Mental Health in Family Medicine 2013;10:29–36

Article

Improving blood and ECG monitoring among patients prescribed regular antipsychotic medications

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ABSTRACT

Aims and methods It is now well established that antipsychotic medications are associated with adverse effects such as metabolic dysfunction, hyperprolactinaemia and cardiac arrhythmias. We completed an audit cycle between 2008 and 2010 to assess whether the implementation of a high-visibility prompt and an educational programme would improve monitoring rates among patients prescribed regular antipsychotics admitted to a 59-bedded psychiatric hospital in West Sussex.

Results There was an improvement in monitoring rates for most audit standards. The greatest improvement was seen in measurement of random plasma glucose and cholesterol levels. Rates improved irrespective of the risk of metabolic dysfunction. However, prolactin measurement remained static and the ECG recording deteriorated.

Clinical implications There appears to be a growing awareness of the need to screen for metabolic dysfunction among patients prescribed regular antipsychotic medication. A high-visibility prompt and educational programme helps to increase monitoring rates. However, more needs to be done to improve the mortality and morbidity rates among this patient subpopulation.

Keywords: antipsychotic medication, metabolic dysfunction, monitoring

Introduction

It is now well established that severe mental illness (SMI) is associated with poorer physical health outcomes.[1] For example, people with schizophrenia die on average 10–15 years earlier than the general population, and the majority of this premature mortality is a result of cardiovascular risk.[2,3] Although it is true that the lifestyle choices of those with SMI contribute to the inflated cardiovascular risk, there is now firm evidence for the iatrogenic induction of metabolic syndrome by the use of regular antipsychotic medication.[4,5] Patients receiving regular antipsychotics show a two- to threefold increase in the incidence of metabolic dysfunction and a similar increase in the point prevalence of diabetes mellitus compared with the general population.[6,7]

Due to the mounting evidence for the metabolic side effects of antipsychotic medication, there has been increasing recognition of the need for effective monitoring of cardiovascular risk factors in this subgroup of patients.[8] In addition, antipsychotics may induce hyperprolactinaemia, with consequent adverse effects on sexual well-being and osteoporosis if treatment is prolonged.[9,10] Monitoring recommendations have been adopted by nationally recognised guidelines as well as being enshrined in the policy of several NHS trusts, including our own (details are available from the author on request).[11,12] However, several studies have demonstrated that such recommendations are poorly adhered to in community outpatient settings.[13,14] We wanted to examine equivalent monitoring rates among patients

prescribed regular antipsychotics who had been admitted to a local inpatient facility.

The admission of a person with SMI to a psychiatric hospital represents a unique opportunity for physical health checks to be carried out. Unfortunately, this opportunity is rarely grasped.[15] Research has begun to focus on the underlying causes of the poor uptake of guidelines, and has identified barriers to monitoring protocols, including uncertainty about clinical responsibility, lack of confidence in interpreting the results, and limited access to basic medical equipment.[14]

Various methods have emerged to combat these barriers, with varying degrees of success. Runcie *et al* showed that the circulation of an algorithm among doctors, drawn up with the consensus of senior psychiatrists, endocrinologists, dietitians and pharmacists, did little to improve monitoring rates among psychiatric inpatients.[16] However, a one-page monitoring prompt and educational programme worked effectively among community outpatients.[17] Both of these studies were conducted between 2004 and 2005, and the interventions were implemented over 5 years ago. Since then, there appears to have been a growing awareness among psychiatrists of the impact of antipsychotic prescribing. We wanted to investigate whether a similar high-visibility prompt and a low-grade educational programme would improve monitoring patterns for psychiatric inpatients.

Methods

An audit cycle was implemented in a 59-bedded psychiatric hospital in West Sussex between November 2008 and January 2010. The hospital consists of four acute wards (two general adult wards, one ward for older adults with functional mental health problems, and one ward for adults with organic psychiatric disorders).

All patients resident within the hospital on 8 November 2008 were included in the initial audit. Responsible clinicians had been made aware of the intention to perform the audit, and consent had been obtained to examine the medical records of their patients, but the exact date of the audit was not revealed. Patients were only excluded if they were not prescribed regular antipsychotics. Patients were not excluded on the basis of age or diagnosis, or if they were administered depot antipsychotics, to ensure greater external validity.

A data collection tool was used to gather information on patient demographics, diagnoses, antipsychotic prescribed, reason for antipsychotic prescription, baseline blood tests and ECG monitoring, and continuation blood tests. Information was collected by retrospective inspection of the clinical records and computer-held records of blood tests. The latter allowed blood monitoring information to be gathered from several years previously, but was limited to monitoring practices within the catchment area of our hospital.

Monitoring patterns were investigated for adherence with the *Maudsley Prescribing Guidelines*, 9th edition and also with the local recommendations of the Sussex Partnership NHS Foundation Trust.[11,12] It was agreed that full blood count (FBC), urea and electrolytes (U&Es), liver function tests (LFTs), thyroid-stimulating hormone (TSH) levels, corrected calcium (CCa) levels, random plasma glucose (RPG) levels, fasting cholesterol (Chol) levels, prolactin (PRL) levels and an electrocardiogram (ECG) should be performed in all patients at baseline and annually thereafter. Our trust advises the measurement of baseline TSH and CCa, due to the effects that abnormalities in these two biochemical markers can have on cardiac rhythm, although these tests are not included in the monitoring regime recommended in the *Maudsley Prescribing Guidelines*, 9th edition. For patients on clozapine, the audit standard required FBC to be performed according to the guidelines of the issuing authority.

It was considered that glucose should be measured at 1 month, 6 months and yearly thereafter for patients newly started on clozapine or olanzapine, and that cholesterol should be monitored 3-monthly for the first year in all patients on second-generation antipsychotics. The number of patients in whom this standard could be evaluated was limited, as only a small proportion of patients were admitted during the first-year window following antipsychotic prescription. Similarly, annual monitoring practices could only be evaluated in those who had been administered regular antipsychotic medication for more than a year. These continuation and annual blood checks are often performed in the community. Although it is recommended that electrocardiograms should be performed annually, we did not investigate whether these were being carried out, as general practices often record follow-up electrocardiograms and we did not have access to primary care records.

Following the first audit, the results were presented to the local consultant body and head pharmacist. A discussion was held to brainstorm methods to improve monitoring practices. It was agreed that a one-page monitoring prompt would be drawn up and posted in all wards in the doctors' office, the nurses' office and the clinical areas (see Figure 1). Access to medical equipment was not a major barrier to monitoring practices in our hospital,

Protocol for monitoring of patients on *regular* antiphychotics

Remember: It is the duty of the **prescribing doctor** to ensure that drugs *they* have prescribed are monitored appropriately.

BLOODS & TESTS	Baseline	Monthly monitoring 1	2	3	4	5	6	7	8	9	10	11	Annually	Thereafter
FBC	■	Clozapine: FBC weekly for 18 weeks					Clozapine: fortnightly from 18 weeks until the end of one year						■	Cloz: monthly
U&Es	■												■	Annually
LFTs	■												■	Annually
TSH	■												■	Annually
CCa^{2*}	■												■	Annually
Glucose	■	Cloz Olan					■						■	Annually Cloz: 6mts
Lipids	■			■			■			■			■	Annually
PRL	■												■	Annually
ECG	■	Perform ECG 3-monthly if high risk of cardiac disease, polypharmacy or high doses. ECG is essential when starting haloperidol *and with every change in its dosage.*											■	Annually

KEY: ■ = perform the test; Cloz = clozapine; Olan = olanzapine; PRL = prolactin level; CCa^{2*} = corrected calcium level.

Specific exclusions from monitoring:
Haloperidol: annual lipids and annual glucose
Amisulpride/sulpride: LFTs

Clozapine: PRL
Olanzapine: <20mg daily: PRL
Aripiprazole: does not need monitoring of any lipids, PRL or ECG.

The guidelines regarding ECGs:
QT_c > 500ms is an *absolute* contraindication for any antipsychotic except aripiprazole.
QT_c > 450ms in men and > 470ms in women is a *relative* contraindication. In this case, ECGs need to be performed every 3 months.

