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Psychiatric Bulletin (2002), **26**, 170–172

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Co-prescribing of atypical and typical antipsychotics – prescribing sequence and documented outcome

AIMS AND METHOD

To evaluate patterns of antipsychotic co-prescription and to establish documented outcome, we reviewed 1441 in-patient and community prescriptions written in a large mental health trust. For patients co-prescribed regular atypical and typical antipsychotics for longer than 6 weeks, medication histories were taken and case notes examined to determine sequence of prescribing, documented outcome and reasons for co-prescription.

RESULTS

Fifty-three patients had been co-prescribed aytpical and typical antipsychotics for more than 6 weeks. In 62% of cases the atypical drug had been prescribed first and a typical drug added later. The most frequently documented reason for co-prescription was that symptoms persisted when prescribed a single antipsychotic. Clinical outcome was documented for 64% of patients: 45% of the total number treated showed some improvement, with seven of 53 patients noted to have shown improvements in psychotic symptoms.

CLINICAL IMPLICATIONS

Co-prescription of aytpical and typical antipsychotics often occurs as a consequence of poor outcome with single drug treatment. In this study there was minimal evidence to suggest that co-prescription improved outcome to an important extent. There remains little support for co-prescription of antipsychotics but considerable evidence to suggest that such practice worsens adverse effect burden. Co-prescription of atypical and typical antipsychotics should be avoided in all but very exceptional circumstances.

In practice, typical and atypical antipscyhotics are commonly co-prescribed (Ereshefsky, 1999; Taylor *et al*, 2000*a*) despite clear evidence that such prescribing substantially increases the use of anticholingeric medication (Taylor *et al*, 2000*a*,*b*). This increased frequency of anticholinergic prescribing is an accepted marker of an increased frequency or severity of acute extrapyramidal side-effects (EPS), presumably brought about by additional blockade of striatal dopamine D_2 receptors (Kapur *et al*, 2001).

Very few data support the supposed therapeutic benefits of atypical–typical co-prescribing. As far as we are aware, only one randomised controlled trial has been conducted in this field (Shiloh *et al*, 1997) and this showed only a modest benefit for the addition of sulpiride to clozapine therapy. Other supporting data are rather less compelling (Yuzda, 2000), being derived largely from case studies or case series (e.g. Mowerman & Siris, 1996).

Thus, co-prescription of atypical and typical antipsychotics continues to be widespread in the face of weak evidence of benefit and rather stronger evidence of a deleterious effect on tolerability. Little or nothing is known of the reasoning behind decisions to co-prescribe, the sequence of prescribing or of the documented outcome of co-prescribing in everyday practice.

This study was undertaken to evaluate these elements of co-prescribing of atypical and typical antipsychotics.

The study

In the first quarter of 2001 we reviewed all prescriptions written for patients of the South London and Maudsley NHS Trust. This review included all in-patients and community patients whose medication was supplied by trust pharmacies, but excluded out-patients and patients obtaining medication from community pharmacies.

All patients co-prescribed regular atypical antipsychotics with any other regular antipsychotic for longer than 6 weeks at full treatment doses were identified. For these patients, prescribing details and medication histories were recorded and patient notes examined to determine demographic data, documented reasoning for co-prescribing and documented outcome.

Findings

We examined 1441 prescriptions and uncovered 53 patients (4%) fulfilling the criteria above. Their mean age

https://doi.org/10.1192/pb.26.5.170 Published online by Cambridge University Press

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Table 1. Details of first and second antipsychotic prescribed

First antipsychotic prescribed	*n*	Second antipsychotic added	*n*
Clozapine	21	Amisulpride	10
Olanzapine	9	Sulpiride	9
Quetiapine	2	Olanzapine	9
Risperidone	1	Risperidone	7
Flupentixol decanoate	5	Haloperidol	4
Fluphenazine decanoate	3	Droperidol	4
Haloperidol decanoate	3	Clozapine	3
Zuclopenthixol decanoate	3	Quetiapine	3
Pipotiazine palmitate	1	Clozapine	3
Droperidol	3	Pipotiazine palmitate	2
Chlorpromazine	1	Chlorpromazine	1
Sulpiride	1	Thioridazine	1

Table 2. Documented reasons for co-prescribing

	n	%
Residual symptoms on single antipsychotic	35	66
Adverse effects of typical drug	5	9
Patient request	3	6
Adverse effects of atypical drug	2	4
Non-compliance with oral medication	2	4
Different mechanism of action required	1	2

was 40.5 years (range 21–71) and 34 (64%) were male. All had a diagnosis of schizophrenia or schizoaffective disorder.

