous other studies in bipolar disorder. The results have been inconsistent. The benefits appear to be most suggestive for bipolar depression rather than for mania. However, the area that has the most evidence in mood disorders and psychiatry in general is major depressive disorder (MDD). The greatest number of studies with omega-3 fatty acids have been double-blind, placebo-controlled trials looking at them adjunctive to standard antidepressants. The majority of those studies show a benefit of omega-3 versus placebo in that context.

To my knowledge, there has not been a study looking at omega-3 versus another adjunctive treatment. However, at least two large meta-analyses of the mood disorder literature show a statistically significant benefit of omega-3 fatty acids versus placebo in double-blind placebo-controlled trials.²,³

What kind of studies need to be conducted before use of omega-3 fatty acids will be accepted as an effective intervention?

One of the major limitations of the studies to date are generally size. Many of the studies do not have the power to demonstrate the results that we would hope to see. In general, treatment studies in depression have a pretty high placebo response rate, usually quoted as between 30% to 40%. That means that in order to see a true effect of a treatment, we need to have enough patients where there would be a statistically significant difference between those who received the intervention and those who received placebo. The largest studies to date looking at omega-3 fatty acids have still been relatively small. Some of the studies have included only ~20 subjects in a randomized controlled trial. In order to have definitive information, we need to have studies that include enough patients.

Another topic where omega-3 fatty acids have not been adequately studied is in terms of prevention of mood episodes. One area that is rich in the literature is looking at omega-3 fatty acids in terms of epidemiology and mood disorders. Those studies suggest that there might be preventative benefits. However, to date, we do not have treatment studies that follow through on that area of study.

Are there any side effects of omega-3 fatty acids?

Mild gastrointestinal (GI) symptoms are the most common, and there probably is an effect of dose and quality of the preparation. Some of the early studies looking at omega-3 fatty acids had very high doses. For example, in Stoll and colleagues’ first study in bipolar disorder,¹ patients received >9 g/day of Omega-3 fatty acids—14 capsules/day—which was a really tremendous amount to take on a daily basis.

In the studies that have been conducted for patients with mood disorders, lower doses appeared most effective. Many studies showed a benefit, in terms of adjunctive studies, of 1–3 g/day, which is a much smaller number of capsules in MDD. The main possible side effects, aside from GI upset, are mild nausea or diarrhea, which appear to be dose related. Many of the products are flavored and encapsulated differently; sometimes simply switching brands can alleviate side effects.

Are there any cardiovascular benefits from taking omega-3 fatty acids?

They are well established for cardiovascular benefits. Just like the general population, patients with psychiatric disorders who are looking for treatments are going to be at risk for cardiovascular problems. Having a psychiatric diagnosis is associated with increased risk because such individuals are more prone to smoking or not exercising enough. It is nice to be able to offer treatments that would provide overall general health benefits and may provide some relief in terms of mood disorders or other psychiatric disorders. It makes sense, while we are waiting for definitive evidence that omega-3 fatty acids are beneficial for mood disorders, to recommend products that have general health benefits. The American Heart Association recommends that Americans consume omega-3 fatty acids at least twice a week. Those with cardiovascular risk should consume at least 1 g/day.

Are any other supplements or approaches besides omega-3 fatty acids effective in helping patients with psychiatric disorders or symptoms?

The evidence for exercise as an add-on therapy is very strong. Epidemiologic data and treatment studies show the likely benefit of adding exercise to a regimen. There is no downside in terms of general health benefits and there is a potentially large upside in terms of health benefits and tolerability.

There is very compelling data for the efficacy of S-adenosyl-L-methionine (SAM-e). The biggest downside with SAM-e is that it is expensive. SAM-e is a major donor of methyl groups in the human body. It has been studied in double-blind placebo-controlled trials as a monotherapy for MDD. Primarily, it has exhibited benefit over placebo. It was initially studied intramuscularly, but is also available in an oral formulation. It has been studied in doses between 400–1,600 mg/day. When studied head-to-head with antidepressants, primarily tricyclic antidepressants, it has been found to be better tolerated. However, there is less data comparing SAM-e with newer antidepressants.
Does folate work well as an antidepressant?

The studies published to date suggest folate is an adjunctive treatment rather than a monotherapy. There is not much evidence that folate, in and of itself, is an antidepressant. However, low folate levels have been associated with higher levels of depressive symptoms, and adding folate has been demonstrated to speed up the response to an antidepressant, particularly fluoxetine.

Is there any way that a consumer or prescriber could know what kind of quality control is involved when prescribing SAM-e or omega-3?

This hits on a major issue. There is a difference in the regulatory requirements for pharmaceuticals versus food supplements regarding both claims that can be made and the amount of regulation in terms of purity. There is a large burden on consumers to know what they are purchasing and how to take the product.

Some, but not many, formulations of some of the supplements are available by prescription, which puts them in the class of requiring a greater level of regulation and oversight. Some companies have quality assurance information. It is unclear to what level that is accessible to the general public, but it is possible for the research community to obtain some of that data. For example, in the process of putting in grants, quality assurance information can be provided. However, I am not sure that is readily available. Certainly, individuals could ask for it. Some companies may even have that posted on their Websites. Still, I think that this puts a very tremendous burden on consumers.

Some people use vitamins and supplements because they want to believe that they do not need medication, when in fact they do. Do you feel this is an ethical conflict adequately addressed in the field?

The situation is complicated and multifactorial. There are often patient preferences and desires to avoid medication. It may be that patients have certain beliefs about medication or diagnoses. I think that part of the problem that we are up against in psychiatry is that there is great stigma often to being on medication, having a diagnosis, or obtaining treatment from a psychiatrist.

The area of CAM particularly raises some of these ethical concerns because a lot of the treatments are widely available without a prescription. While CAM treatments may vary in cost from inexpensive to relatively expensive, they are often accessible in terms of not requiring patients to access formal mental health treatment.

There is often a drive for patients to self-diagnose and self-treat, at risk of not getting appropriate treatment. It is a very important ethical issue that many patients might spend a lot of time suffering and a lot of money on treatments that are not effective. It is important in psychiatry and in medicine in general that we make sure that healthcare providers are educated about CAM so that they know what would be appropriate treatments and what the risks and benefits of different CAM treatments might be. We do not do a good enough job educating medical students, residents, and physicians in practice about different treatments, risks, benefits, and appropriate use of many of these treatments.

In parallel, I think we also need to make sure that the public is educated about psychiatric disorders and do what we can to decrease stigma, so that there is less of a barrier for patients getting full appropriate evaluations and knowing about their full treatment options.

If individuals really want to pursue CAM treatments for psychiatric disorders, I believe strongly that care should be in collaboration with a healthcare provider who can help monitor effectiveness and safety for the individual patient. Effects for the individual should be evaluated at intervals so that patients who are not doing well can continue to assess their options.

REFERENCES