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LETTERS TO THE EDITOR

Letter to the Editor

Sirs.

Clozapine-induced neuroleptic malignant syndrome not recurring with olanzapine, a structurally and pharmacologically similar antipsychotic

A patient with schizophrenia had neuroleptic malignant syndrome (NMS) with clozapine. Retreatment with olanzapine, which has a structure and a pharmacological profile of activity similar to those of clozapine (Owens and Simpson, 1998), was not followed by recurrence of NMS. A MEDLINE search found only the report of one patient with a possible clozapine-induced NMS retreated with olanzapine without recurrence of NMS (Ahmed *et al*., 1998).

A 32-year-old man, with schizophrenia for 15 years, had been taking clozapine, 600 mg/day, for 5 years. Psychotic symptoms had improved. He had been clinically stable for 3 years, when there was the rapid onset of fever (39.5°C), muscle pains, rigidity, acute confusional state, tachycardia, labile blood pressure, elevated creatine phosphokinase (CPK) (3473 U/L), diaphoresis, granulocytosis (92.3 per cent), and lymphocytopenia (4.8 per cent). These symptoms were found not to be due to another substance or a neurological or other general medical condition following clinical and laboratory investigations. Fever did not improve with antibiotics. Clozapine was discontinued, and he was treated with dantrolene for 1 week. NMS disappeared in 10 days. Due to the worsening of psychotic symptoms following clozapine discontinuation, olanzapine, 20 mg/day, was started 10 days later. During the following 2 months NMS did not recur.

The clinical picture met DSM-IV (American Psychiatric Association, 1994) and other (Gurrera, 1999) criteria for NMS. The similarities of the structure and the pharmacological profile of activity between clozapine and olanzapine (Owens and Simpson, 1998) should have induced the treating psychiatrists to avoid olanzapine to treat psychosis. However, NMS did not recur with olanzapine, suggesting that olanzapine may be safe after clozapine-induced NMS, despite these similarities. While NMS with clozapine has been reported (Sachdev *et al*., 1995), only one report of olanzapine-induced NMS, following the treatment of a psychotic patient with a recent NMS caused by haloperidol and levomepromazine (Burkhard *et al*., 1999), was found on MEDLINE. Only the report of one patient, with a possible clozapine-induced NMS retreated with olanzapine without recurrence of NMS (Ahmed *et al*., 1998), was found on MEDLINE. The treatment of psychosis following NMS has always been a problem for fear of inducing a NMS recurrence with another antipsychotic. The reported 30 per cent risk of recurrence on re-exposure to neuroleptics may be minimized by delaying rechallenge by 2 weeks post NMS. This is achieved by using an antipsychotic of an alternative class, or by switching to an atypical antipsychotic (Meltzer and Fatemi, 1998). The present report suggests that olanzapine may be safe alternative after clozapine-induce NMS for the treatment of psychotic symptoms.

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REFERENCES

Ahmed, S., Chengappa, K. N. R., Rama Naidu, V., Baker, R. W., Parepally, H. and Schooler, N. R. (1998). Clozapine withdrawal-emergent dystonias and dyskinesias: a case series. *Journal of Clinical Psychiatry*, **59**, 472–477.

American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition. American Psychiatric Association, Washington, DC.

Burkhard, P. R., Vingerhoets, F. J. G., Alberque, C. and Landis, T. (1999). Olanzapine-induced neuroleptic malignant syndrome. *Archives of General Psychiatry*, **56**, 101–102.

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Gurrera, R. J. (1999). Sympathoadrenal hyperactivity and the etiology of neuroleptic malignant syndrome. *American Journal of Psychiatry*, **156**, 169–180.

Meltzer, H. Y. and Fatemi, S. H. (1998). Treatment of schizophrenia. In *The American Psychiatric Press Textbook of Psychopharmacology*, 2nd edition, Schatzberg, A. F. and Nemeroff, C. B. (Eds), American Psychiatric Press, Washington, DC, pp. 747–774.

