

How much medicine is prescribed for the side effects of psychotropics?

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- **OBJECTIVE** — To examine the nature and frequency of medicines prescribed to forensic and rehabilitation inpatients to manage the side effects of psychotropic medicines.
- **SUBJECTS AND SETTING** — 153 inpatients in the forensic and rehabilitation service of a large, independent psychiatric hospital.
- **DESIGN** — A retrospective review of drug charts and case notes and a structured interview with consultant psychiatrists.
- **RESULTS** — Of the 143 patients prescribed psychotropics, 94 (65.7 per cent) were prescribed medicines for side effects related to these drugs. Prescription of side effect medicines was associated with a higher number of psychotropic prescriptions, prescription of antipsychotics (particularly in high doses), polypharmacy and prescription of clozapine. The most common side effect medicines were those prescribed to treat extrapyramidal motor disorders (in 30.1 per cent of patients), constipation (24.5 per cent) and hypersalivation (22.4 per cent). In 38.2 per cent of cases the psychiatrist said that it would be unwise to continue with the psychotropic if the side effect medicine had to be discontinued.
- **CONCLUSION** — When antipsychotics, especially clozapine, and multiple psychotropics are prescribed, further medicines may be required to manage their side effects. Sometimes side effect medicines will be necessary to enable safe continuation of the psychotropic. This has implications for informed patient consent. Pharmacists have an important clinical role in the multidisciplinary team, which includes advising on the management of the side effects of psychotropics.

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All medicines have side effects but some are more serious than others and may lead to withdrawal of the medicine or prescription of other medicines to counteract the adverse effects. Psychotropic medicines can often be identified as the definite or probable cause of side effects (eg, clozapine causes hypersalivation and typical antipsychotics cause extrapyramidal side effects), or as a contributing factor to a side effect or condition (eg, atypical antipsychotics contribute to weight gain and glucose intolerance). The side effects of psychotropics can cause significant patient distress,^{1,2} reduce compliance^{3,4} and lead to the development of serious physical disorders.⁵

We are unaware of any other published studies examining medicines prescribed for the side effects of psychotropics.

Method

This study was approved by the hospital's medical advisory and clinical audit committees.

St Andrew's Healthcare, Northampton, is a 450-bed charitable psychiatric hospital providing inpatient treatment for patients with a wide variety of psychiatric disorders. We studied patients in the forensic and rehabilitation service (nine locked wards and two open wards). Most of these patients are detained under the Mental Health Act (1983) and have been transferred from other psychiatric hospitals because they require treatment and rehabilitation in a secure setting. Approximately half of the patients have been compulsorily admitted to psychiatric hospital via the criminal justice system.

In March 2006, details of current, regular and as required prescriptions were obtained from each patient's current drug chart, and demographic data were collected from the patients' case notes.

Patients prescribed high dose antipsychotics were identified using the method described by Yorston and Pinney.⁶ The dose of each regular antipsychotic a patient was prescribed was expressed as a percentage of its British National Formulary maximum recommended dosage. If the patient was prescribed more than one regular antipsychotic, the percentages were added together to give a total percentage dose. A patient was considered to be prescribed high dose antipsychotics if the total percentage dose exceeded 100 per cent.

The clinical pharmacist interviewed each patient's consultant psychiatrist, inquiring about the patient's clinical diagnosis, which medicines were being prescribed for the direct treatment of the mental disorder and which were being prescribed to treat the side effects of psychotropics. For example, sodium valproate was classed as a psychotropic when used as a mood stabiliser, but where prescribed as an antiepileptic for clozapine-induced seizures it was classed as a side effect medicine. Medicines were only classed as side effect medicines if the psychiatrist believed the psychotropic was definitely or probably causing or contributing to the side effect in question. The psychiatrist was also asked about the nature of the side effects and the relationship of the psychotropic to the side effect medicine, for example, whether the psychotropic would have to be withdrawn if the side effect medicine had to be discontinued.

Results

In March 2006 there were 153 inpatients in the forensic and rehabilitation service. Of these, 108 (70.6 per cent) were male. The median age was 35 years (range 21–60 years) and the median length of stay was 2.7 years (range 0.1–21.8 years). A total of 145 patients (94.8 per cent) were involuntary patients and 86 (56.2 per cent) had a diagnosis of schizophrenia. There were 10 patients who were not prescribed any psychotropics and were thus excluded from the subsequent analysis, leaving a study population of 143 patients.

