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.*

Although antidepressants and anxiolytics are frequently used together to treat depression in the acute phase, how effective is the concomitant use of these drugs?

The acute phase of depression is often accompanied by anxiety, irritability, insomnia and anxiety disorders. As a result, the concomitant use of an anxiolytic agent with an antidepressant is often necessary. Selective serotonin reuptake inhibitors (SSRIs) are currently the first-choice therapy for depression, but insomnia, irritability and anxiety sometimes occur in the early stages of treatment. As these symptoms may result in early dropout or delays in the antidepressive response, the concomitant use of an anxiolytic is considered helpful. Benzodiazepines (BZDs) alleviate symptoms associated with anxiety and irritability and do not aggravate core symptoms such as anhedonia and, thus, can lead to short-term improvement in depression and rapid alleviation of patient distress. However, some patients feel unable to stop taking BZD anxiolytics even when remission of depression has been achieved. This tendency is expected to be even stronger in patients with a high degree of neuroticism, a well-known premorbid personality trait associated with depression.

To investigate the benefits of the concomitant use of antidepressants and BZDs, Furukawa et al (*Cochrane Database Syst Rev* 2000;[4]: CD001026) conducted a meta-analysis of 9 randomized comparative studies involving 4–6 weeks of continuous treatment. The combination-therapy group was found to be less likely to drop out of treatment than the antidepressant-alone group (relative risk reduction 37%). The dropout rate due to adverse drug reactions was also low (relative risk reduction 48%). The combined effects were most evident in week 1. When assessed at week 4, combined treatment was still more efficacious, with a response rate of 63% compared with 38% for monotherapy. However, no difference was identified between groups at weeks 6–8.

The azapirone anxiolytic agents do not cause dependency; however, when we investigated the effects of the concomitant use of tandospirone and clomipramine, which displays a potent serotonin-reuptake inhibiting action, no significant differences between concomitant administration of both drugs and clomipramine monotherapy were noted in the initial stages of treatment, even up to week 8 (Yamada et al, *Psychiatry Clin Neurosci* 2003;57:183-7). Because azapirone anxiolytics require several weeks before any effect on anxiety is exhibited, there is little clinical reason for their concomitant use in the initial stages of depression treatment to target anxiety and irritability. Rather, the use of concomitant azapirone anxiolytics should be thought of as a way to augment SSRI therapy. Concomitant use of buspirone with SSRIs such as fluoxetine, citalopram and paroxetine has already been reported to augment the effects of SSRIs for treatment-resistant depression. Azapirone anxiolytics are thought to act as agonists on 5-HT_{1A} receptors. It is possible that azapirone anxiolytic agents not only stimulate postsynaptic 5-HT_{1A} receptors but also suppress compensatory overactivity and inhibit further serotonin depletion by acting on autoreceptors.

In conclusion, the concomitant use of antidepressants and BZDs may be useful in the first few weeks of treatment to bring about rapid improvement and to reduce the dropout rate. After a few weeks, BZDs should generally be withdrawn. In contrast, there is little clinical reason for the concomitant use of azapirone anxiolytics in the initial stages of treatment of depression. Instead, their use should be considered as a way to augment SSRI therapy.

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Competing interests: None declared.

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.