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M. HARRINGTON, P. LELLIOTT, C. PATON, C. OKOCHA, R. DUFFETT AND T. SENSKY

The results of a multi-centre audit of the prescribing of antipsychotic drugs for in-patients in the UK†

AIMS AND METHOD

Forty-seven UK mental health services participated in a 1-day audit of prescribing of antipsychotic drugs. Audit standards were derived from national guidelines and consensus statements.

RESULTS

Of the 3132 patients, 20% were prescribed a total dose of antipsychotic medication above that recommended by the *British National Formulary*. The majority of case notes failed to record an indication for high-dose prescribing or that the patient had been informed; only 8% had undergone an electrocardiogram. Forty-eight per cent of patients were prescribed more than one antipsychotic drug.

CLINICAL IMPLICATIONS

Antipsychotic prescribing for in-patients often runs counter to existing guideline recommendations. It is likely that many patients who are prescribed high doses or polypharmacy are unaware that their prescription is out of line with guideline recommendations and is inadequately monitored.

In the UK, 23 antipsychotic drugs are available on prescription, many by more than one route. Most side-effects of these drugs are dose related, cause substantial morbidity and may contribute to poor treatment adherence (American Psychiatric Association, 1997). It remains unclear whether the risk of sudden death, acknowledged to occur with antipsychotic drugs, is dose related (Royal College of Psychiatrists, 1997). Existing research offers limited guidance on optimal prescribing in individual circumstances. However, reviews have concluded that, in general, the use of high doses or of polypharmacy (simultaneous use of more than one antipsychotic drug) offers little, if any, benefit over moderate doses of a single drug, in relation to the disadvantages (Royal College of Psychiatrists, 1993). This evidence has influenced the development of national guidelines and consensus statements.

Method

Development of the audit standards

Five English-speaking countries have published national guidelines or consensus statements that refer to the prescribing of antipsychotic drugs (American Psychiatric Association, 1997; EPPIC Statewide Services, 1999; New Zealand Ministry of Health, 1996; Royal College of Psychiatrists, 1993, 1997; Working Group for the Canadian Psychiatric Association and the Canadian Alliance for Research on Schizophrenia, 1998). All advise against the use of high doses other than in exceptional circumstances. Four make a similar, explicit recommendation in respect of polypharmacy. Audit standards were derived from these documents and were presented to, and agreed by, a separate 'expert panel' of psychiatric pharmacists and psychopharmacologists. The standards audited, and the measures used to audit them, are shown in Table 1.

Dose

The *British National Formulary* (*BNF*; British Medical Association & Royal Pharmaceutical Society of Great Britain, 1999) states a maximum recommended dose, or a dose range for all antipsychotic drugs except trifluoperazine. The Royal College of Psychiatrists' consensus statement (Royal College of Psychiatrists, 1993) recommends that, when an antipsychotic is given at a dose above the

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BNF limit the decision should be made by a fully trained psychiatrist; the patient should be informed and his/her consent obtained; an electrocardiogram (ECG) should be performed; regular pulse, blood pressure and temperature checks should be made; and fluid intake should be monitored. A trial of a high-dose prescription should not last longer than 3 months. If there has been no improvement, the dose should be reduced back to within the standard range.

Polypharmacy

The *BNF* advises against polypharmacy. However, the College consensus statement suggests that there are some occasions when it is appropriate to give more than one antipsychotic drug concurrently for short periods. These include when changing gradually from one drug to another and when giving a more sedative and/or injectable antipsychotic drug to someone who is very agitated and who is already prescribed another antipsychotic drug on a regular basis.

High dose caused by polypharmacy

The College consensus statement clearly states that high-dose prescribing may occur because of the additive effects of two antipsychotic drugs that are prescribed concurrently. There are two methods of calculating whether the 'total dose of antipsychotic drug' exceeds the recommended level. One is to convert the doses of the drugs into 'chlorpromazine equivalents' and add these. The other approach, which was used in this audit, is to convert the prescribed dose to its percentage of the upper recommended dose (or maximum dose) for each drug and then to add the percentages (Yorston & Pinney, 2000). When the sum exceeds 100, the patient is considered to be receiving a high dose.

