Managing schizophrenia: an update

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Atypical antipsychotic drugs offer hope to schizophrenics and their families. Controversy continues over their cost-effectiveness but patient surveys suggest increased compliance and thus improved mental health. This article reviews schizophrenia management, exploring the consequences of failing to adopt modern therapies in hampering compliance and stigmatizing the mentally ill.

Schizophrenia remains the most devastating of the chronic serious mental illnesses, placing a tremendous strain upon sufferers and their families alike. It affects both sexes, all races, cultures and social classes equally, with men first presenting between the ages of 15 and 25 years and women about 10 years older. The annual incidence is about 1–2 per 10 000, about twice that of epilepsy, and approximately 250 000 people in the UK are currently sufferers (Cochrane Schizophrenia Group, 1999).

The lifetime risk is almost 1%, increased in near relatives of schizophrenics (Gottesman and Shields, 1982). Its florid psychotic presentations with delusions and hallucinations generally follow a relapsing and remitting course, but about a quarter of patients develop a 'defect state' in which personality is gradually eroded leading to lack of motivation and poor social functioning. Yet, with increasingly effective treatments, the outlook for sufferers has improved considerably over the past 50 years.

SCHIZOPHRENIC PATIENTS IN THE COMMUNITY

Between 1955 and 1991, the number of psychiatric beds in the UK fell from 155 000 to 59 000, partly as a result of advances in treatments using antipsychotic drugs from the early 1950s (Muijen and Hadley, 1995). The move towards community-based care in the late 1970s hastened the closure of beds and saw a four-fold increase in numbers of community psychiatric nurses during the 1980s, with widespread establishment of community mental health teams. Nevertheless, in 1992 it was estimated that approximately one in seven schizophrenic patients require hospital admission, costing half the annual expenditure on schizophrenia care (Kavanagh et al, 1995).

The increasing presence in the community of people who would previously have spent much of their time in hospital has increased public awareness of severe mental illnesses such as schizophrenia but a few highly publicized enquiries into homicides have served to increase public fear and stigmatization of schizophrenics generally. This is ironic since most of these enquiries have involved individuals who were not suffering from schizophrenia. In fact schizophrenics are more likely to be at risk themselves, having a 1.6 times increased mortality rate, doubled incidence of violent death and nine times the rate of suicide of the general population (Harris and Barraclough, 1998).

In September 1999, the government published the National Service Framework for Mental Health with the stated aim of affording mental health 'the same priority as coronary heart disease' (Department of Health, 1999). Seven standards were set out, of which four and five were about effective services for those with serious mental illness, including schizophrenia. Within these, the concept of community care was expanded to include models for crisis response and engagement of patients, particularly assertive community treatment. To these can be added improved drug treatment, particularly using atypical antipsychotics, which has made management more effective and medication easier to tolerate through a reduction in adverse effects (Department of Health, 1999).

Significant controversy surrounds these new drugs which are considerably more expensive than the conventional, or typical, antipsychotics. With an average cost of £1000 per patient per year, resistance to their use has been encoun-

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tered from some health authorities and a proportion of GPs (Taylor et al, 1999). Studies have questioned claims of greater efficacy but it has been difficult to gainsay the views of schizophrenic patients who, in surveys by the National Schizophrenia Fellowship, have emphatically endorsed the atypical antipsychotics as being less troublesome to take than any other antipsychotic drugs (Kapur and Remington, 2000; Roach, 2000). The mental health charity MIND have been running a yellow card scheme, mirroring that of the British National Formulary, wherein patients report side-effects of their medications to MIND, a reaction to the view that many doctors do not explore sufficiently the patient's experience of taking medication.

ANTIPSYCHOTICS: THE STATUS QUO

Antipsychotic drugs offer the most effective treatment for schizophrenia. Acting on central nervous system receptors, including dopamine and serotonin, they provide relief from the majority of positive symptoms.

Typical antipsychotics

Typical antipsychotics block dopamine D_2 receptors post-synaptically, and are licensed for the acute and maintenance treatment of schizophrenia and other psychoses. Most have been around for many years and are familiar to all doctors but concerns over safety, particularly the risk of cardiac arrhythmias with drugs such as thioridazine and droperidol which prolong the QT interval, have raised questions over their continued use.

Chlorpromazine, haloperidol, trifluoperazine and zuclopenthixol are still widely used and provide relief from psychotic symptoms within 2–6 weeks of commencing. Although effective, these drugs have unpleasant side-effects ranging from sedation, constipation, blurred vision, urinary retention and dry mouth, to hypotension with postural dizziness and impotence. Hyperprolactinaemia, leading to galactorrhoea, is produced by interference with the dopamine-mediated hypothalamic regulation of prolactin secretion. Distressing movement disorders are also commonly associated with short- and long-term use of these drugs and include extrapyramidal side-effects (EPS) with its gait disturbances, mask-like face, tremor and reduced movement. Akathisia, occurring in up to 75% of people (Cochrane Schizophrenia Group, 1999), involves a sense of inner restlessness, often expressed as a need to pace, together with mood disturbances and uneasiness. Dyskinesias, involuntary, repetitive movements often involving localized muscle groups such as the face/mouth, trunk or limbs, occur with an annual incidence of 5% (Cochrane Schizophrenia Group, 1999).

