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Venlafaxine and paroxetine in treatment-resistant depression

Sir: Poirier & Boyer (1999) suggest their comparative trial showed some evidence of superiority of venlafaxine over paroxetine in treatment-resistant depression. Examining the previous antidepressants used throws considerable doubt on this conclusion.

Sixty-six per cent of the venlafaxine group and 65% of the paroxetine group had previously been treated with a selective serotonin reuptake inhibitor (SSRI). As venlafaxine is the only serotonin–noradrenaline reuptake inhibitor (SNRI) available, none of the patients will have previously taken an SNRI. Most of the patients in the study have already found one SSRI ineffective: we should not be surprised that paroxetine tended to be less helpful.

Although numbers would be small it would be interesting to examine response rates for the patients who had not been treated with an SSRI previously. I suspect a difference may not be apparent in this group.

Despite reservations, I note that the study does throw some light on a common clinical problem. Psychiatrists generally look to drugs of a different class when one medication has been unhelpful. This study supports this practice, at least in the use of venlafaxine rather than another SSRI when treatment with a first SSRI has failed.

Poirier, M. F. & Boyer, P. (1999) Venlafaxine and paroxetine in treatment-resistant depression. Double-blind, randomised comparison. *British Journal of Psychiatry*, **175**, 12–16.

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Authors' reply: In response to Dr Gregson, while approximately two-thirds of patients in the venlafaxine and paroxetine groups had received an SSRI previously, 69% of the venlafaxine group and 73% of the paroxetine group had also received a tricyclic antidepressant (TCA) previously. No differences in response were noted between treatment groups among patients previously treated with a TCA. Although not strictly considered as SNRIs, the TCAs exhibit a range of activity on serotonin, noradrenaline, or combined serotonin–noradrenaline reuptake.

We agree with Dr Gregson that the results of our study support the use of an antidepressant of a different pharmacological class in patients who have failed to respond to an SSRI.

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Urinary detection of olanzapine – an aid to compliance

Sir: With increasing use of oral atypical antipsychotic drugs and the current absence of injectable preparations, it is to be expected that the use of depot medication will decline (Liberman, 1988). With this comes the increased importance of ensuring patient compliance with medication.

Previous analysis of serum olanzapine levels has primarily been concerned with the pharmacokinetics and clinical response to particular levels (Perry *et al*, 1997; Prieto *et al*, 1997; Berna *et al*, 1998), and these results are, as yet, not useful for everyday clinical practice.

We report that in a carefully selected group of patients, monitoring of the presence or absence in urine of a particular antipsychotic may help to confirm compliance with prescribed medication. This will provide greater confidence (in professionals, the patient and the community) that people are being treated for their mental disorder appropriately. It is important to state that at this stage we are looking at a qualitative test for presence or absence of the drug, not a quantitative test, which may have more relevance to efficacy and effectiveness of treatment. The use of urinary testing, rather than blood testing, should generally be more acceptable to patients. It should also help to ensure that there is no confusion between periodic urinary testing for the presence of olanzapine and the routine blood monitoring that is required for potentially dangerous drugs such as clozapine.

The method currently used to screen for olanzapine involves gas chromatography/mass spectrometry, and concentrations can be detected down to at least 100 µg/l using this method (I. Marsh, personal communication, 1999). Urine (5 ml) is extracted using a Toxilab extraction tube, Toxi-tube A (Microgen Products, Lake Forest, CA). The organic extract is evaporated to dryness under nitrogen and reconstituted in 100 µl butyl acetate. The extract is then analysed by gas chromatography/mass spectrometry using a Hewlett-Packard HP6890/5973 system. Extract (1 µl) is injected onto a HP-5MS capillary column (30 m × 0.25 mm × 0.25 µm) and analysed in scan mode using a temperature program starting at 85°C and ramping to 280°C at 10°C per minute with a final temperature hold of nine minutes. Olanzapine is then identified by retention time and mass spectral data.

The normal elimination half-life of 32.4 hours for olanzapine should allow variable or inconsistent compliance to be detected within a reasonable period of time. The absence of clinically active metabolites further strengthens the appropriateness of the test. A mass balance study showed that approximately 57% of radiolabelled olanzapine appeared in the urine, principally as metabolites (data provided by manufacturer).

We believe we may be the first to use clinically a form of testing of urine for the presence of olanzapine. The mode of monitoring has been to discuss the situation with patients when they are in remission, to ask whether they agree to submit to random testing at various points in their community care. Obviously, patient consent can be withdrawn at any time, which may suggest that compliance is poor. If the result is positive, we have discovered that it has strengthened the therapeutic alliance between patient and doctor. We believe this is particularly valuable in cases where patients have previously shown a high degree of dangerousness when in relapse. The limitation is, of course, that quantification is not undertaken, which would mean that even very low urine levels may be detected as positive. However, as an initial first step to aiding compliance, or perhaps what is more correctly called concordance with antipsychotic medication, we believe that this form of therapeutic drug monitoring (Olesen & Linnet, 1998) could present a major step