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Letters to the editor

Withdrawal symptoms associated with paroxetine

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Paroxetine is a potent selective serotonin reuptake inhibitor (SSRI), with a half-life of approximately 1 day. Withdrawal syndromes have been reported to occur with other SSRIs, including fluoxetine, sertraline and fluvoxamine (Szabadi, 1992; Louie et al, 1994; Einbinder, 1995). More recently, paroxetine has been implicated in similar withdrawal syndromes. We wish to add a further three cases to those described previously (Barr et al, 1994; Debattista and Schatzberg, 1995; Pyke, 1995).

The patients involved were three physically healthy women (aged 25–42 years). Each had an uncomplicated diagnosis of major depression, and was treated as an outpatient. Paroxetine was commenced at a dose of 20 mg/day and was tolerated well by all patients. One patient's medication was increased to 40 mg/day after some time. Paroxetine was the only medication prescribed and was continued over a treatment period of 8–12 months. All patients responded well, with full remission of symptoms in two cases, and the other patient showing a partial response. In two cases, following agreement on discontinuation of treatment, paroxetine was reduced to 10 mg/day for 2 weeks, continued on alternate days for a further 2 weeks and then discontinued. Both of these patients reported symptoms of dizziness, vertigo, headache, tremor and a subjective sense of gait instability and 'jitteriness' on discontinuation of their medication. One patient left work abruptly because she felt so unwell. The symptoms persisted for approximately 5–7 days.

The third patient had been prescribed 40 mg/day and on reaching the end of her supply, found she had mislaid her prescription. She experienced similar withdrawal symptoms on omitting her medication. On recommencing paroxetine at 20 mg daily, her symptoms resolved. She currently remains on this dose.

Paroxetine is more antimuscarinic in effect than other drugs of the SSRI class. It has been suggested that withdrawal symptoms encountered may be mediated by cholinergic rebound (Pyke, 1995), similar to that occasionally seen in abrupt discontinuation of tricyclic antidepressants. Debattista and Schatzberg (1995) discount this suggestion, arguing that it is unlikely that low doses of a relatively weak antimuscarinic agent such as paroxetine could result in substantial cholinergic rebound. They suggest that it is more likely that these symptoms represent serotonin rebound phenomena. The similarity of some of the symptoms reported to those seen in the serotonin syndrome (eg, tremor, restlessness, etc) could support this hypothesis.

What is again striking from a clinical point of view, is the appearance of withdrawal symptoms despite gradual tapering of dose over a 4 week period. It is clear that some patients may require very gradual reduction of medication to low doses over a period of some weeks.

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Louie AK, Lannon RA, Ajari LJ. Withdrawal reactions after sertraline discontinuation. *Am J Psychiatry* 1994;151:450–1

Pyke RE. Paroxetine withdrawal syndrome. *Am J Psychiatry* 1995;152(1):149–50

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Possible delayed venlafaxine withdrawal reaction: two case reports

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Withdrawal reactions to the antidepressant venlafaxine have been described (Faraii and Lauer, 1996). We report two cases of possible venlafaxine withdrawal reaction with delayed onset of symptoms.

In the first case, Mr A, 42 years old, had a history of more than 10 years of dysthymia. He had incessant suicidal ideation with recurrent suicidal threats, but had never made any drastic suicidal attempt. Several antidepressant drugs had been tried with limited success. After 5 months on 150 mg venlafaxine daily, he was admitted to our hospital due to increased anxiety and feelings of unbearable loneliness. The dose of venlafaxine was decreased to 75 mg daily and discontinued 2 days later, when instead citalopram 10 mg daily was started. After a further 9 days of treatment, seemingly more stable, Mr A was on a planned leave to his home. There, he experienced the most intense anxiety attack he ever had, with overwhel-

ming suicidal impulses. With a knife, he cut off his left hand almost entirely, feeling no pain when cutting. After extensive surgical intervention, the hand was saved. He gradually returned to his habitual state.

