Psychopharmacology for the Clinician
Psychopharmacologie pratique

To submit questions for this regular feature, please send them to the Journal of Psychiatry & Neuroscience / Revue de psychiatrie & de neuroscience, *Canadian Medical Association, 1867 Alta Vista Dr., Ottawa ON K1G 3Y6, Canada; fax 613 729-9545; jpn.office@sympatico.ca Please include details of any relevant case and your name, address, telephone and fax numbers as well as your email address.*

Should thyroid replacement therapy be considered for patients with treatment-refractory depression?

There is a well-established association between depressive illness and the thyroid axis. One of the most consistent findings reported is that 10%–15% of depressed patients will have grade II subclinical hypothyroidism (i.e., normal levels of circulating thyroxine [T4] and triiodothyronine [T3], with elevated thyrotropin [TSH]). The exact clinical significance of this observation is not fully understood.

Ms. A was a 43-year-old woman who presented with evidence of a major depressive disorder. Routine thyroid screening revealed a modest elevation of TSH at 8.3 mU/L with normal T4 and T3 levels. She was given a trial of a serotonin reuptake inhibitor but failed to respond after 6 weeks of adequate treatment. A subsequent trial of a second selective serotonin reuptake inhibitor was also unsuccessful. Treatment with triiodothyronine (T3) was instituted at 25 µg/day, in addition to her antidepressant. She responded robustly to the addition of the thyroid hormone during the second week of augmentation and was feeling well with no symptoms of depression.

T3 has been used to augment antidepressant response. Most of the literature suggests that it is effective in patients who are euthyroid. There are approximately 12 studies that consistently show that T3 augmentation is effective in about 50%–60% of cases. However, most studies were open and uncontrolled and all involved tricyclic antidepressants rather than the more commonly used classes of antidepressants today.

In the case of Ms. A, there are 2 possible explanations for the effectiveness of T3 as an antidepressant augmentation strategy. The first is that it potentiated the therapeutic effect of the selective serotonin reuptake inhibitor irrespective of thyroid status. The second is that the T3 was thyroid hormone replacement therapy to correct the subclinical hypothyroidism. The first explanation is a well-documented finding. The second is controversial. There is no clear evidence that correction of subclinical hypothyroidism either reverses depression or corrects treatment-resistant depression. However, there are data suggesting that subclinical hypothyroidism may reduce the rate of antidepressant response in patients with major depressive disorder. Furthermore, there is at least a theoretical argument that depressed patients with subclinical hypothyroidism may, in fact, have a clinical manifestation of thyroid disease, as depression and depressed mood are commonly associated with thyroid illness, particularly hypothyroidism. Regardless of which of these explanations is true, varying degrees of hypothyroidism may, in fact, increase vulnerability to depression and reduce the rate of antidepressant response.

Although one would not recommend thyroid replacement therapy for all cases of modest elevations of TSH in the presence of a treatment-refractory depression, it should be considered to improve the chance of therapeutic success with antidepressant therapy. In the event that thyroid replacement therapy is considered, one could either opt for T4 or T3. T3 may be a more effective antidepressant, but is not routinely used for thyroid replacement. On the other hand, T4 is generally the thyroid hormone used for replacement therapy, but its effectiveness in major depression in euthyroid patients is less well documented.

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The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided.