Letters
Correspondance

Vitamin beef

The clinical review by Milly Ryan-Harshman and Walid Aldoori in the April 2008 issue of *Canadian Family Physician* requires comment.[1] While I appreciate the efforts of the authors to review such a huge, unwieldy topic, I think one of the several dangers in doing so is that certain key elements are not covered. I refer in particular to the section on B12 and mental health. It appears that there is a huge volume of literature that has not been researched by the authors regarding this topic, and I note that prolific authors (such as Coppen and Bottiglieri, for example) are not even mentioned in the bibliography. Yet their contributions to the literature on vitamin B12, folic acid, *S*-adenosylmethionine, homocysteine, and depression are of paramount importance. Therefore, I think that Ryan-Harshman and Aldoori's conclusion that B12 is "unlikely to substantially alter cognitive function or depression" is both inaccurate and unfair.

The other issue I have with review articles such as this one is the attempt to single out one particular element as having a beneficial effect. This attempt is inappropriate and unlikely to produce valid results, especially regarding vitamins and minerals. Vitamins and minerals work in concert; they work synergistically. Nowhere is this more evident and important than in the 1-carbon methylation cycle, which involves folic acid, vitamin B12, and homocysteine. This cycle, in and of itself, requires no less than 6 or 7 cofactors that must work together, in concert, for appropriate methylation of neurotransmitters and other important intermediates, as well as to remove toxic by-products. In fact, I would suggest that it is impossible to even consider vitamin B12 in relation to the treatment of depression without considering folic acid, *S*-adenosylmethionine, and vitamin B6, as well as tetrahydrobiopterin. This is notwithstanding the contribution that the methylenetetrahydrofolate reductase polymorphism would make.

For future clinical reviews in which nutrients are being considered, I think it would be worthwhile for both the editors and the authors to consider the synergistic aspects of medicine and direct themselves away from the outdated concept that there is one specific treatment for one disease.

For an excellent recent review of depression, folic acid, and vitamin B12, I would refer the readers to the paper by Coppen and Bolander-Gouaille entitled "Treatment of depression: time to consider folic acid and vitamin B12."[2]

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Medications for obesity

In his article on the use of medication in the management of obesity, Dr Sharma states that "there is now abundant evidence from pharmacologic trials that drugs such as orlistat, sibutramine, and rimonabant (a newer compound), when added to lifestyle interventions, can help patients maintain clinically meaningful weight loss for more than 2 years."[1] There are no citations given for this conclusion. The unstated implication is that these drugs can help achieve clinically meaningful results in terms of morbidity and mortality.

One of us searched the Cochrane Library for reviews about the effects of medication on weight-loss maintenance. There was 1 general review about the use of medication[2] and 1 for each of the 3 drugs that Dr Sharma mentions.[3-5] None of these 4 reviews provide any evidence that the use of these medications results in clinically meaningful patient outcomes, including noticeable average weight loss. The general review examined orlistat and sibutramine. In pharmacotherapeutic trials, of all the participants who withdrew from therapy during the weight-loss phase of the study, 33% were taking orlistat and 43% were taking sibutramine. These people were not followed up with and their outcomes were not reported at the end of the trial period, even though it is a common and ethical practice to follow-up with trial participants and obtain information on key outcomes despite early discontinuation of treatment. As a result, their weight gain or loss was not included in the efficacy estimates. This degree of incomplete reporting negates any scientific conclusions drawn from these studies. The authors of the review concluded that longer and more methodologically rigorous trials were required to fully evaluate any potential benefit of these weight-loss drugs.[2]

In one of the other studies, the rimonabant group had a similar attrition rate of approximately 40% of participants at the end of 1 year.[5] The authors cautioned that results regarding weight loss needed to be viewed tentatively owing to the methodologic limitations of the trials. Their conclusion was that "studies with longer follow-ups after the end of treatment and of more rigorous quality should be done before definitive recommendations can be made regarding the role of this new medication in the management of overweight or obese patients."

Beyond the issue of the role, if any, of these medications in the management of obesity, this also raises questions about the editorial process at *Canadian Family*

Physician. Editors must ensure that strong claims are not published unless there is supporting evidence. In particular, editors should prevent publication of assertions that claims are supported by evidence when they are not.

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Response

Dr Lexchin and colleagues correctly note that the data on the long-term benefits of antiobesity medications are perhaps not as robust as I made them out to be. There is no doubt that high dropout rates and lack of follow-ups are severe methodologic shortcomings of studies in this field. Nevertheless, from the long-term data available, weight maintenance (especially in per-protocol analyses) in participating individuals appears substantially superior to the nonpharmacologic controls of these studies.[1]

A seemingly modest 5% to 10% reduction in body weight (achieved in most pharmacologic trials) is generally associated with clinically meaningful improvements in risk factors (of obesity) and quality-of-life indicators.[2]

The key challenges of pharmacotherapy are how to match the right patient with the right drug and how to ensure long-term compliance and adherence to the medication in order to maximize the benefits. Obesity is a remarkably heterogeneous condition; the expectation that any one drug will work for all patients with obesity is probably unrealistic.

I fully agree with Dr Lexchin and his colleagues that more research is needed to discover the best use of these medications; nonpharmacologic strategies are clearly unsuccessful in providing long-term control of this condition.[3]

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