For the purpose of the audit, the maximum daily dose for trifluoperazine was taken to be 50 mg.

Recruitment of sites

In February 1998, all UK adult mental health services were invited to take part in the audit; 47 did so. Services from every part of the country and from every main socio-demographic group (inner city, urban, mixed and rural) participated. They included one private hospital and one high security hospital. A total of 241 psychiatric wards (154 acute admission, 69 rehabilitation and 18 forensic) were involved. All wards were primarily for the treatment of people aged 18–65.

The audit

Local staff used a pro forma to collect information about all in-patients who were prescribed antipsychotic medication on 5 October 1998. This included details of all prescriptions for antipsychotic medication (drug, daily dose and route of administration). For each prescription, it was noted whether the drug was to be administered routinely or whether it was to be given 'as required' at the discretion of nursing staff. Frequency of administration was recorded for antipsychotic drugs prescribed as depot injections and, for zuclopenthixol acetate, the dose prescribed in the previous 72 hours.

Data collectors used a checklist to collate information from case files for comparison of practice with the standards set out in Table 1.

Data collection and management

Staff from each site attended a workshop at which the audit standards and methods for data collection were presented and discussed. Completed forms were returned to the Royal College of Psychiatrists' Research Unit where the data were analysed using SPSS for Windows, version 8.

Results

Returns gave information about prescribing practice relating to 3132 in-patients.

Frequency of prescribing of high doses and polypharmacy

Antipsychotic medication at a total dose above the *BNF* recommended daily limit was prescribed to 613 patients (20%). For only a small minority of cases (n=34; 5.5% of those prescribed a high dose) was this due to the prescription of a single type of antipsychotic drug at a high dose. For the remainder, high-dose prescribing was due to a combination of two or more types of anti-psychotic drug. If only antipsychotic drugs prescribed for routine administration were considered, 318 patients (10% of the total sample) were prescribed a high dose.

In all, 1487 patients (48%) were prescribed more than one antipsychotic drug on the census day. The results of the audit are summarised in Table 1.

Discussion

As there was no random selection of the participating services, the cohort may not be fully representative. However, units from all parts of the country took part and the sample is large, containing perhaps 15–20% of all people in a psychiatric hospital on the census day. This estimate is extrapolated from the bed numbers for England (Department of Health, 1998).

Why are high-dose prescribing and polypharmacy so common?

The finding that patients in hospital are commonly prescribed high doses is consistent with six smaller scale audits or surveys of psychiatric in-patients carried out in the UK over the past decade (Chaplin & McGuigan, 1996; Krazucki & McFarlane, 1996; Milton *et al*, 1998; Newton *et al*, 1997; Warner *et al*, 1995; Yorston & Pinney, 1997). These studies involved 1084 patients prescribed anti-psychotic medication, 32% (n=344) of whom were prescribed a high dose.

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Table 1. Audited standards and the findings

Standard	Cases *n* (%) Eligible	Missing	Included	Audited measure	Cases meeting standard *n* (%)
High-dose prescribing					
If a patient is prescribed a trial of high-dose antipsychotics, the clinical indications should be documented in the patient's notes	613	112 (18)	501 (82)	Clear statement of indications	212 (42)
The decision to commence a patient on a high dose of antipsychotic medication is the responsibility of the patient's consultant. A decision to start an elective trial of high-dose antipsychotic medication must be made by the patient's consultant or by a deputy who is on the specialist register	613	112 (18)	501 (82)	Decision recorded to prescribe above recommended dose Where decision was recorded, decision made by consultant	163 (33) 153 (94)
Patients should be informed that they are receiving a trial of a high dose of antipsychotics (or an explanation of why they were not informed should be documented)	613	112 (18)	501 (82)	Records show that patient was informed Explicit statement why patient has not been informed	90 (18) 15 (3)
An electrocardiogram (ECG) to exclude significant cardiac disease or prolonged QT intervals should be performed prior to commencing patients on high-dose antipsychotics (or an explanation for not doing so should be documented)	613	112 (18)	501 (82)	Evidence from records that ECG performed Statement in notes that ECG could not be performed	40 (8) 10 (2)
If a patient is prescribed high-dose antipsychotic drugs for 3 months, the outcome by the end of this time should be documented in the patient's notes			214	Clear statement of outcome Records show outcome reviewed in the light of the original indications	147 (69) 95 (44)
Polypharmacy					
Two or more antipsychotic drugs should only be given concurrently as part of a considered treatment plan. Indications include: (a) when a single antipsychotic has failed to control symptoms; (b) while switching a patient between different antipsychotics; (c) covering a period of acute exacerbation	1487	101 (7)	1386 (93)	Patients fulfilling criterion (a) Patients fulfilling criterion (b) Patients fulfilling criterion (c) Patients meeting none of the criteria	826 (60) 290 (21) 411 (30) 311 (22)

A number of factors need to be considered when interpreting the findings from the multi-centre audit, they are as follows.

The sample is cross-sectional

This means that it will contain a higher proportion of patients with longer lengths of stay, and probably higher levels of disturbance and disability, than a cohort of consecutive admissions. Also, the audit gives no indication of longitudinal patterns of prescribing. The potential impact of this is illustrated by the finding that 12% of patients on more than one antipsychotic were in the process of being switched from one antipsychotic to another.

Ward conditions

About two-thirds of the patients were on acute admission wards. The rate of admission to these wards has increased considerably over the past 15 years despite a reduction in bed numbers. This has resulted in people who are severely disabled and highly disturbed being concentrated on these wards. Some of the prescribing might therefore reflect the use of antipsychotics to control behaviour, in the context of a disturbed ward environment, rather than the rational treatment of psychotic symptoms. Furthermore, the need to free up beds for new admissions creates pressure to discharge people quickly. This might encourage rapid escalation of doses or the premature addition of a second type of antipsychotic drug. The commonest reason given for the use of polypharmacy was that a single drug had failed to control symptoms. It is not known how often the trial of a single antipsychotic drug had lasted >6 weeks, as recommended by a number of national guidelines.

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Medication given at the discretion of nurses

The decision as to whether medication should be given at levels exceeding those recommended by the *BNF* had, in effect, been left to nursing staff in about half of cases where a doctor had prescribed a high dose. This was through the writing up of 'as required' medication. The audit neither determined whether this was intentional (see below) nor whether nursing staff were sufficiently trained in psychopharmacology to make such decisions. The writing of 'as required' could also lead to the unintentional and unknowing administration of a high dose (Milton *et al*, 1998).

Psychiatrists might not be aware that they are prescribing high doses

For two-thirds of patients to whom it applied, the case notes contained no explicit statement that *BNF* limits had been exceeded. This might reflect sub-optimal record keeping, a lack of awareness or a combination of both. Nearly 95% of high-dose prescribing was due to polypharmacy. It is possible this represents a second cause of 'covert' high-dose prescribing wherein clinicians lose sight of total additive dose when they give more than one type of drug at the same time (Tyson *et al*, 1999).

Prescribers might disagree with the guidelines

When an audit highlights significant divergence from recommended practice, the 'validity' of the guideline should be reconsidered as well as the behaviour of clinicians. The research base for the guidelines, which informed this audit, is not strong and there might also be questions about the extent to which the research findings can be extrapolated to the real-life clinical situations encountered in modern British psychiatry. Also, the recommendations for maximum doses take no account of patient factors, such as age, gender, ethnicity, body mass, smoking or other medication that might influence response or side-effects. Furthermore, there are apparent inconsistencies between *BNF* maximum recommended doses and comparisons between drugs based on commonly used tables of equivalence. This is particularly important, given the extent to which high-dose prescribing is associated with polypharmacy.

