



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., HOGARTH, 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 D₂ 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 Clozanyl 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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The forms themselves did later mention that the haemoglobin was falling, but the warning was condensed on the left side below the blood parameters at the bottom of the form. Asterisks were not used. By contrast, however, the status 'green' was in block capitals in open space on the opposite side of the page, drawing the reader's eye to it instantly. This patient has subsequently undergone investigation and treatment for anaemia.

This is another example of a false sense of security gained by relying upon CPMS monthly blood counts. Had they been routine local blood tests then medical staff would have, in my view, assessed each form more thoroughly, paying attention to more than one parameter – as opposed to the solitary concern about a fall in white cell count. The CPMS form needs to have a different layout so as to allow for other abnormalities to be drawn to the doctors' attention sooner.

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Driving in Somerset

Sir: I agree that to deprive older people of transport could seriously inconvenience them (*Psychiatric Bulletin*, December 2000, **24**, 469), however, the new General Medical Council guidelines – *Confidentiality; Protecting and Providing Information* (2000) specifically states that "The Agency [DVLA] needs to know when driving licence holders have a condition which may now, or in the future, affect their safety as a driver. . . . If patients refuse to accept the diagnosis or the effect of the condition on their ability to drive, you can suggest that the patients seek a second opinion, and make appropriate arrangements for the patients to do so. You should advise patients not to drive until the second opinion has been obtained."

No, I do not want to alienate older people with mild cognitive impairment, but I do feel that we have a duty to the public in assessing and monitoring these people. They can, after all, have a driving assessment arranged through regional test centres if they feel they want to appeal against advice not to drive.

GENERAL MEDICAL COUNCIL (2000)
Confidentiality; Protecting and Providing Information. London: GMC.

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Urinary detection of olanzapine and its limitations

Sir: Sander (*Psychiatric Bulletin*, January 2001, **25**, 33) is correct in pointing out some of the limitations of urinary detection of olanzapine as a proxy for compliance, as previously described by myself (Coates, 1999, 2000). Currently, only a negative result shows non-compliance, whereas a positive result is open to various interpretations. I am presently studying two ways of potentially addressing these shortcomings, which may prove helpful.

First, I am investigating the quantification of the urinary levels of olanzapine, rather than just using a qualitative test. This should provide more of an indication of the actual compliance when levels are ascertained. Second, the measurement of urinary metabolites, either quantitatively or qualitatively, may lead to a more sophisticated approach in the future. In particular, 10-N-glucuronide is the most abundant metabolite but 4'-N-desmethylolanzapine is correlated to clearance (Callaghan *et al*, 1999) and this may give a better indication of a person's recent compliance.

Currently, however, non-detection of urinary olanzapine remains the best objective test of non-compliance and with these further developments it may prove to be even more valuable in clinical practice.

CALLAGHAN, J.T., BERGSTROM, R. F., PTAK, L. R., *et al* (1999) Olanzapine. Pharmacokinetic and pharmacodynamic profile. *Clinical Pharmacokinetics*, **37**, 177–193.

COATES, J.W. (1999) Urinary detection of olanzapine – an aid to compliance. *British Journal of Psychiatry*, **175**, 591–592.

— (2000) Urinary detection of olanzapine – an aid to compliance confirmed. *Psychiatric Bulletin*, **24**, 316.

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National Service Framework

Sir: As Deahl *et al* (*Psychiatric Bulletin*, June 2000, **24**, 207–210) recently pointed out, whether those considering committing suicide will use NHS Direct, and therefore lower the number of suicides and meet a standard of the *National Service Framework (NSF) for Mental Health* (Department of Health, 1999), is uncertain. How NHS Direct will be used by people for mental health related problems of any nature is also uncertain, even though there is an emphasis on its use for this client group in the NSF.

In order to work towards the implementation of the NSF we carried out a small pilot study in one NHS Direct site to learn more about how people with mental health related problems were using the service. For the period of 1 week we collected data on all mental health related calls to the site. This was done by asking nurses to complete data forms for every mental health call, and by looking at the presenting complaints of all other calls to pick up any that were obviously mental health related. We identified 33 mental health related calls during the week, which accounted for 2.6% of the workload. Given that nurse advisers did not complete a data collection form for every mental health call, and that the data on presenting complaints were unreliable, we were able to estimate that mental health is more likely to account for approximately 4% of NHS Direct's workload.

The 33 calls related to 24 callers, the majority of whom (67%) were calling on their own behalf. Of these 24, 37.5% presented with more than one problem, some of which were complex and time consuming for nurse advisers to deal with. Just over one-third of the calls were prioritised as either immediate or urgent, the same figure not urgent, and the majority (66%) were referred to another service. This differed to all calls received during the study period where 57% were prioritised as not urgent and only 43% were referred onto another service.

The study demonstrated that NHS Direct is being used by people for their mental health problems and already performing one of the tasks in the NSF of enabling this client to contact another service. How well this task is being undertaken is something that needs to be monitored. Work is currently underway to evaluate the £1 million investment the Government has given to ensuring NHS Direct can meet this task, and results will be available shortly.

DEPARTMENT OF HEALTH (1999) *National Service Framework for Mental Health. Modern Standards and Service Models*. London: Department of Health.

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Personal psychotherapy, training and psychodrama

Sir: I read with interest Chris Mace's views on the relevance of personal psychotherapy to training (*Psychiatric Bulletin*, January 2001, **25**, 3–4). As a specialist registrar in general adult psychiatry, I have recently started psychodrama training as my special interest. When Moreno, the founder of psychodrama and philosophical antagonist