In 33 patients (62%) an atypical antipsychotic had been prescribed first and another antipsychotic added to it. Clozapine was first prescribed in 21 of these patients, olanzapine in nine, quetiapine in two and risperidone in one. For the other 20 patients (38%) a typical antipsychotic was first prescribed (depot 15, oral typical five patients) (see Table 1 for details).

The reason for co-prescribing was documented for 48 (91%) patients. Documented reasons are given in Table 2.

Clinical outcome of co-prescribing was documented for 34 (64%). Overall, 24 patients (45%) were noted to have shown some improvement in any symptom domain. Documented evidence of improvement in psychotic symptoms (delusions, hallucinations and thought disorder) was noted in seven cases (13%). Psychotic symptoms were clearly not improved in 27 patients (51%). In one case (2%) an improvement in adverse effects was documented. For 10 patients (19%) documentation clearly indicated that no improvement of any kind had been observed.

Comment

The main findings of this study were that co-prescription was undertaken largely in an attempt to improve symptoms and that clinical outcome, where documented, was variable but unremarkable. Where response to treatment was documented, improvements in psychotic symptoms were uncommon. Indeed, most documented changes were trivial (examples included: sleep improved, more settled and less distracted).

As discussed earlier, atypical–typical co-prescription is for the most part poorly supported by published literature. However, augmentation of clozapine with sulpiride has some clinical trial backing (Shiloh *et al*, 1997) and attempted augmentation with any drug is probably supportable if clozapine has proved insufficiently effective alone (Chong & Remington, 2000). In 21 of 53 cases examined here, another drug was added to clozapine therapy; of these, only five had had documented improvements in psychotic symptoms. In another 12 cases, typical drugs were added to existing atypical (non-clozapine) therapy, largely in an attempt to improve psychotic symptoms. Improvement in psychotic symptoms was documented in only two cases. Clozapine may have been a more appropriate choice in these cases, since only one of these 12 had previously received the drug.

In seven of 53 cases studied here, co-prescription had arisen from an apparent desire to improve adverse effects. In most cases it was clear that the intention was to withdraw the poorly tolerated drug once the second drug had been established, but this had not been done. In only one patient was there documented improvement in adverse effects – the addition of olanzapine to fluphenazine depot reduced the severity of oro-facial dyskinesia.

Documentation of clinical change was poor – outcome could not be determined for 34% of patients in the sample. Where clinical change was documented, it was limited to brief descriptions of alterations in symptoms or adverse effects. In no case was monitoring or documentation systematic and no validated rating scales of any kind had been used.

In this study, co-prescription of atypical and typical antipsychotics rarely led to documented improvement in psychotic symptoms. Augmentation of clozapine with, for example, sulpiride, is probably valid where clozapine alone has failed, but all other co-prescription should probably be avoided. Prospective, randomised evaluations of antipsychotic polypharmacy are needed.

https://doi.org/10.1192/pb.26.5.170 Published online by Cambridge University Press

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Declaration of interest

D.T. has received research funding from various manufacturers of atypical antipsychotics and the Department of Health, and consultancy fees and honoraria for presentations received from AstraZeneca, Janssen–Cilag, Novartis, Pfizer and Eli Lilly. S.M. has received consultancy fees and honoraria for presentations from Eli Lilly and Novartis; S.M. has received research funding from Pfizer; and E.W. has received honoraria for presentations from Eli Lilly.

