High-dose antipsychotic treatment in clinical practice

A review, audit and survey of consultant psychiatrist opinions

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Aims and method A trust-wide audit of antipsychotic prescription was conducted in order to investigate the prevalence of high-dose treatment in a population with schizophrenia and assess compliance with Royal College of Psychiatrists' guidelines on the use of high doses. Details of antipsychotic medication were recorded and in cases of high-dose treatment compliance with the College's guidelines was assessed.
Results Sixteen out of 361 patients (4%) were receiving high-dose medication. At re-audit this figure fell to four patients (1%). High-dose treatment comprised of a combined depot and oral medication in most cases. There was poor compliance with the College's guidelines.
Clinical implications The study stresses the importance of monitoring patients on high-dose antipsychotics, particularly when taken in combination.

The prescription of antipsychotic medication above limits recommended by the manufacturers, as documented in the *British National Formulary* (BNF; British National Formulary, 1997), has been a topic of debate over the past few years (Brotman & McCormick, 1990; Hirsch & Barnes, 1994; Sillifant *et al*, 1997). There is a consensus that high-dose treatment (prescription exceeding BNF limits) is warranted in some instances, despite the lack of research evidence to back this up (Mortimer, 1994). Allied with this are concerns that some patients are maintained on high-dose treatment unnecessarily. Associated risks include increased extrapyramidal side-effects and there have been reports of increased mortality due to cardiac conduction abnormalities (Mehtonen *et al*, 1991). To minimise the incidence of unnecessary high-dose treatment and to promote effective safeguards in instances where high dose treatment is warranted, the Royal College of Psychiatrists issued a consensus statement incorporating extensive guidelines on the use of high-dose treatment (Thompson, 1994).

The consensus statement recommended regular auditing of antipsychotic prescribing practice at a local level, and the results of such audits have been published by a number of authors. Yorston & Pinney (1997) audited a sample of 113 in-patients and 113 community and rehabilitation patients in south Buckinghamshire. Ten per cent of in-patients, and 4% of community and rehabilitation patients were prescribed regular high-dose antipsychotics. This represented 7% of the total patient population. In these cases adherence to the College's guidelines was poor. At re-audit the number of patients receiving high-dose treatment fell to six (3%).

Krasucki & McFarlane (1996) did a cross-sectional study on all in-patients at a psychiatric hospital in south London. Of the 92 patients receiving antipsychotic medication, 14 (15%) were on high doses. Electrocardiogram (ECG) checks recommended by the College's guidelines had been administered to only four (28%) of these patients.

Warner *et al* (1995) audited the prescriptions of patients on nine wards of a psychiatric hospital in Surrey. The first phase of the audit showed that 44% of patients were receiving antipsychotic medication which, when converted to chlorpromazine equivalents, was above BNF limits. This figure did not decrease at re-audit (42%), although there was a reduction in the prescription of 'megadoses' (>4000 mg of chlorpromazine equivalent daily) between the two audit phases.

The present audit sought to evaluate prescribing practice in the light of the College's guidelines, and to compare prescribing practice in East Yorkshire with previously published audit findings. Our focus was on all patients with schizophrenia, as they represent a more homogenous group than had been studied in previous audits. In addition, we surveyed consultant psychiatrists' opinions of the College's guidelines to see if this had any bearing on compliance with them.

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Method

Phase 1

Details of patients with a clinical diagnosis of schizophrenia were ascertained from patient information systems, community teams and acute units within Hull and Holderness Community Health NHS Trust. Name, age and gender were recorded in addition to details of illness and medication.

Antipsychotic dosages were recorded from case notes and converted to a percentage of maximum recommended dose according to the *British National Formulary* (BNF, 1997). Where patients were prescribed more than one antipsychotic, percentages were summed to give an aggregate percentage of the BNF (1997) maximum for each drug. This novel method of calculating total dosage using aggregate percentages was originally used by Yortson & Pinney (1997) and was preferred to the traditional way of expressing dosage in terms of chlorpromazine equivalents as this method has been shown to provide inconsistent estimates of antipsychotic potency (Dewan & Koss, 1995).

