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The study

The descriptive study took place in the Wandsworth Assertive Community Treatment Team, which has a case-load of 105 patients with a severe psychotic illness who have been difficult to engage with treatment. The majority (75) have a diagnosis of paranoid schizophrenia and many of them have been non- or partially-responsive to antipsychotic medication.

The study group comprised 26 patients with a diagnosis of schizophrenia who were treatment refractory (prior unsuccessful treatment despite the use of at least two antipsychotics prescribed at adequate dose for an adequate duration) or treatment intolerant (severe or untreatable neurological or other adverse reactions such as tardive dyskinesia), and who were initiated on clozapine in the course of clinical practice. Those refusing to come into hospital to start clozapine were started at home. Hospital-based initiation of clozapine is widely practised so our study concentrated on those patients starting at home, describing the process and any adverse events experienced.

A locally-agreed policy has been developed regarding commencement of clozapine at home. A full medical history is taken and full physical examination carried out, including weight, pulse, temperature and blood pressure. In particular, any history or evidence of cardiovascular problems, epilepsy or haematological disorders is sought. The initial full blood count is taken. Once the CPMS agrees that clozapine can be started, treatment begins on a Monday. The patient is given 12.5 mg of clozapine. A member of the team stays with the patient in his/her own home for at least the first 6 hours and the pulse, temperature and blood pressure are taken every hour. The team senior house officer (SHO) visits on this first day.

For the rest of the week, the patient is visited at home each day and given clozapine, which is increased by 12.5 mg every day. Physical observations are taken daily. The SHO visits on day 3 or 4. A member of the team (most of whom are trained in venesection) takes a second blood test at home on the third day.

The clozapine dose is gradually increased depending on clinical response and side-effects, aiming for a minimum dose of 300 mg, although some patients are maintained on lower doses. During the first week the clozapine is given in one dose, although it may be divided at a later date depending on the adverse effects experienced by the patient and his/her preference for the type of dosing regime.

Results

Of the 26 patients started on clozapine during the study, 14 began treatment without requiring a hospital admission. Two of these were 'restarts', having been on clozapine at some time in the past. One who was eligible for home initiation did not actually start clozapine for some time because his baseline blood pressure was found to be extremely low (see below). Clozapine treatment was started by 12 patients while in hospital. All of this group

were considered too unwell to be in the community at the time. Of those actually started on clozapine at home, only one attempt was abandoned, because the patient went on to refuse daily access to her house.

Of the 14 patients started at home, 7 complained of no problems at all. Five patients complained of sedation and one had nausea and vomiting. Four complained of dizziness; of these, two had blood pressure recordings within normal limits, but two had low blood pressures on the first day (both 90/50). One of these patients was taken to the ward for 6 hours. Side-effects or adverse events did not cause the start of clozapine treatment to be abandoned for any patients; 10 of the 13 patients are still on clozapine (the others having become non-compliant at a later date).

Case vignettes

Case 1

A 62-year-old woman, compliant with oral antipsychotic medication, shows only minimal response and suffers constant auditory hallucinations and paranoid delusions. As a result she rarely leaves the house and eats very little (both behaviours are secondary to delusional beliefs). She refuses to come into hospital but has been willing to start clozapine. At the first attempt to start clozapine at home treatment was not started because her baseline blood pressure was found to be 60/40. She has been thoroughly investigated by the physicians. They feel that her hypotension is due to poor diet and she has been given a high-salt diet. Clozapine is being started very gradually, at 6.25 mg increments over time. She is now on 100 mg a day, her blood pressure is within normal limits, and she has experienced no hallucinations for 6 weeks.

Case 2

A 45-year-old woman lives in a low-support hostel. She has negative symptoms, severe functional deficit and social withdrawal. The usual policy for initiating clozapine at home was enhanced by the availability of hostel staff in the evening and at night-time. She was successfully established on clozapine with no adverse side-effects and is now returning to the care of the local community mental health team.

Case 3

A 40-year-old man has a mild learning disability and paranoid schizophrenia. Owing to his learning disability, a long time was spent preparing him for the introduction of clozapine, with information being regularly repeated and reinforced. Clozapine was started successfully in the community; he experienced some initial nausea and dizziness but this abated by the second week. He is maintained in the community on a dose of 600 mg. Although he continues to express delusional beliefs, he no longer displays the disturbed behaviour seen prior to starting treatment.