Most patients (127, 83 per cent) were receiving regular antipsychotic medicine. A mood stabiliser was being taken by 49 patients (32 per cent) and an antidepressant by 57 (37.3 per cent). Of the patients prescribed psychotropics, 94 (65.7 per cent) were receiving medicine for the side effects of psychotropics and 49 (34.3 per cent) were not. Table 1 (p136) compares the characteristics of patients prescribed side effect medicines with those who were not, and the other medicines they were prescribed.

Prescription of side effect medicines appeared to be associated with a higher number of psychotropic prescriptions, being prescribed atypical, typical or high dose antipsychotics, being prescribed clozapine and antipsychotic polypharmacy.

In total, there were 180 prescriptions for atypical antipsychotics and 144 prescriptions

Table 1: Comparison of patients prescribed medicines for side effects with those not prescribed medicines for side effects (N=143)

Variable	Patients prescribed side effect medicine (N=94)		Patients not prescribed side effect medicine (N=49)	
	No.	%	No.	%
Male	72	76.6	26	53.1
Involuntary patient	88	93.6	48	98.0
Diagnosed with schizophrenia	74	78.7	18	36.7
Prescribed antipsychotics	92	97.9	35	71.4
Prescribed high dose antipsychotics	39	41.5	6	12.2
Prescribed two or more antipsychotics	52	55.3	8	16.3
Prescribed a typical antipsychotic	26	27.7	5	10.2
Prescribed an atypical antipsychotic	87	92.6	31	63.3
Prescribed clozapine	57	60.6	5	10.2
Prescribed a mood stabiliser	36	38.3	13	26.3
Prescribed an antidepressant	33	35.1	24	49.0
Other patient details				
Age in years	Median 35.5 (range 21–60)		Median 36 (range 22–56)	
Length of stay in years	Median 2.7 (range 0.1–21.8)		Median 2.7 (range 0.1–15.3)	
Number of regular plus as required psychotropics	Median 4 (range 1–7)		Median 3 (range 1–6)	

for the side effects of these drugs. There were 62 clozapine prescriptions and 124 prescriptions for clozapine-related side effect medicines. The corresponding figures for typical antipsychotics, antidepressants and mood stabilisers were 50:37, 63:9 and 53:1, respectively.

The nature of the side effects caused by psychotropics and details of the medicines prescribed to treat them are outlined in Table 2 (p137). The most common side effect medicines were those prescribed to treat extrapyramidal motor disorders, hypersalivation and constipation. Some patients were receiving multiple side effect medicines (median = 1.5, range 1–7).

In total, there were 191 prescriptions for side effect medicines. In each case the psychiatrist believed there was a definite link between the psychotropic, the side effect and the medicine for the side effect. In 85 (44.5 per cent) instances the psychiatrist said the side effect medicine was being used to

treat side effects that were definitely caused by a psychotropic. In 33 (17.2 per cent) instances the psychiatrist said the side effects were probably caused by a psychotropic and in 73 (38.2 per cent) instances the psychiatrist said a psychotropic was contributing to the condition for which the side effect medicine was being prescribed. In 73 (38.2 per cent) instances the psychiatrist said that if the side effect medicine had to be discontinued then the related psychotropic would probably or definitely have to be discontinued.

Discussion

In this survey, two-thirds of patients prescribed psychotropics were also prescribed one or more medicines for a wide variety of side effects. Antipsychotics, in particular clozapine, led to the prescription of most of the side effect medicines, especially when given in high doses or when multiple antipsychotics were prescribed. Clozapine is

known to cause unpleasant and potentially serious side effects.^{7,8} Antidepressants led to the prescription of relatively few side effect medicines and mood stabilisers even fewer. Most of the antidepressants that required prescription of side effect medicines were selective serotonin reuptake inhibitors. These have been linked to an increased risk of gastrointestinal bleeding and a need to co-prescribe gastroprotective medicines.⁹

The strength of the relationship between the psychotropic and side effect medicine varied. Sometimes the relationship was clear (eg, clozapine and hypersalivation) and sometimes the psychotropic was only contributory to the physical condition (eg, atypical antipsychotics and hyperlipidaemia). In over one third of cases the side effect medicine was integral to the treatment for mental illness and not purely for the patient's comfort, ie, if the side effect medicine had to be stopped the psychotropic would also have to be discontinued.

