Audit of out-patients on 'higher dose' antipsychotics

John R. Taylor and Ian B. Cookson

Standards developed from the Royal College of Psychiatrists' consensus statement on the use of high-dose antipsychotics were audited. The baseline survey and two completed audit cycles are described showing improvement in the monitoring and management of out-patients on higher dose depot antipsychotics. Initially the main problem was poor attendance at hospital appointments. Practice was changed by (a) medical staff becoming more assertive and visiting non-attenders at home; (b) a phlebotomist visiting patients at home. Deinstitutionalisation has relocated many patients with chronic psychoses into the community, but services, including the ancillary services, have sometimes been slow to follow. This audit found that the most effective change was the provision of services to patients in their own home.

The Royal College of Psychiatrists' consensus statement on the use of high-dose antipsychotic medication (Thompson, 1994) suggested that it should be used to set local standards that could then be audited. High doses are known to increase side-effects, but there is no clearly established relationship with sudden death (Kane, 1994) despite public concern (Hirsh & Barnes, 1994). The evidence for efficacy of high doses is limited and not supported by controlled studies (Thompson, 1994), but the possibility that some patients may benefit has not been ruled out (Kane, 1994). Cookson (1987) reported that, in a group of patients who were thought to have improved on a higher dose, there was increased relapse when the dose was reduced.

The consensus statement defined 'high dose' as a total daily dose which exceeded the advisory upper limit for general use in the *British National Formulary* (BNF) or product licence. Warner *et al* (1995) highlighted the problem of deciding whether a patient is on high-dose antipsychotics, for the purpose of audit, using the above definition. 'Higher dose' in this paper is defined as equivalent to a depot dose of flupenthixol 200 mg fortnightly or greater. This dose is well within the BNF limit for flupenthixol but is around the BNF limit for equivalent doses of the other depot antipsychotics (British Medical Assocation & Royal Pharmaceutical Society, 1995). It is also roughly equivalent to 1000 mg chlorpromazine daily (Foster, 1989) which is the BNF upper limit for chlorpromazine.

The study

Following an initial survey in 1994 of 32 patients on 'higher doses' of depot antipsychotics, and the publication of the consensus statement, a system was introduced for all patients on higher dose depots to be reviewed three-monthly at the out-patient clinic, and for the patient's physical state, routine bloods and electrocardiogram (ECG) to be checked annually at the depot clinic.

Standards based on the consensus statement were formally agreed in April 1995 when a baseline survey was also completed. These standards were that all out-patients on higher dose depot antipsychotics should have:

(a) clinical review by a psychiatrist at least six-monthly;
(b) the Manchester Scale completed by a psychiatrist at least six-monthly;
(c) the dose of antipsychotic changed on a fixed scale depending on symptoms;
(d) physical examination annually (including weight, smoking and alcohol);
(e) ECG annually;
(f) blood tests annually, including hepatic and renal function.

Patients who refused physical investigations were deemed to have met the audit standard if the refusal was clearly documented in the notes. The Manchester Scale is a short and simple rating scale designed for chronic psychotic patients, which is sensitive to change and includes a record of side-effects (Krawiecka *et al*, 1977). If the patient had marked positive symptoms (i.e. a score of 3 on delusions, hallucinations or incoherence, or a combined score of 4) the dose was increased on a fixed scale. If patients were asymptomatic, or had not benefited from a higher dose, then the dose was reduced until they were maintained on 200 mg flupenthixol fortnightly or equivalent. Further reductions were not made because of concern that this would increase the risk of relapse (Cookson, 1987).

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Results

Characteristics of the patients

The mean age of the 24 patients on higher dose antipsychotics during the audit period was 47.1 years and two-thirds were male (15/24). They had diagnoses of either schizophrenia (21/24) or schizoaffective disorder (3/24). The mean duration of illness was 20.8 years and the average time on a depot was 8.6 years. The majority (21/24) were prescribed doses of flupenthixol decanoate within BNF limits (mean 371 mg fortnightly). The three cases receiving fluphenazine decanoate were all receiving doses outside BNF limits (mean 258 mg fortnightly). A third of patients were on additional oral antipsychotics, but the dose only exceeded 100 mg in chlorpromazine equivalents in four cases. The other four patients were receiving a small dose of thioridazine at night as a hypnotic.

Results of the audit

The results of the baseline survey in April 1995, and the first and second cycles of the audit in October 1995 and April 1996, are shown in Table 1. Over 90% of the patients were clinically reviewed during the last six-month audit period and a modified Manchester Scale, which included a record of medication and side-effects, was completed on nearly all of these patients. All the patients met the standard for routine bloods by the end of the audit, but only two-thirds met the standards for physical examination and ECG. Over 80% of patients met the standard for dose change after the first cycle but this had fallen back to the baseline level by the time of the second cycle. The final dose was increased in 30% and decreased in 43% of patients compared with baseline. This was reflected in a fall in the mean dose of flupenthixol decanoate to 313 mg fortnightly. The use of other treatment options was limited, for the majority of patients, by poor compliance, and only one patient was changed to an atypical antipsychotic during the audit period.

Abnormalities found during the physical investigations

Four ECGs had minor abnormalities that required no action. Five patients had abnormal blood results that required referral to the physicians or back to the GP. These were: (a) a 58-year-old man with a glucose level of 20.2 mmol/l and an alanine transaminase (ALT) of 36 U/l, gamma glutamyltransferase (GGT) of 189 U/l, and alkaline phosphatase (AlkP) of 163 U/l; (b) a 48-year-old man with glucose of 14.9 mmol/l; (c) a 31-year-old man who was a known heavy drinker whose liver enzymes had deteriorated to ALT 131 and GGT 213; (d) a 39-year-old man with a slightly raised GGT of 78 and ALT of 40; (e) a 23-year-old man with a GGT of 60 and ALT of 37.