In the second case, Mr B, 53 years old, had been treated with venlafaxine for 7 months because of a mixed anxious-depressive state. Most of the time, the dose was 150 mg daily. The effect was initially good, but declined when side effects such as impotence became disturbing. It was then decided to stop venlafaxine, and the dose was tapered from 150 mg daily to 0 during 2 weeks. During the tapering period, he had nausea and paresthesias. A week after the last dose of venlafaxine, he began experiencing dizziness which became rapidly worse. He had never suffered from this before. He could not perform his usual activities, and reported falling and hurting himself several times. His general practitioner could not find any physical cause. Cardiovascular function and laboratory tests were normal. His other medication, zolpidem 10 mg for insomnia, was unchanged all the time. After about 5 weeks of a somewhat fluctuating course, the dizziness gradually decreased, and after 7 weeks he felt normal.

Mr A's behaviour could perhaps be attributed to extremely increased anxiety caused by 10 mg citalopram, but we do not know of any such case reports. The symptoms of Mr B during the tapering period were similar to some of those described by Louie et al (1996). These authors also describe withdrawal symptoms of psychotic quality. The extreme anxiety of Mr A seemed to approach psychotic intensity.

Both patients experienced unusual and disturbing symptoms starting about 1 week after their last dose of venlafaxine. Obviously, we can not claim for certain that these late symptoms were indeed part of a withdrawal reaction. However, in both cases the time coincidence seems noteworthy. Our cases may alert clinicians to be aware of possible similar emergence of new symptoms after discontinuation of venlafaxine.

After the first version of this letter was submitted, we have noted some more cases of possible venlafaxine withdrawal reactions. Such cases may add emphasis to recommendations of careful tapering of venlafaxine (Faraii and Lauer, 1996; Louie et al, 1996).

Faraii A, Lauer TE. Possible venlafaxine withdrawal syndrome (letter). *Am J Psychiatry* 1996;153:576

Louie AK, Lannon RA, Kirsch MA, Thomas BL. Venlafaxine withdrawal reactions (letter). *Am J Psychiatry* 1996;153:1652

Client satisfaction in a clozapine clinic

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The use of clozapine is complicated because of the need for mandatory hematological monitoring which may affect patient compliance (Meltzer, 1992; Paton and Wolfson, 1995). Patients prescribed clozapine need to be informed about possible side effects, as well as the need for hematological monitoring. A clozapine clinic was set up in our hospital in order to fulfill these requirements and also to monitor clinical progress. The aims of this study were first to measure client satisfaction with the new service, and second to examine the relationship between client satisfaction and clinical outcome. A clozapine clinic was developed in our hospital in order to centralize the administration and hematological monitoring of clozapine, and to follow clinical progress, and detection of side effects. The clinic is staffed by a senior registrar and two members of nursing staff. Patients attend on an appointment basis. The mental state of each patient is assessed at each visit as well as their full blood count, blood pressure and weight. After each visit, clinic staff liaise with each patient's consultant regarding their clinical progress, which provides continuity of care for the patients. Patients return later in the week or 2 weeks later to collect their medication. Patients attending the clinic fulfilled DSM-III-R criteria for schizophrenia, which was confirmed as treatment refractory. Psychopathology was assessed initially, and after 6 months by means of the Brief Psychiatric Rating Scale (BPRS). Client satisfaction was also measured at 6 months, using the Client Satisfaction Questionnaire (CSQ-8) (Larsen et al, 1979). The CSQ-8 is a measure of general satisfaction with services and was developed to provide a brief, standard assessment procedure suitable for use in a wide variety of service settings. The CSQ was administered to patients by a psychiatrist (LH), who was not involved with the clozapine clinic. Data was analyzed using SPSS. There was a total of 28 patients (19 males and nine females) attending the clinic during the study period. All patients agreed to participate in the study. The age range of patients was 19–65 years with a mean of 32.8 (SD: 14). The mean initial BPRS score was 65 (SD: 14) and this decreased to a mean of 46 (SD: 12) following 6 months of clozapine therapy ($P \leq 0.0001$). The mean dose of clozapine used was 400 mg (SD: 150 mg). The mean client satisfaction score was 27.4 (SD: 3.5), indicating high levels of satisfaction. The decrease in mean BPRS scores at 6 months correlated inversely with the client satisfaction scores ($r = -0.32$, $P \leq 0.05$). The importance of recognizing the consumers' view when planning psychiatric services has been previously noted (Murphy, 1988). This study demonstrates that patient satisfaction levels in a specialized clozapine clinic are high. A significant reduction in BPRS scores followed treatment with clozapine. Client satisfaction as measured by the client satisfaction questionnaire, and symptom reduction measured by the BPRS are positively associated.

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