Correspondence

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Antidepressant withdrawal syndrome

Sir: Pacheco *et al* (1996) report five more cases of paroxetine withdrawal and highlight the general phenomenon of a withdrawal syndrome associated with selective serotonin reuptake inhibitors (SSRIs). A withdrawal syndrome has been reported with all major classes of antidepressants. Indeed, the incidence of the antidepressant withdrawal syndrome following discontinuation of imipramine has been estimated to be from 21% to as high as 100% (Lejoyeux *et al*, 1996) and with monoamine oxidase inhibitors to be 32% (Tyrer, 1984). A withdrawal syndrome has been reported with all of the SSRIs; however, to date, the majority of reports have concerned paroxetine (see Table 1).

Despite the greater incidence of reports concerning paroxetine it is, in the absence of comparative placebo-controlled trials, impossible to determine definitively which antidepressant is more likely to provoke this syndrome. However, in a recent study which incorporated a terminal placebo-controlled discontinuation phase, 34.5% of the group who had previously received paroxetine reported an adverse event on discontinuation compared with 13.5% of patients who had previously received placebo (Oehrberg *et al*, 1995). Paroxetine may be more likely to provoke antidepressant withdrawal because of a combination of a relatively short half-life and more potent anticholinergic effects. However, it remains important to be aware of this phenomenon with all antidepressants, and the gradual dosage reduction advocated by Pacheco *et al* may need to be widely applied to those antidepressants which have relatively short half-lives.

In view of the belief widely held by patients that antidepressants are addictive, it is important to reassure patients that these drugs do not produce tolerance and drug dependence like the benzodiazepines do.

Lejoyeux, M., Ades, J., Mourad, I., et al (1996) Antidepressant withdrawal syndrome. *CNS Drugs*, **5**, 278–292.

Oehrberg, S., Christiansen, P. E., Behnke, K., et al (1995) Paroxetine in the treatment of panic disorder. A randomised, double-blind, placebo-controlled study. *British Journal of Psychiatry*, **167**, 374–379.

Pacheco, L., Maio, P., Aragues, E., et al (1996) More cases of paroxetine withdrawal syndrome (letter). *British Journal of Psychiatry*, **169**, 384.

Tyrer, P. (1984) Clinical effects of abrupt withdrawal from tricyclic antidepressants and monoamine oxidase inhibitors after long term treatment. *Journal of Affective Disorders*, **6**, 1–7.

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Table 1 Plasma elimination half-lives, Committee on the Safety of Medicines (CSM) reports of withdrawal reactions, and withdrawal reactions per million prescriptions for serotonin specific reuptake inhibitors (SSRIs)[1]

SSRI	Half-life (active metabolite)	CSM reports of withdrawal reactions	Withdrawal reports/ million prescriptions[2]
Citalopram	36 hours	2	143.9
Fluoxetine	2–3 days (7–15 days)	36	13.3
Fluvoxamine	15 hours	12	21.02
Paroxetine	20 hours	679	237.78
Sertraline	26 hours (36 hours)	44	35.22

1. Information supplied by NHS Executive Northern and Yorkshire Regional Drug and Therapeutics Centre.
2. These figures are approximations based on fees and on a sample of 1 in 200 prescriptions (1989–1990). Data from 1991 onwards cover all prescriptions dispensed by community pharmacists, appliance contractors, dispensing doctors and prescriptions submitted by prescribing doctors for items personally administered.

Graded dosage calendar packs for psychiatric medication

Sir: I wish to urge the pharmaceutical industry to introduce graded dosage calendar packs for psychiatric medication requiring staged changes in dose, and for psychiatric drugs which are often prescribed in subtherapeutic doses by general practitioners and inexperienced junior doctors.

Suitable drugs would thus include tricyclic and certain other antidepressants, some newer antipsychotics, carbamazepine and reducing-dose chlordiazepoxide for alcohol detoxification. Accurate compliance would be easier for patients, particularly those with impaired concentration, memory or motivation. Effective and continued treatment would be encouraged and make unnecessary discontinuation less likely. The complexity and costs of prescription and dispensing would thus be minimised.

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Recent registration and referrals from general practitioners

Sir: We noted that an explicit reason for referral from general practitioners (GPs) to the out-patient clinic may be that the patient is newly registered or not well known to the GP; increasingly, we gained the impression that patients who had recently registered with the GP were over-represented among those referred to our outreach clinic.

Our general adult psychiatric out-patient clinic for patients aged between 20 and 64 years served North-East Edinburgh. The time between registration and the date of the referral letter was established in 50 consecutive non-urgent new referrals, that is, those who had never before been seen by the psychiatric service in Edinburgh (21 patients) or those who had been re-referred after a gap of six months or more (29 patients). The sample consisted of 28 women (mean age 36 years) and 22 men (mean age 36 years) who had been referred by 31 GPs from 15 general practices.

Nine patients (18%) had been registered for one month or less, four (8%) for between one and three months, five (10%) for 3–12 months and 32 (64%) for 12 months or more. The general practice medical records were not available at the time of referral for any of the patients who