Establishing cost-effectiveness of atypical neuroleptics†

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Aitchison & Kerwin's (1997) report, of a small-sample 'before and after' cohort study of clozapine therapy, provides a useful approach to handling costs when comparing treatments. It takes into account both direct and indirect costs and savings. While research reports that compare the benefits of treatments without any reference to cost are still common, Aitchison & Kerwin's study demonstrates that it is not difficult to obtain costing data. Clinical decisions are often made in ignorance of the relative costs of different treatment options, yet with the gap between needs and resources getting ever wider, it can be argued that it is unethical to compare the benefits of treatments without also comparing their costs. Is it fair to promote or to prescribe a treatment with marginally greater efficacy but much higher costs than another treatment? To do so is to forego the opportunity to give benefit to another patient in need, or indeed to give greater benefit to the same patient in other ways.

Aitchison & Kerwin (1997) attempt to assess the cost-effectiveness of clozapine in a cohort of treatment-refractory schizophrenics over three years. Does this study increase our knowledge of the cost-effectiveness of clozapine? The sample is small, and data collected retrospectively are compared with data collected prospectively. Neither subjects nor observers were blind to the treatment regimes. We will argue, therefore, that the study results are not much better than anecdotal.

There is already available much better evidence from at least 14 short-term double-blind comparisons that clozapine is more effective than standard neuroleptics in treatment-refractory schizophrenia. But the margin of difference is not all that great, with only 13% of patients better off in terms of the mean response rate from all these studies (Baldessarini, 1991). Also, we need to know how long any benefits are sustained in the treatment of chronic and severe illness. Unfortunately, existing larger, prospective studies of the cost-effectiveness of the new neuroleptics have had a tendency to look only at the immediate effect on symptoms and at comparative occurrences (not the cost) of side-effects.

While small-sample, open studies may be justified as pointers in the early days of availability of new drugs like clozapine and risperidone, they are hardly worth repeating years later, lest they suggest that the growing use of these drugs is based on good evidence. The evidence that is required must come from large-sample, randomised, controlled trials over a long period. The randomised controlled trial is the gold standard, and it must compare costs as well as benefits over many months (if not years) for treatment-resistant or drug-intolerant patients with schizophrenia. Multi-centre collaboration may be required to produce sufficiently large samples.

Such evidence is essential in view of the degree and duration of suffering caused by treatment-refractory schizophrenia, and the costs of clozapine and risperidone compared with those of the typical neuroleptics (clozapine £2000 per annum including laboratory monitoring, and risperidone £1500 per annum at the proposed optimum dose of 6 mg/day). It may turn out that these significant extra costs of drug treatment are justified in extra benefits and lower costs elsewhere, if these new treatments result in shorter hospital stays with lower dependency, fewer side-effects (which have associated costs), better patient compliance, improved functioning in the community and improved quality of life (which can also be costed).

Those who argue that naturalistic studies, such as that of Aitchison & Kerwin (1997), are enough and that prolonged randomised controlled trials are not ethically justified should consider the counter-argument. It is unethical not to carry out such studies when the relative risks, benefits and costs of a long-term treatment for a serious condition are not established. Hippocrates would turn in his grave at the idea that doctors need only intend to do good, and to do no harm without studiously seeking to verify. And he would probably spin even faster at the idea that doctors should exhaust effort and resources in relieving the suffering of one patient without seeking to conserve time and resources for relieving the suffering of others.

The Cochrane Collaboration Schizophrenia Group has two systematic reviews under way: one comparing the effectiveness of clozapine versus 'typical' drugs (Essali *et al*, 1997); and another comparing the effectiveness and side-effects of risperidone with those of placebo, conventional neuroleptic drugs, and new (atypical) neuroleptics in the treatment of schizophrenia (Song, 1997). Currently, there are no randomised controlled trials with adequate numbers and follow-up comparing risperidone with clozapine, and there are no published long-term studies of risperidone (Anonymous, 1993).

HEALTH TECHNOLOGY ASSESSMENT

In January 1997 the NHS Standing Group on Health Technology[1] has called for proposals in two areas: first, a systematic review focusing on the question, 'How do the new neuroleptics compare in effectiveness and cost-effectiveness?', which is expected to be completed within 12 months of the research being commissioned; and second, primary research to determine the cost-effectiveness of risperidone and clozapine and the conventional neuroleptics in relation to treatment-refractory or drug-intolerant patients. The NHS Centre for Reviews and Dissemination at the University of York will be conducting the systematic review, and those applying for the primary research (for which short-listing will take place in September 1997) are expected to liaise closely with the Centre. There are no fixed limits on the duration of primary research projects or on funding within the Health Technology Assessment programme, and proposals are expected to be tailored to address the problem fully. At the same time, there is a pressing need within the NHS for this information and so research is normally expected to be completed within three years (except where longer-term follow-up is necessary).

†See pp. 125–130, this issue.

1. For further information contact the Programme Manager, The National Co-Ordinating Centre for Health Technology Assessment (01962-863511); http://www.wiphm.soton.ac.uk/hta.

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Such a research initiative is timely, for these drugs have been around for some years and their use is becoming widespread. It is often emphasised to students that randomised controlled trials are essential to deal with unknown influences and biases, but it is the known and certain biases of those carrying out research that are more likely to produce misleading results. Consciously or unconsciously, researchers tend to want the new treatment to work well so that they can herald a major step forward in therapy.

REFERENCES

Aitchison, K. J. & Kerwin, R. W. (1997) Cost-effectiveness of clozapine. A UK clinic-based study. *British Journal of Psychiatry*, **171**, 125–130.

Anonymous (1993) Risperidone and remoxipride for schizophrenia. *Drugs and Therapeutics Bulletin*, **31**, 101–102.

Baldessarini, R. J. & Frankenburg, F. R. (1991) Clozapine. A novel antipsychotic agent. *New England Journal of Medicine*, **324**, 746–754.

Essali, A., Resk, E., Wahlbeck, K., *et al* (1997) Clozapine for schizophrenia compared to 'typical' neuroleptic drug treatment. In *Schizophrenia Module of the Cochrane Database of Systematic Reviews* (update 2 December 1996) (eds C. Adams, J. De Jesus Mari & P. White). Available in the Cochrane Library (database on disk and CD Rom). *The Cochrane Collaboration; Issue 1*. Oxford: Update Software.

Song, F. (1997) Risperidone for schizophrenia. In *Schizophrenia Module of the Cochrane Database of Systematic Reviews* (update 2 December 1996) (eds C. Adams, J. De Jesus Mari & P. White). Available in the Cochrane Library (database on disk and CD Rom). *The Cochrane Collaboration; Issue 1*. Oxford: Update Software.

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