Phase 2

In order to improve awareness of health risks associated with high dose treatment and to improve adherence to the College's guidelines, all consultants in the trust were written to with both a summary of the audit and details of the original College guidelines. In addition, the audit findings were disseminated at research meetings involving consultants and trainees in psychiatry. Patients identified as receiving high-dose treatment were re-assessed by their consultant or by A. M. M. in the Department of Psychiatry, University of Hull. Following these measures a re-audit was undertaken approximately six months after completion of the first phase of the audit.

Survey

In order to investigate factors which affect compliance with the College's guidelines, a brief questionnaire was constructed and sent to all the consultant psychiatrists in Hull and Holderness and East Yorkshire Community Health NHS Trust. Consultant psychiatrists whose practices were not included in the original audit were included in the survey in order to increase numbers and therefore give a more representative summary of opinion (n=12). This wider sample of consultant psychiatrists included child and adolescent psychiatrists, old age psychiatrists and general psychiatrists from a neighbouring trust.

Results

Phase 1

The total number of patients clinically diagnosed with schizophrenia who were receiving antipsychotic medication was 361 (231 males, 130 females). In total, 16 patients were on high-dose antipsychotic medication (4%: 10 males, six females). Ten of these patients were receiving high-dose treatment of between 100% and 150% of the BNF maximum, three patients were receiving high-dose treatment of between 150% and 200% of the BNF maximum, and the remaining three patients were receiving high-dose treatment of between 200% and 270% of the BNF maximum. High-dose treatment comprised of a depot and oral antipsychotic combined (12 cases), depot only (two cases) and a depot and two oral antipsychotics combined (two cases). At the time of audit, patients had spent between one month and eight years on high-dose treatment (mean: two years three months). High-dose antipsychotics were prescribed with similar frequency across all age ranges (19–29 years: 5%; 30–39: 3%; 40–49: 6%; 50–59: 4%; 60–69: 6%).

There was little compliance with the College's guidelines. In particular, guidelines concerning: regular electrocardiogram (ECG) and general health checks, second opinion, written consent and thorough record-keeping were followed in less than half of cases (see Table 1). In addition,

Table 1. Guidelines for high-dose treatment and consultant compliance

Royal College of Psychiatrists' guidelines	Percentage of cases where guidelines were adhered to (n=16) Yes	No
High dosage discussed with multi-disciplinary team	50	50
Written consent obtained	13	87
Thorough record of decision kept	44	56
Second opinion sought	6	94
Presence of health contra-indications to high-dose treatment[1]	25	75
Potentially harmful polypharmacy[1]	0	100
Regular electrocardiogram checks	6	94
Dosage increased gradually	69	31
Regular general health checks done	6	94
Progress reviewed regularly	87	13

1. These items do not refer to consultant compliance with guidelines, but to the percentage of high-dose cases who had contra-indications to high-dose treatment or were being treated with potentially harmful polypharmacy.

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there were possible contra-indications to high-dose treatment in four of the 16 cases (three patients over 60, one with obesity).

Phase 2

Four of the original 16 patients were still receiving high-dose treatment (1% of the overall population with schizophrenia). However, in all of these cases attempts had been made to reduce medication and this was successfully being done in three of the four cases. Attempts at reducing the medication in the fourth patient had been unsuccessful, resulting in relapse, and as a consequence their medication had increased. Three of these patients were still prescribed both an oral and depot antipsychotic. All were considered treatment resistant and living in the community. There had been no improvement in adherence to the College's guidelines for those patients receiving high-dose medication.

Survey

All consultants approached returned the questionnaires. Results of the survey are shown in Table 2.

Comment

Incidence of high-dose treatment

In our audit, 4% of patients receiving antipsychotic medication were on dosages in excess of BNF limits. This figure fell to 1% at re-audit. These findings show a lower rate of high-dose prescription than that reported by Yortson & Pinney (1997) who used the same method of calculating total dosage. Patients who remained on high-dose treatment at re-audit were considered treatment-resistant and although high-dose treatment can be justified in these circumstances, there are a number of alternatives to high-dose treatment which should be considered (Thompson, 1994).