Owens, M. J. and Simpson, G. M. (1998). Atypical antipsychotics. In *The American Psychiatric Press Textbook of Psychopharmacology*, 2nd edition, Schatzberg, A. F. and Nemeroff, C. B. (Eds), American Psychiatric Press, Washington, DC, pp. 323–348.

Sachdev, P., Kruk, J., Kneebone, M. and Kissane, D. (1995). Clozapine-induced neuroleptic malignant syndrome: review and report of new cases. *Journal of Clinical Psychopharmacology*, **15**, 365–371.

Sirs,

Ginkgo biloba in the treatment of sexual dysfunction due to antidepressant drugs

In depression, impairment of libido, other sexual functions and, in the male erection and ejaculation, are integral components of the illness. Even when the depression responds to treatment with antidepressant drugs (ADs) sexual function often does not improve, being perpetuated by the majority of ADs themselves. This may occur in as many as 67 per cent of patients (Segraves, 1998).

Ginkgo biloba is a herbal extract of the 'Maidenhair tree' and is used to enhance memory, particularly in the elderly (Le Bars *et al.*, 1997). Following reports from the USA that AD-induced sexual problems in individual patients had responded to *Ginkgo biloba* (Cohen and Bartlik, 1998), a small prospective pilot study was initiated to treat 14 patients suffering from this problem, for six weeks with a dose of 240 mg daily. Sexual dysfunction before and after treatment was measured by the sexual stress questionnaire from the Wheatley Stress Profile (WSP), a validated instrument that measures: loss of libido, stress therefrom, effects on sexual relationship, physical problems, guilt, masturbation and in females dysparunia and fear of pregnancy (Wheatley, 1990). These extra items for females were included, since males rarely complain of either. Sleep was recorded by the Sleep Questionnaire of the WSP which measures: sleep onset, times waking, early morning waking, duration of sleep and waking mood.

Two patients dropped out after the first assessment, leaving 12 to continue the trial. Unusually, males predominated over females in the proportion of 2 to 1, with a mean age of 42.4 years (range 27–66, CI 35.5–49.3). Specific serotonin re-uptake inhibitors (SSRIs) were the ADs mainly in use (67 per cent). Respectively these were: fluoxetine 20 mg for 3, 4, 30, 76 weeks; paroxetine 40 mg for 4, 4, 12, 24 weeks; hypericum 500 mg for 52 weeks and 1000 mg for 74 weeks; amitriptyline 300 mg for 8 weeks and clomipramine 100 mg for 12 weeks. All patients complained of severe or complete loss of libido, whilst in males the physical problems were: inability to achieve or maintain an erection (7), premature ejaculation (1), failure or delay in ejaculation (2). Of the females: one had no physical problems, but the other three complained of anorgasmia. Apart from antidepressant medication, no other drugs were taken during the trial. Assessments were made at baseline and after 3 and 6 weeks of treatment respectively. The results are shown for the main measures of: Hamilton Anxiety (max = 56) and Depression (max = 52) Scales, Sex (max = 24) and Sleep (max = 10) in Figure 1.

The paired *t*-test was used to measure significance over time and there was improvement on all these items, but this was only statistically significant for anxiety between weeks 0 and 6 ($p < 0.05$, CI 0.4–5.6) and the sex total for weeks 0–3 ($p < 0.01$, CI 0.1–4.8) and weeks 0–6 ($p < 0.01$,

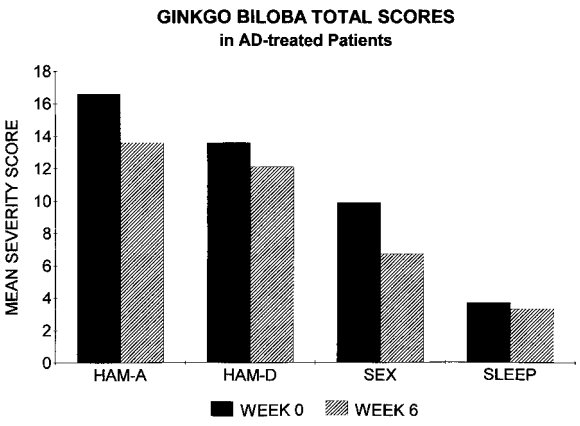

Figure 1.