Discussion

Fourteen patients are now established on clozapine, having started it at home. Our team already had a culture of assertive medication management with many patients being given their medication daily in their own homes; our clozapine policy has evolved within this culture. The criteria for starting clozapine are within the UK prescribing restrictions (Novartis, 2001), but do not follow the more stringent Kane criteria (Kane *et al*, 1998). It is felt that the Kane criteria were appropriate when demonstrating the efficacy of clozapine in a randomised controlled trial, but in practice they are too restrictive and delay access to the drug despite concerns that such a delay may reduce eventual effectiveness (Kerwin & Lofts, 1993). The approach involves a great deal of coordination and input from key workers and the junior doctor on the team. Using a team approach spreads the burden, especially on the first day, making the operation more practical.

To some extent this protocol provides a framework for positive risk-taking as the CPMS recommends hospitalisation to start clozapine and the team's responsible medical officer (RMO) is required to take responsibility for any adverse events. We feel that the potential benefits to the patient justify this risk. We have experienced no serious problems thus far. Some patients have experienced nausea, dizziness and drowsiness, but these have not prevented them being managed at home. If two days of clozapine are missed, the CPMS recommends that administration be restarted from a dose of 12.5 mg. This means that regular daily contact needs to be established and maintained. Clearly this can be a challenge with some of this patient group and for one it meant the attempt had to be abandoned.

We believe that for assertive outreach services, working long-term with very disabled patients with psychosis, one indicator of good practice is the number of patients who are maintained on clozapine or who have been tried on it in the past. This reflects a commitment to providing evidence-based care. We have now established a quarter of our case-load on clozapine, half of whom started without requiring admission to hospital. A further two patients have since come to the team, having been started on clozapine at the local day hospital.

Obviously, there are a substantial number of patients for whom community initiation would be unsuitable. Although we would always review each case on its merits we would be unlikely, for example, to try community initiation in someone with a history of epilepsy (similar to a history of epilepsy or withdrawal seizures being usual exclusion criteria for community alcohol detoxification).

Overall, the experience has been a positive one for the team. It is certainly labour-intensive, but we feel that

it is worth it in the long-run as we have found that once patients are established on clozapine many go on to show substantial improvement, thus requiring less clinical input. We recognise that our policy requires a level of time commitment that a generic community mental health team could not provide. However, our policy has been amended for use in the day hospital and several teams are starting clozapine in this way.

Ultimately a clinical decision has to be made, weighing up the potential risks of this policy against its benefits – especially as the RMO needs to take responsibility. We feel that in a select patient group the risk is justified and that by commencing clozapine in this way we have given our patients a chance to receive a treatment of proven benefit.

Declaration of interest

M.F. spoke at events organised by Novartis Pharmaceuticals on two occasions during 2000 and 2001, for which he received reimbursement of expenses and a fee of £200 for each event. He has facilitated a workshop on clozapine in assertive outreach and community initiation at two Clozaril Nurse Summits.

References

- AITCHISON, K. J. & KERWIN, R. W. (1997) Cost-effectiveness of clozapine. A UK clinic-based study. *British Journal of Psychiatry*, **171**, 125–130.
- GRACE, J., BELLUS, S. B., RAULIN, M. L., *et al* (1996) Long-term impact of clozapine and psychosocial treatment on psychiatric symptoms and cognitive functioning. *Psychiatric Services*, **47**, 41–45.
- JOHNSON, C. G., LITRELL, R. N. & MACGILL, A. H. (1994) Starting patients on clozapine in a partial hospitalisation programme. *Hospital and Community Psychiatry*, **45**, 264–268.
- KANE, J., HONINGFIELD, G., SINGER, J., *et al* (1988) Clozapine for the treatment-resistant schizophrenic: a double-blind comparison with chlorpromazine. *Archives of General Psychiatry*, **45**, 789–796.
- KERWIN, R. & LOFTS, F. (1993) Clozapine in the management of schizophrenia. All schizophrenic patients would benefit. *BMJ*, **307**, 199–200.
- NOVARTIS (2001) *Clozaril®. Summary of Product Characteristics*. Camberley: Novartis Pharmaceuticals UK.
- PERCUDANI, M., FATTORE, G., GALLETTA, J., *et al* (1999) Health care costs of therapy – refractory schizophrenic patients treated with clozapine: a study in a community psychiatric service in Italy. *Acta Psychiatrica Scandinavica*, **99**, 274–280.
- ROSENHECK, R., CRAMER, J., XU, W., *et al* (1997) A comparison of clozapine and haloperidol in hospitalised outpatients with refractory schizophrenia. *New England Journal of Medicine*, **337**, 809–815.
- STEIN, L. & TEST, M. A. (1980) Alternative to mental hospital treatment. (1) Conceptual model, treatment program, and clinical evaluation. *Archives of General Psychiatry*, **37**, 392–397.

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