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Depression after Cyproheptadine: MAO Treatment

To the Editor:

Cyproheptadine has been reported to be effective in the treatment of anorgasmia induced by the administration of tricyclic antidepressants (Sovner 1984; Steele and Howell 1986), monoamine oxidase inhibitors (MAOIs) (DeCastro 1985), or fluoxetine (McCormick et al 1990). It has been postulated that cyproheptadine's efficacy in treating this symptom is caused by the blockade of serotonin receptors.

The administration of cyproheptadine for the treatment of antidepressant-induced sexual dysfunction has recently been associated with a recurrence of depressive symptomatology in a series of three patients treated with fluoxetine (Feder 1991), as well as with the reversal of therapeutic benefit in two patients with bulimia nervosa, also treated with fluoxetine (Goldboom and Kennedy 1991).

We report here a case of recurrence of depressive symptoms after administration of cyproheptadine in a patient who received full therapeutic benefit from treatment with phenelzine.

Mr. C. is a 37-year-old man who presented for diagnosis and treatment of chronic depressive symptomatology. Upon evaluation, he was severely depressed, with a blunted affect, as well as mood irritability, and a history of chronic impulsive self-injurious behavior, usually during the periods of more severe depression. A 17-item Hamilton Depression Rating Scale (HDRS) score of 38 was obtained on initial evaluation. Although no actual suicide attempts were reported, he described almost constant suicidal ideation, which he resisted by increasing his physical activity until exhaustion.

During the year prior to evaluation, he had been attending weekly outpatient psychotherapy. Concomitant with the psychotherapeutic intervention, several medication trials had been attempted, including desipramine, imipramine and nortriptyline, without relief of depressive symptoms. Trazodone was reported of limited benefit, with a mild reduction in depressive symptomatology, but severe sedation and orthostatic hypotension necessitated discontinuation of this agent. A trial of fluoxetine significantly reduced symptomatology after 6 weeks, but was also poorly tolerated due to severe agitation and anxiety.

In addition to a referral for cognitive-behavioral therapy, phenelzine was initiated, to a maximum dose of 75 mg per day. After 5 weeks on this regimen, his depressive symptomatology remitted (HDRS score = 4). Suicidal ideation and self-injurious behavior, as well as the demanding, impulsive, and irritable style noted in the initial presentation, were also markedly diminished.

Concomitant with the resolution of his depressive symptomatology, the patient reported difficulties in sexual activity, with delayed ejaculation that later progressed to anorgasmia. Treatment with cyproheptadine was initiated at a daily dose of 4 mg in an attempt to reduce his sexual dysfunction. Within 3 days of initiating this medication, nearly complete recurrence of depressive symptomatology was observed. No improvement of anorgasmia was reported

by the patient. Discontinuation of cyproheptadine promptly reduced his depressive symptoms (HDRS scores decreased from 22, 5 days after cessation of cyproheptadine, to 6, 12 days after discontinuing treatment). At the present time, the patient reports a moderate degree of delayed ejaculation, although he is no longer anorgasmic.

We report here an instance of recurrence of depressive symptomatology 3 days after the administration of cyproheptadine in a patient who had responded fully to treatment with the MAOI phenelzine. This phenomenon has been reported previously, in a similarly rapid time course (few hours to 4 days), in three patients responsive to the serotonin-reuptake blocker, fluoxetine (Feder 1991). Cyproheptadine may lead to a reversal of clinical benefit when administered for the treatment of antidepressant-induced anorgasmia. Close observation of patients treated with this regimen is suggested.

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Sodium Valproate Augmentation of Fluoxetine or Fluvoxamine Effects

To the Editor:

Fontaine et al (1991) described the addition of lithium to fluoxetine in the treatment of refractory depression. This is likely to be a major advance if lithium augments the action of fluoxetine without producing a potentially dangerous hyperserotonin syndrome (CSM 1989). For cases in whom there are contraindications to the use of lithium carbonate, the introduction of sodium valproate may be considered. The use of sodium valproate in the treatment of affective illness has been previously described (Emrich et al 1985), but it also appears to have an augmenting effect on the specific serotonin reuptake inhibitors fluoxetine and fluvoxamine. Two cases are described in some detail.

Case 1

A 57-year-old woman was referred with a 2-month history of panic attacks and depression with weight loss, sleep disturbance, and feelings of guilt. The general practitioner treated the woman with imipramine, which caused a rash, and benzodiazepines. Treatment with clomipramine, then with clomipramine and tryptophan, was not completely effective and she was unable to stop the diazepam because of continuing feelings of anxiety. There was also a severe tremor so these drugs were gradually withdrawn. A course of electroconvulsive therapy (ECT) helped temporarily but was followed by a rapid deterioration. Eighteen months after initial referral, fluoxetine was started and was increased gradually to 20 mg TID, and nifedipine, which might have been maintaining the depression, was discontinued. The patient was discharged on fluoxetine 60 mg mane only, but 3 weeks later reported severe depression, wakening with panic at 5:00 A.M., diurnal variation of mood, and poor appetite. Fluoxetine was reduced to 20 mg mane, sodium valproate was added, and 4 weeks later there was a marked improvement. Six weeks after the introduction of valproate the patient was completely free from pan-