Polypharmacy

Twelve of the patients who were originally on a high-dose were prescribed an oral and a depot antipsychotic concurrently. Two patients were prescribed a depot in addition to two oral antipsychotics. The remaining patients were prescribed depot medication only. This practice of polypharmacy has no clear rationale, and can be particularly dangerous at high dose levels as the metabolism of antipsychotics when given together is unpredictable and can lead to extreme blood plasma concentrations. Any ad-

Table 2. Survey of consultant psychiatrist opinions of the Royal College of Psychiatrists' guidelines

Questions	Consultant responses (*n*=12)
1. Were you aware of the College's guidelines on the use of high-dose neuroleptic medication?	92% Yes 8% No
2. In your experience, in what percentage of patients is high-dose treatment warranted?	55% Less than 1% of patients 20% Less than 5% of patients 27% Less than 10% of patients
3. In cases where high-dose treatment is warranted, are your patients monitored in line with the College's guidelines?	64% Said they don't have patients on high-dose treatment 27% Yes 8% No
4. What do you feel are the practical limitations to the implementation of the guidelines?	35% None 27% Patient adherence 18% Time/resources 9% Problems obtaining second opinion 9% Difficulties following up patients
5. In terms of safeguarding the patients' health, which of the College's guidelines do you feel are of most clinical importance (respondants were not restricted to one guideline)?	73% Regular electrocardiogram checks 45% Health contra-indications to high-dose treatment 45% Potentially harmful polypharmacy 45% Regular general health checks performed 45% Written consent obtained 36% Dosage increased gradually 27% High dosage discussed with team
6. Which of the guidelines do you feel of least clinical importance?	45% All important 18% Regular general health checks performed 18% Second opinion sought 18% High-dose treatment discussed with team

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verse consequences of high-dose polypharmacy may be legally indefensible, particularly given our findings of low adherence to the College's safeguards. At re-audit three patients were still receiving high-dose polypharmacy. This is currently under review.

Adherence to the College's guidelines

In cases of high-dose treatment we found little adherence to the College's guidelines. This finding concurs with previous audits. Yorston & Pinney (1997) found poor compliance with guidelines regarding: regular ECG and general health checks; regular progress review; multi-disciplinary team involvement; record kept of treatment decision; written consent obtained from the patient. Similarly, Krasucki & McFarlane (1996) found a very low rate of compliance (23%) with the guideline advising regular ECG checks for patients receiving high-dose medication.

This general lack of adherence to the College's guidelines suggests that they have had limited success in improving clinical practice. In our region, this finding is not due to a lack of awareness of the College's guidelines as all of the consultants who were included in the audit were aware of them, as were 92% of the wider sample of consultants who were surveyed. This concurs with the findings of Yorston & Pinney (1997) who reported that even in cases where few of the guidelines were followed, consultants did express an awareness of them.

Perhaps the lack of compliance with the guidelines reflects practical limitations on their application. Indeed 64% of consultants surveyed felt that this was the case: patient compliance; time/resources; problems obtaining a second opinion; and difficulties following up patients were all reported as hindering compliance with the guidelines. Practical difficulties such as these have been reported in previous audits. Sillifant *et al* (1997) had to sedate two patients with learning disabilities before routine investigations could be carried out. Similarly, ECG technicians and equipment had to be borrowed from another trust. Furthermore, in the audit by Krasucki & McFarlane (1996) some doctors knew that ECG should be carried out on patients on high doses, but reported they did not have time to get the apparatus to the ward to do it.

Another possible explanation for non-compliance to the guidelines may be that consultants were unaware of their patients who were receiving high-dose treatment. This suggestion is consistent with our study findings because some consultants reported that they did not have any patients on high-dose treatment, whereas our audit revealed that they did. This lack of awareness of patients on high-dose treatment may occur in circumstances where patients receive both oral and depot medication and the consultant does not calculate total dosage. In addition, with case-loads constantly changing it may be sometimes difficult to keep track of the medication of all the patients within a practice. There is some support for this suggestion in our study as the consultant psychiatrist who had the largest number of high-dose cases (seven) also had the largest case load, which included a recent influx of the patients from a colleague who had left the trust.

Recommendations for practice

It is hoped that the use of high-dose antipsychotics, particularly in combination, will fall further, and that the guidelines on monitoring of patients on high doses will eventually be rendered obsolete. Until then it is incumbent on consultant psychiatrists to manage their workload in order that such patients are not missed, and that attempts are made to reduce both dose and polypharmacy while ensuring that the guidelines are followed as closely as possible.

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