References

CHONG, S. A. & REMINGTON, G. (2000) Clozapine augmentation: safety and efficacy. *Schizophrenia Bulletin*, **26**, 421–440.

ERESHEFSKY, L. (1999) Pharmacologic and pharmacokinetic considerations in choosing an antipsychotic. *Journal of Clinical Psychiatry*, **60**(Suppl 10), 20–30.

KAPUR, S., ROY, P., DASKALAKIS, J., *et al* (2001) Increased dopamine D2 receptor occupancy and elevated prolactin level associated with addition of haloperidol to clozapine. *American Journal of Psychiatry*, **158**, 311–314.

MOWERMAN, S. & SIRIS, S. G. (1996) Adjunctive loxapine in a clozapine resistant cohort of schizophrenic patients. *Annals of Clinical Psychiatry*, **8**, 193–197.

SHILOH, R., ZEMISHLANY, S., AIZENBERG, D., *et al* (1997) Sulpride augmentation in people with schizophrenia partially responsive to clozapine. A double-blind, placebo-controlled study. *British Journal of Psychiatry*, **171**, 569–573.

TAYLOR, D., MACE, S., MIR, S., *et al* (2000*a*) A prescription survey of the use of atypical antipsychotics for hospital inpatients in the United Kingdom. *International Journal of Psychiatry in Clinical Practice*, **4**, 41–46.

—, MIR, S. & KERWIN, R. (2000*b*) Prescribing in schizophrenia. Evaluating the effect of introducing a new treatment protocol. *Psychiatric Bulletin*, **24**, 106–108.

YUZDA, M. S. K., (2000) Combination antipsychotics: what is the evidence? *Journal of Informed Pharmacotherapy*, **2**, 300–305.

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Psychiatric Bulletin (2002), **26**, 172–174

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Use of atypical antipsychotics by consultant psychiatrists working in forensic settings

AIMS AND METHOD
Atypical antipsychotics have less neurological side-effects than the older drugs but are only available as oral preparations. This may limit their use in forensic patients. We sent a postal questionnaire to all consultant psychiatrists working in forensic settings in the UK to determine their views.

RESULTS
The response rate was 60%. Respondents tended to overestimate the benefits and underestimate the side-effects of the atypical antipsychotics. The majority often prescribed atypical antipsychotics and depots together. Psychoeducation and serum level monitoring were used to optimise/monitor compliance by 50%.

CLINICAL IMPLICATIONS
Using atypical antipsychotics as monotherapy is problematic in forensic settings. The extent of polypharmacy means that patients may experience the side-effects of both typical and atypical antipsychotics. More could be done to facilitate and monitor compliance.

The atypical antipsychotics have equivalent efficacy to the older drugs but less neurological side-effects. This has led some to recommend atypical antipsychotics as first-line agents in schizophrenia, although this stance is controversial (Geddes *et al*, 2000). Clozapine is uniquely effective in treatment-resistant schizophrenia (Kane *et al*, 1988).

The National Service Framework for Mental Health (Department of Health, 1999) states that all patients have the right to receive the most effective treatment and further recommends that all patients should be assessed to see if they might benefit from the reduced neurological side-effects of the newer drugs.

In the UK, forensic psychiatrists provide care primarily for mentally disordered offenders, most of whom are referred through the criminal justice system. Although such patients may have lengthy hospital admissions, the majority are eventually cared for in the community.

Atypical antipsychotics are currently available only as oral formulations. This complicates their use in forensic settings where the potential consequences of non-compliance can be significant, both for the patient and for others. Both clozapine and risperidone have been used with some success in the special hospitals (Special Hospitals' Treatment Resistant Schizophrenia Research Group, 1996), but little is known about the use of these drugs by psychiatrists based in medium-secure settings or caring for community-based forensic patients.

We aimed to survey the views and practice of all consultant psychiatrists working in forensic settings in the UK.

Method

We designed a semi-structured questionnaire that explored prescribing patterns for in-patients and

https://doi.org/10.1192/pb.26.5.170 Published online by Cambridge University Press