Three other patients needed their bloods rechecked, due to raised glucose or thyroid-stimulating hormone, but no further action was required. Another patient was already being followed up by the physicians for alcoholic liver disease, probably cirrhosis, with low platelets secondary to hypersplenism. His platelets were 60, GGT 542 and ALT 40.

Eighteen patients (of 22) had their flupenthixol levels checked. All results were within the expected range and there was no evidence of either unusually high or low levels.

Two of the physical examinations were abnormal. One 58-year-old man was referred to his GP with mild hypertension and obesity. The only other abnormality was the man with probable cirrhosis who was wheezy and oedematous.

Comments

Review of the standards

The Manchester Scale was easy to use and was helpful in monitoring patients' progress. It is likely to be replaced by the Health of the Nation Outcome Scale in the future, as it will be impractical to complete two similar scales.

The consensus statement recommended that the ECG should be checked three-monthly but

Table 1. Audit of out-patients on 'higher dose' antipsychotics

Standards	April '95 *n* (%)	Oct '95 *n* (%)	April '96 *n* (%)
Cinical notes	20 (87)	20 (87)	21 (95)
Manchester Scale	4 (17)	19 (83)	19 (86)
Dose change	14 (61)	19 (83)	14 (64)
Physical[1]	9 (39)	12 (52)	17 (77)
ECG[2]	9 (39)	12 (57)	15 (68)
Bloods[2]	10 (43)	13 (57)	22 (100)
Total (%)	23 (100)	23 (100)	22 (100)

1. Includes three patients with documented refusal.
2. Includes four patients with documented refusal.

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made it clear that the guidelines were intended to be "informative and facilitatory rather than prescriptive" (Thompson, 1994). It has been suggested that an ECG should be done three-monthly if the chlorpromazine dose equivalent is higher than 1000 mg, and that the dose should be reduced if the QTc is over 400 ms (Krasucki & McFarlane, 1996). While these guidelines may be suitable for in-patients who may have just started on antipsychotics, we feel that our standard of annual ECGs and a QT cut-off of 500 ms is more suitable for out-patients on large but stable doses of depot antipsychotics. Three of our patients had QTc intervals over 400 ms, but the information available suggests that 400 ms is too short to be an acceptable upper limit (Thomas, 1994). The Committee on Safety of Medicines (1996) recommends that the relevant drug should be stopped if the ECG shows a QT interval of greater than 500 ms or if an episode of torsade de pointes is recorded. Our standard is also compatible with current BNF advice that ECGs need to be repeated "periodically".

The only investigations that detected significant abnormalities were the routine blood tests. Two patients were diabetic and five had abnormal liver enzymes. In two cases the abnormal liver enzymes were probably secondary to alcohol misuse, but in three cases there was no obvious cause and it is possible that these changes were drug-induced. After discussion with a physician it was decided to continue all these patients on their 'higher dose' antipsychotics.

There are no clear guidelines about which blood tests are required for patients on high-dose antipsychotics. The consensus statement suggested that hepatic and renal impairment were relative contraindications and that hydration or urea and electrolytes should be checked regularly (Thompson, 1994). In addition we checked the glucose and thyroid function as part of a general health screen, and a full blood count in view of the small risk of neutropenia or agranulocytosis.

The physical examinations failed to detect any new abnormality apart from one patient with mild hypertension. This standard has now been changed to a baseline physical when starting on higher dose antipsychotics. The updated standards for monitoring out-patients on higher dose antipsychotics are shown in Table 2.

Improvements in clinical practice

This study shows the effectiveness of audit in improving the standard of the monitoring of both the mental and physical state of patients on 'higher dose' antipsychotics. Although this audit only involved 24 patients under the care of one consultant, it clearly shows that audit can help a community psychiatric team to improve its clinical practice. After the first cycle of the audit it became clear that the main problem was poor attendance at hospital appointments. Two changes were made to improve clinical practice. Medical staff became more assertive and arranged to visit patients who failed to attend their out-patient appointments at home. The second change was the introduction of a domiciliary phlebotomy service where a phlebotomist was accompanied by a community psychiatric nurse to take blood from patients in their homes.

All the out-patients in the audit had a chronic psychosis. In the past many of this group would have been long-term in-patients and it would have been relatively easy to monitor both their physical and mental state. There is evidence that assertive community programmes are effective at looking after this group of patients, but ancillary services are still mainly based in hospital buildings and are often inflexible. There will always be a minority of patients who refuse physical investigation, and the risks of these patients continuing on higher dose antipsychotics need to be assessed individually.

Considerable improvements were seen by the time the second cycle of the audit was completed in April 1996. All patients now met the standard for routine bloods and nearly all had been clinically reviewed. It is planned that medical staff will continue to visit non-attenders at home to review their physical and mental state. In addition it is hoped to train the community psychiatric nurses in phlebotomy and the use of a mobile ECG machine. The main disadvantage of this approach is that it reduces the amount of time they can spend on

Table 2. Suggested standards for out-patients on 'higher dose' depots

(1)	Case-note entry within six months.
(2)	Manchester Scale/HoNOS six-monthly (completed by doctor after clinical review).
(3)	Dose changed on a fixed scale (depending on the level of symptoms).
(4)	Baseline physical examination on starting (including obesity, smoking and alcohol).
(5)	ECG annually. Monitor QT interval and stop higher dose depot if QT is greater than 500 ms.
(6)	Blood tests annually (U & Es, LFTs, FBC, TFTs and glucose).

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other activities. The alternative would be greater availability to domiciliary phlebotomy and ECG services.

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