Although probably no more effective in the treatment of positive symptoms of schizophrenia, atypical antipsychotics may be more effective for the disabling negative symptoms of apathy, ambivalence and social withdrawal. In addition, they mostly lack the potential to cause EPS and other movement disorders commonly associated with typicals. The improved side-effect profile results in atypical antipsychotics being safer and better tolerated, with consequently improved compliance. It is important to consider this, particularly in the light of a recently-published meta-analysis of studies comparing typicals and atypicals which concluded that there was no clinically significant superiority in the efficacy or tolerability of atypical over typical antipsychotics (Geddes et al, 2000). The point missed was that the virtual absence, at standard dose, of EPS is possibly the most important factor affecting compliance and outcome from treatment (Kapur and Remington, 2000). The presence of EPS is related to poor outcome, depression, tardive dyskinesia, poor social integration and secondary negative symptoms and may increase suicide risk through damaging quality of life (Casey, 1995).

Atypical antipsychotics

Currently available atypical antipsychotics are amisulpride, clozapine, olanzapine, quetiapine, risperidone and zotepine. Their side-effects include sleep disturbance, weight gain, dizziness and agitation; zotepine may also prolong QT interval and lowers seizure threshold. Weight gain has been a potential problem for all antipsychotics, leading to increased morbidity from hypertension, cardiac disease and diabetes. Clozapine and olanzapine show this more with an average gain of 4.45 kg and 4.15 kg respectively over 10 weeks (Allison et al, 1999) and patients should be informed of this and given advice concerning a healthy diet and exercise before commencing. The cause is possibly serotonin-mediated through impairment of the utilization of energy and fat storage; there appears to be a return to baseline weight on discontinuation. Weight gain with one compound does not predict weight gain with others.

Currently available in the USA and Sweden, the novel atypical ziprasidone is expected to receive its licence in the UK within the next year. It would appear to have a significant advantage over other drugs of this group in showing weight gain and rises in prolactin comparable to those in a placebo group. Its control

of positive and negative symptoms of schizophrenia would appear to be equivalent to other atypicals (Arato et al, 1998; Allison et al, 1999).

Cardiac complications

Recent restrictions on the use of thioridazine and pimozide have resulted from concerns over their prolongation of QT intervals. The use of thioridazine has recently been restricted to second-line treatment of schizophrenia only and doctors are recommended to arrange an electrocardiogram (ECG) for all patients taking this drug, to change to another preparation if possible, and to arrange regular ECGs, particularly before dose increase. It is likely that all typical antipsychotics prolong QT intervals to some extent, and there are particular problems with parenteral chlorpromazine, once beloved of general practitioners as a rapid tranquiliser (Yap and Camm, 2000). Haloperidol is a safer alternative but its sister compound, droperidol, has recently been withdrawn for similar reasons. The first parenteral atypicals will soon be available.

Non-responders

Approximately 30–40% of people on typical or atypical antipsychotics fail to respond adequately. Clozapine may be effective in this group. First marketed in the 1960s and withdrawn in 1975 because of unexplained deaths, it was later reintroduced as the only atypical whose action is distinct from other atypicals and all typicals. Its major drawback is its side effect of agranulocytosis in 0.5–2% of patients. Some 40–60% of schizophrenics with symptoms resistant to other antipsychotic treatment respond to clozapine and most cope with its other side-effects of weight gain and hypersalivation. It is of benefit in negative symptoms and the only drug licensed for treatment-resistant schizophrenia, but it is the province of specialist mental health services (Cochrane Schizophrenia Group, 1999).

PSYCHOSOCIAL TREATMENTS

Some 20–40% of schizophrenics prove resistant to all standard antipsychotic treatments; some as a result of refusal to take medication because of side-effects or lack of insight. Others show a partial response and are left with residual positive symptoms such as hallucinations or delusions, many with negative symptoms. These are an extremely vulnerable group, often severely disadvantaged in dealing with neighbours, benefits, housing and the myriad manifestations of bureaucracy required of those incapable of earning a living. The residual symptoms are stigmatizing as are the side-effects, particularly movement disorders, exhibited by many such people. Many become estranged from families and friends and a significant proportion are made homeless. The proportion of the homeless population with schizophrenia has been estimated at around 30% (Craig and Timms, 1995).

Many such individuals can be helped through the use of interventions designed to address issues of social functioning, insight and coping with symptoms. A variety of psychosocial interventions are available with good studies of outcome in terms of quality of life, reduced disability, greater integration into the community and thus reduced stigma. Such approaches are a mainstay of community working with schizophrenic patients and carers and have been adapted for use in the assertive community treatment setting. The burden on families of schizophrenics is a major consideration and the National Service Framework has underlined the need to support relatives and carers, as well as sufferers, through family interventions.

