the columns

correspondence

Low dose typical antipsychotics – a brief evaluation

Sir: We were disturbed by David Taylor's article in the December 2000 issue of the *Psychiatric Bulletin* (vol. **24**, pp. 465–468). The paper comes across as a somewhat selective interpretation of current knowledge on this highly controversial and very topical issue. This paper clearly supports a particular point of view, giving selective weight to some studies and downplaying the importance of those that do not fit with the author's hypothesis. Some important recent studies on the issue have been completely omitted (e.g. Kapur *et al*, 2000) and the findings of the study by McEvoy *et al* (1991) are presented in such a way that the principal message of the paper is obscured. It is also regrettable that the author chooses not to consider the opinions of those leaders in the field with a different point of view (Kulkarni & Power, 1999) and seems to disregard the side-effects of the second-generation antipsychotics altogether.

We believe that, at this time, there is insufficient evidence to come to the kind of conclusions that the author has come to and that the paper is more of a statement of personal opinion than of scientific fact. There has never been a real dose-finding study with haloperidol (or most of the traditional antipsychotics) and no proper evaluation of low-dose traditional antipsychotics *v.* second-generation antipsychotics. Until properly designed studies are done, it would probably be wise not to come to premature conclusions. The harsh reality is that, for most patients in the world, medications like haloperidol are the only option. Finding the optimal dose of the so-called typical antipsychotics is something that should be pursued with vigour. This issue is far from resolved and a more balanced evaluation of the current state of knowledge would be welcome.

KAPUR, S., ZIPURSKY, R., JONES, C., *et al* (2000) Relationship between dopamine D(2) occupancy, clinical response, and side effects: a double-blind PET study of first-episode schizophrenia. *American Journal of Psychiatry*, **157**, 514–520.

KULKARNI, J. & POWER, P. (1999) Initial treatment of first-episode psychosis. In *The Recognition and Management of Early Psychosis* (eds P. D. McGorry & H. J. Jackson), pp. 184–205. Cambridge: Cambridge University Press.

McEVOY, J. P., HOGARTHY, G. E. & STEINGARD, S. (1991) Optimal dose of neuroleptic in acute schizophrenia. A controlled study of the neuroleptic threshold and higher haloperidol dose. *Archives of General Psychiatry*, **48**, 739–745.

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Author's reply: Oosthuizen and colleagues essentially repeat caveats outlined in the original article and make some more specific observations. The study by Kapur and co-workers (2000) appeared during the publication process of the article and so could not be included. This important trial of 22 patients with first-episode schizophrenia found that the likelihood of efficacy, hyperprolactinaemia and extrapyramidal symptoms increased significantly at striatal dopamine D_2 receptor occupancies by haloperidol of 65%, 72% and 78%, respectively. However, the difference in occupancy between efficacy and adverse effects was said to correspond to less than 0.5 mg/day haloperidol for a given patient. Thus, although this study appears to have discovered a 'therapeutic window' for haloperidol, it is unlikely to be clinically relevant, especially given the inter-individual variability in occupancy in patients given the same dose and the impracticality of receptor occupancy evaluation in clinical practice. It may also explain why the trials cited in the original article could not separate therapeutic and adverse effects.

In regard to the study by McEvoy *et al* (1991), it is difficult to see how the findings were misrepresented. Of 106 subjects given haloperidol 2 mg daily, 49 (46%) showed "an increase in cogwheel rigidity from baseline" at this dose and 15 of these required a dose decrease because of "excessive rigidity". Of 48 patients continued on the "neuroleptic threshold" dose, four were removed "due to severe EPSEs". The study did suggest that increasing to dosage above the neuroleptic threshold "did not lead to greater improvement in measures of psychosis but . . . regularly lead to significant increases in distressing extrapyramidal side effects". However, no justification is given for the numbers of subjects recruited, so equivalence in efficacy certainly cannot be assumed. Overall, this study demonstrated that extrapyramidal symptoms (albeit largely mild ones) were induced at very low doses of haloperidol; doses that were effective but that were by no means proven to be optimally so. Moreover, extrapyramidal side-effects and efficacy seemed again to be inexorably linked.

As your correspondents point out, this issue is far from resolved. However, the burden of proof surely now lies with those who support the continued widespread use of typical antipsychotics. If data relating to atypical drugs are to be scrutinised and criticised from every angle, then the sparse data supporting the existence of a 'therapeutic window' for typical antipsychotics are inevitably liable to potent censure. In this respect, it is noteworthy that Oosthuizen and colleagues present no cogent data to counter the conclusions of the original article but resort instead to vague and unsubstantiated accusations of bias.

Late awareness of anaemia in a patient receiving clozapine

Sir: Having read the letter by Ali and Adeyemo (*Psychiatric Bulletin*, November 2000, **24**, 432), showing the hazards of Clozanil Patient Monitoring Service (CPMS) full blood count monitoring by paying too much attention to the 'green' status, I would like to point out another clinically relevant and related pitfall.

One of my patients with chronic schizophrenia, aged 61, has been on clozapine for 3 years. His blood tests were all passed as green. One day we spotted a haemoglobin of 8.5 g on the CPMS form. His normal value had been 13 g. There had been a steady fall over 6 months that nobody had detected as the patient was asymptomatic and the medical staff were focusing on the prominently labelled green status.

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