

Clozapine for the treatment of levodopa-induced psychosis and dyskinesia in Parkinson's disease

Sir – Jalenques and Coudert¹ present a very interesting case study and review of the literature on the use of clozapine in the treatment of levodopa-induced psychosis and dyskinesia in Parkinson's disease.

We were, however, surprised by the omission of any explicit reference to the risk of agranulocytosis with clozapine. This rare but potentially fatal side effect is of considerable interest to clinicians. A fatality rate of up to one in 300 has been estimated prior to the introduction of routine blood monitoring.² Because of this serious unwanted effect, clozapine is indicated only in patients unresponsive to, or intolerant of, conventional antipsychotic drugs.³

It is the clinical experience of one of us that such patients can often be managed with conventional antipsychotic drugs, which have the additional advantage of being considerably cheaper than clozapine.

Other antipsychotic drugs are available for the treatment of psychosis in Parkinson's disease, such as sulpiride, which have less pronounced extrapyramidal side-effects. It is our view that such drugs should be used before resorting to clozapine.

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Authors' reply

Sir – Hughes, Mindham and Ross emphasise the guidelines concerning prescriptions of clozapine which is indicated only in patients unresponsive to, or intolerant of, conventional antipsychotic drugs. Obviously, if patients can be managed with conventional neuroleptics, the use of clozapine should not be considered.

We are, however, surprised by the incidence of agranulocytosis these authors underline. Recent data by Alvir and Lieberman¹ should be mentioned: the Clozaril Patient Management System reported two patients who died after developing agranulocytosis in the cohort of 11,555 patients who received clozapine in the United States from February 1990 to April 1991. The haematologic monitoring system, both necessary and effective, induces greater effort and costs than conventional neuroleptics. But an exact evaluation needs to take into account a global cost including duration of hospitalisation, social cost, etc.²

The management of levodopa psychoses generally requires first a reduction in parkinsonian medications or a 'drug holiday'. Electroconvulsive therapy should also be considered.

An antipsychotic drug should be only added in patients whose psychosis fails to respond to, or who cannot tolerate, a reduction in medication. Such an addition makes sense only if the psychiatric benefits outweigh the adverse effects.

Even low-potency neuroleptics with mild extra-pyramidal adverse effect profiles have been implicated in inducing parkinsonism and even relatively low doses of low-potency neuroleptics have induced marked exacerbation of parkinsonism in idiopathic Parkinson's disease (PD).³ In particular, comparative studies of sulpiride in psychiatric patients reported similar extrapyramidal effects when compared to other neuroleptics.^{4,6}

The work of Alberts *et al*⁷ concerning the adverse effects in 65 clinical trials involving 2,851 patients receiving sulpiride, reported neurological events in 366 patients, among them rigidity, akathisia, acute dystonia and generalised dyskinesia. Thus, it would be of interest to perform and publish comparative studies on sulpiride and other neuroleptics in the treatment of psychosis in PD in order to clarify the clinical experience.

Lastly, while we agree that clozapine must only be used in limited situations, our view is that the lack of acute blockade of striatal D2 receptors and the failure of chronic clozapine treatment to suppress striatal dopamine release may account for the lack of worsening effect on PD; and that a specific benefit of clozapine on parkinsonism might be due to an effect on the serotonergic system leading to a release of striatal dopamine. In some particular cases, such properties can be of great benefit for the treatment of psychosis in patients with PD.

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The prediction of suicide and the law on abortion

Sir – In his editorial *The prediction of suicide and the law on abortion*,¹ Kelleher concludes that the research evidence (quoted by him) indicates that medicine and psychology does not have the ability to predict suicide, even with a

moderate degree of accuracy. This sentence is dangerously misleading and fundamentally untrue. The clear inference to be drawn from the editorial is that the Supreme Court in the 'X' case was wrong in concluding that a real and substantial risk existed that Ms 'X' might commit suicide. This conclusion is derived from actuarial and epidemiological type evidence based on surveys of large populations of patients extrapolated to suicide many years later. This is like reviewing the characteristics of the 20,000 two year old race horses presently in training in these islands and attempting to predict those 15 or 20 or so who may eventually qualify for the Derby and may win the race.

The position of the court in the case of Ms 'X' was rather different. Here was a 14 year old raped girl who had been seen several times by an experienced clinical psychologist and who remained adamant in her expressed desire to commit suicide rather than continue with her pregnancy. Such a situation is comparable to the one the punters face when they attend Ascot and place their bets on one of the handful of race horses competing in the Derby.

Consider the situation of the clinical cardiologist. The prediction of imminent death from myocardial infarction may be extremely powerful when made in the context of the Intensive Care Unit but weakens progressively throughout patient departments to general practice. Yet nobody has yet suggested that cardiologists cannot predict heart attacks. Nor would it be advisable that an aged patient with marked ECG changes and three previous heart attacks to engage in marathon running. The fundamental flaw in D. Kelleher's thinking is to extrapolate the prediction of a rare event (suicide) from patient population surveys on the one hand, to prediction by psychiatrists dealing with actively suicidal patients in the context of intensive psychiatric inpatient care.

In the present political atmosphere, Dr Kelleher's conclusions are almost certain to be taken up and quoted by those whose sincerely held beliefs are strongly opposed to the introduction of liberal legislation on the matter. This writer

firmly believes that practising psychiatrists are in fact remarkably efficient in the prediction of suicide, amongst high risk cases. There is a remarkable paucity of reliable research to support this view it must be admitted, but such research is at present being initiated at Galway.

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Reference

1. MJ Kelleher. The prediction of suicide and the law on abortion. *Ir J Psychol Med* 1994; 2: 55-6.

Author's reply

Sir – As a clinician, I welcome Prof Fahy's determination to identify factors, which if universally applied will predict the event of suicide. If he is successful, then he will have achieved something which, to date medicine and clinical psychology has been unable to do.^{1,2,3}

Prof Fahy also confuses the difference between a court judgment and a medical opinion. The court's decision is, in law, true and, therefore, neither he nor I can refer to it as being wrong.

The point of the editorial was simple. At this moment in time, we do not have the ability to predict suicide with a modicum of certainty. Therefore, if the law, on termination of pregnancy within the Republic of Ireland, is to be changed, then, estimation of risk of suicide by clinicians would be an unreliable criterion for allowing such termination.

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Erratum

The paper entitled *A descriptive study of adjustment disorder diagnoses in general hospital* (*Ir J Psychol Med* 1994; 11: 153-7), by Paul Foster and Thomas Oxman contained two errors.

1. The first sentence of the final paragraph on page 155 should read: "With respect to the outcome of the condition, follow up treatment was recommended for 40% of these patients". The figure given in this sentence was erroneously printed as 4%.

2. In table 2 on page 154 the DSM subtype of adjustment disorder for anxious mood should read as 309.24 and not 309.9 as was printed.

Our apologies to the authors.

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