Precautions and consent

Fewer than 10% of patients prescribed a high dose had undergone an ECG. There might be a number of explanations for this:

(a) it might reflect the lack of awareness that a high dose has been prescribed
(b) psychiatrists might be unaware both of the importance of such a test and of the College guideline (Henderson *et al*, 1997)
(c) trainee psychiatrists might not feel proficient in interpreting the results of an ECG (Warner *et al*, 1996).

A lack of awareness of the psychiatrist that a high dose has been prescribed might also partly explain why as many as 80% of patients appear not to have been informed, let alone given their consent. Patients have made allegations of negligence involving doses of antipsychotics outside the *BNF* recommended range (Bradley, 1997). The lack of objective data to support the efficacy of high doses, in conjunction with the lack of informed consent (Brabbins *et al*, 1996) and failure to conduct simple precautionary tests, are likely to make such allegations difficult to defend against.

Prescribing behaviour has probably changed since the 1998 audit owing to the increased use of atypical antipsychotic drugs. This supports the case for further audits of this type.

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Declaration of interest

C. P. has very occasionally received speaker fees from Eli Lilly and Pfizer. Over the past year she has been involved with research projects funded by Novartis, Eli Lilly and Janssen–Cilag, but has not received any personal income from those projects. T. S. has been paid honoraria by numerous pharmaceutical companies for contributing to educational events. In 2000 he attended a meeting as a participant in an advisory board for Pfizer. The views expressed do not necessarily reflect those of the Royal College of Psychiatrists.

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M. HARRINGTON, P. LELLIOTT, C. PATON, M. KONSOLAKI, T. SENSKY AND C. OKOCHA

Variation between services in polypharmacy and combined high dose of antipsychotic drugs prescribed for in-patients†

AIMS AND METHOD

A 1-day census provided an opportunity to examine the variation between 44 mental health services in the frequency of prescribing high doses and polypharmacy of antipsychotic drugs to in-patients on acute psychiatric wards.

RESULTS

The proportion of patients prescribed a high dose ranged 0–50% and simultaneous use of more than one antipsychotic drug ranged 12–71%. A number of case-mix variables explained 26% and 40%, respectively, of the variance between services on these two indicators of prescribing practice.

CLINICAL IMPLICATIONS

Services with high rates of prescription of high dose or polypharmacy might consider a review of clinical practice and of service-level factors that might affect prescribing.

One of the stated aims of the UK Government is 'to reduce unacceptable variations in clinical practice' (Department of Health, 1998). Laudable though this aim is, it begs the questions as to what is an 'acceptable' level of variation and what factors, other than the performance of practitioners, influence variation. The first question becomes easier if the extent of variation can be compared with some standard or norm.

There is a consensus among English-speaking countries in the developed world that high doses or polypharmacy of antipsychotic drugs should be avoided, other than in exceptional circumstances (Harrington *et al*, 2002, this issue). A 1-day census of prescribing provided an opportunity to describe variation between UK mental health in-patient services and the extent to which this guidance is followed.

Method

Data collection and the sample

The database used for this study was that described in the accompanying paper (Lelliott *et al*, 2002, this issue), involving a 1-day census of drugs prescribed to in-patients on psychiatric wards of 49 mental health services. Patients on forensic or rehabilitation wards were not included in this study, reducing the number of mental health services involved to 44. The 2149 patients on acute psychiatric wards who were prescribed an antipsychotic drug were included. The wards were primarily for people aged 18–64.

Data analysis

For each patient, prescribed antipsychotic medication was classified as either standard dose or high dose, as defined in the associated paper by Harrington *et al* (2002, this issue). The unit of analysis was the mental health service. For each service, the percentage of patients in acute wards who were on a high dose of an antipsychotic or polypharmacy was calculated. These percentages were then used as the dependent variable in linear regression analyses to examine how much of the variation between services could be explained by 'case-mix' factors that were known to influence prescribing (Lelliott *et al*, 2002, this issue). These independent variables were mean age, proportion of patients who were male, proportion detained under the Mental Health Act (MHA) and proportion with a diagnosis of schizophrenic or delusional disorder. Although ethnicity had been found not to influence the probability of being prescribed a high dose or polypharmacy, the proportion

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