Table 2: Outline of the side effects experienced by patients prescribed psychotropics (N=143) and the medicine prescribed for these side effects

Side effect	Psychotropic(s) causing the effect	Medicines prescribed for side effect	No. of patients receiving side effect medicine(s) (%)
Extrapyramidal	Clozapine, olanzapine, risperidone, typical antipsychotics	Orphenadrine, procyclidine, trihexyphenidyl	43 (30.1)
Constipation	Amisulpride, carbamazepine, clozapine, olanzapine, SSRI antidepressants, typical antipsychotics, venlafaxine	Bisacodyl, ispaghula husk, lactulose, macrogols, senna, sodium docusate	35 (24.5)
Hypersalivation	Clozapine	Atropine, hyoscine, pirenzepine	32 (22.4)
High cholesterol	Clozapine, olanzapine, typical antipsychotics	Fenofibrate, statins	22 (15.4)
Dyspepsia/ gastrointestinal bleeding	Clozapine, SSRI antidepressants, venlafaxine	Compound alginates, proton pump inhibitors	13 (9.1)
Diabetes mellitus	Clozapine, olanzapine, quetiapine	Gliclazide, insulin, metformin, rosiglitazone	8 (5.6)
Seizures/myoclonus	Clozapine	Lamotrigine, sodium valproate	4 (2.8)
Weight gain	Clozapine	Orlistat, topiramate	2 (1.4)
Tachycardia	Clozapine	Atenolol, propranolol	2 (1.4)
Hypertension	Clozapine	Atenolol, ramipril	1 (0.7)

A previous study of our patient population reported that 33 per cent were overweight and 39 per cent were obese¹⁰ yet only two patients in the current study were prescribed weight reduction medicines. We believe there is reluctance by psychiatrists in the UK to prescribe such medicines, despite the increased morbidity and mortality associated with obesity. Pharmacists can advise psychiatrists about which antipsychotics are least likely to cause weight gain. However, the choice of antipsychotic may be limited for clinical reasons and the patient's history of response. In these circumstances

pharmacists can also suggest the appropriate prescription of weight reducing medicines. Pharmacists, in conjunction with dietitians, may also be able to assist patients with weight reduction strategies.

Implications The findings of this study have a number of implications. When selecting psychotropics, particularly antipsychotics, prescribers and pharmacists need to bear in mind that other medicines may be required to manage any side effects and to allow patients to continue safely to take the medicine. These medicines in turn have their own side effects which may compound the side effects of psychotropics already prescribed. For example, procyclidine prescribed for extrapyramidal symptoms, can worsen the anticholinergic effects of antipsychotics (eg, constipation). Since the prescription of side effect medicines increases the total number of medicines prescribed for a patient, the risk of drug interactions will also increase.

This study also has implications for informed patient consent. The National Institute for Health and Clinical Excellence guideline on bipolar disorder states that patients "should have the opportunity to make informed decisions about their care and treatment".¹¹ The NICE guidance on schizophrenia states that "the choice of

antipsychotic drug should be made jointly by the individual and the clinician responsible for treatment based on an informed discussion of the relative benefits of the drugs and their side effect profiles".¹² In order for patients to be fully informed, they need to be advised about the potential side effects of antipsychotics and that they may require further medicines to be prescribed.

For patients with treatment-resistant schizophrenia, the choice of antipsychotic is by definition reduced. NICE guidance on schizophrenia acknowledges this by recommending the early introduction of clozapine.¹² As we have shown, the use of clozapine frequently results in the prescription of multiple medicines for side effects. The cost implications of side effects also need to be considered. The side effect medicines themselves cost money, as does the additional pharmacy time spent monitoring prescriptions, advising patients and clinicians and dispensing the medicines.

Limitations

We acknowledge that this study has a number of limitations. It was a relatively small study carried out in a specialist inpatient setting. Many of the patients studied were long-stay and had a diagnosis of treatment-

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resistant schizophrenia. Its generalisability to the wider NHS is therefore limited. Since 62 of the patients in this study (40.5 per cent) were prescribed clozapine, this will have had a strong influence on the overall results, because clozapine is well known for its side effect profile.

In addition, it was not unusual for a patient to be on multiple medicines for side effects caused by clozapine. Findings may differ in other forensic rehabilitation units if there are fewer patients prescribed clozapine. A further limitation is that we did not take into account the doses of psychotropic medicines, apart from identifying patients on high dose antipsychotics.

Conclusion

We believe that pharmacists have an important clinical role in the multidisciplinary mental health team which includes advising on the management of side effects caused by psychotropics. Pharmacists have specialist clinical knowledge to advise psychiatrists on the appropriate use, choice and availability of medicines for side effect management.

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