Symptom-focused therapies are mostly based on cognitive behavioural models, and have been particularly effective in managing hallucinations and delusions. They can be used in an individual or group setting and many centres now offer 'voice hearer's' groups. The approach is to teach an individual to learn to live with their abnormal experiences, to ignore them or incorporate them into their lives in a constructive rather than destructive way. Sadly poor access to psychological therapies in many areas, together with their time consumption and cost, has rendered them unavailable to many schizophrenics.

Other approaches are designed to educate and inform about the illness and symptoms and to encourage better compliance leading to treatment alliances and recognition, by the patient of the early signs of relapse with a plan of how to seek help. In such approaches the role of compliance therapy has been important and the advent of 'insight nurses' has provided an ability to improve understanding and compliance with treatment, particularly pharmacotherapies (Cochrane Schizophrenia Group, 2000).

CONCLUSION

With the advent of safer, effective and more tolerable drug treatments, public awareness and a range of psychological interventions, the prospects for managing schizophrenia have improved considerably. It remains, however, the most disabling and stigmatizing of the serious mental illnesses. There continues to be a reluctance to prescribe atypical antipsychotics in many areas, despite their clear superiority over

other drugs, and this is primarily an issue of cost. Campaigning by mental health charities, particularly the National Schizophrenia Fellowship and MIND, is leading to a greater public awareness of these issues. The mental health National Service Framework and Department of Health Impact strategy, aimed at reducing the stigma of mental illness, have yet to bear fruit (Department of Health, 1999). The fundamental aim of treatment for schizophrenia is social reintegration through use of the many and varied pharmacological and psychosocial approaches. Treatment outcomes should be measured only against this goal. **HM**

KEY POINTS

- Schizophrenia is a common serious mental illness associated with deterioration in social, occupational, interpersonal and self-care skills and represents a tremendous emotional burden on families.
- Effective treatment, both physical and psychosocial, has a significant role in reducing pathology and improving prognosis.
- Compliance with antipsychotic medication is the single most important factor in treating schizophrenia.
- Typical antipsychotics are effective and cheap but have disabling short- and long-term side-effects which affect compliance.
- Atypical antipsychotics are more expensive but better tolerated and at least as effective, with some evidence of superiority in negative symptoms.
- Psychosocial interventions have offered major advances, complementing drug treatment in the rehabilitation of sufferers.
- The best management of schizophrenia is undertaken as a partnership between primary care and specialist mental health services.

Conflict of interest: Dr Chris Fear sits on advisory boards for Pfizer and is involved in clinical trials for Pfizer.

Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, Weiden PJ (1999) Antipsychotic-induced weight gain: a comprehensive research synthesis. *Am J Psychiatry* **156(11):** 1686–96

Arato M, O'Connor R, Bradbury JE, Meltzer H (1998) Ziprasidone in the long-term treatment of negative symptoms and prevention of the exacerbation of schizophrenia. *Eur Psychiatry* **13(4):** 303(s)

Casey DE (1995) Motor and mental aspects of extrapyramidal syndromes. *Int Clin Psychopharmacol* **10**(suppl 3): 105–14

Cochrane Schizophrenia Group (1999) Drug treatments for schizophrenia. *Effective Health Care* **5(6):** 1–12

Cochrane Schizophrenia Group (2000) Psychosocial interventions for schizophrenia. *Effective Health Care* **6(3):** 1–8

Craig TKJ, Timms PW (1995) Homelessness and schizophrenia. In: Hirsch SR, Weinberger DR, eds. *Schizophrenia*. Blackwell, Oxford: 664–84

Department of Health (1999) *National Service Framework for Mental Health.* HMSO, London

Geddes J, Freemantle N, Harrison P, Bebbington P for the National Schizophrenia Guideline Development Group (2000) Atypical antipsychotics in the treatment of schizophrenia: systematic overview and meta-regression analysis. *Br Med J* **321:** 1371–6

Gottesman II, Shields J (1982) *Schizophrenia: The Epigenetic Puzzle.* Cambridge University Press, Cambridge

Harris EC, Barraclough B (1998) Excess mortality of mental disorder. *Br J Psychiatry* **173:** 11–55

Kapur S, Remington G (2000) Atypical antipsychotics. *Br Med J* **321:** 1360–1

Kavanagh S, Opit L, Knapp M, Beecham J (1995) Schizophrenia: shifting the balance of care. *Soc Psychiatry Psychiatr Epidemiol* **30:** 206–12

Muijen M, Hadley T (1995) Community care: parts and systems. In: Hirsch SR, Weinberger D, eds. *Schizophrenia.* Blackwell, Oxford: 649–63

Roach JO (2000) Mentally ill people denied choice of drugs. *Br Med J* **321:** 1432

Taylor D, Mir S, Mace S, Hogman G (1999) *Is Cost a Factor – II.* National Schizophrenia Fellowship, London

Yap YG, Camm J (2000) Risk of torsades de pointes with non-cardiac drugs. *Br Med J* **320:** 1158–9