High risk patients are those with positive family histories of cardiac arrhythmias, or those with other risk factors for cardiac disease.

Figure 1 One-page prompt displayed in highly visible clinical areas to improve monitoring of patients on regular antipsychotics.

although training in the use of such equipment, uncertainty about clinical responsibility, and lack of confidence in interpreting the results were, so the prompt concentrated on these factors. In addition, all new trainees were educated during their induction programme about the importance of monitoring patients on regular antipsychotics with a half-hour talk.

Monitoring practices were re-audited on 23 January 2010. The results were analysed using Microsoft Windows Excel 2007 (version 12) and an online statistical calculator (GraphPad QuickCalcs).[18] The chi-squared test of independence (with Yates' correction due to the small sample sizes) or Fisher's exact test were used to compare the categorical variables as appropriate. Fisher's exact test was used when at least one cell had a value less than 5. Two-sided *P*-values were generated for all comparisons, except where no change was seen between the 2008 and 2010 audits. Statistical significance was taken to be a *P*-value of less than 0.05.

Results

Of the 59 inpatients in the first audit, 36 individuals were on regular antipsychotic medication. These represented about half of all patients on the older persons' wards, and over two-thirds of those on the general adult wards. When the audit was repeated 14 months later, the 13-bedded ward for adults with organic mental illnesses had been temporarily closed. However, of the total of 46 inpatients, 38 (82.6%) were prescribed regular antipsychotic medication. The demographics of the patient populations were similar for the two audits (see Table 1).

In 2008, three patients (8.3%) had been prescribed more than one regular antipsychotic. It was difficult to establish the date of first antipsychotic prescription in 11 patients (28.2%), either because the medication had been prescribed several years ago or because the patients had moved into the local area from a long distance. However, these patients were still investigated to ensure that annual blood monitoring was being performed. In 2010, again three

Table 1 Demographics of the two audit populations

Baseline data	2008 (n = 36)	2010 (*n* = 38)
Mean age (SD) (years)	55.6 (20.35)	54.6 (17.22)
Men, *n* (%)	18 (50.0)	16 (42.1)
Women, *n* (%)	18 (50.0)	22 (57.9)
White British ethnicity, *n* (%)	35 (97.2)*	35 (92.1)†
Median duration of admission at time of audit (days)	24 (range 1–318)	30 (range 1–249)
Most common antipsychotics used (grouped according to risk of metabolic dysfunction)		
Olanzapine, *n* (%)	15 (38.5)	12 (30.0)
Quetiapine, *n* (%)	10 (27.8)	10 (25.0)
Risperidone/amisulpride/sulpiride, *n* (%)	5 (12.8)	5 (12.5)
First-generation antipsychotics‡, *n* (%)	5 (12.8)	4 (10.0)
Most common diagnoses		
Schizophrenia/schizoaffective disorder, *n* (%)	14 (38.9)	12 (31.6)
Bipolar affective disorder, *n* (%)	5 (13.9)	9 (23.7)
Unipolar depression, *n* (%)	7 (19.4)	6 (15.8)
Dementias, *n* (%)	7 (19.4)	2 (5.3)
Most common reason cited for antipsychotic use		
Psychotic symptoms, *n* (%)	25 (69.4)	27 (71.1)
Agitation, *n* (%)	8 (22.2)	11 (28.9)

* One patient was of Mediterranean ethnicity.
† One patient was Black African, one was Mediterranean and one was Israeli Jewish.
‡ The most common first-generation antipsychotic used was chlorpromazine, but others were prochlorperazine, trifluoperazine, benperidol, zuclopenthixol, flupenthixol, fluphenazine and pipothiazine.

patients were prescribed more than one regular antipsychotic (7.9%). It was difficult to establish the date of first antipsychotic prescription in 13 patients (34.2%).

Seven patients with dementia were prescribed antipsychotic medication in 2008. This decreased to two patients in 2010, probably due to the temporary closure of the ward for older adults with organic mental illness.

Baseline FBC, U&Es and LFTs were measured in approximately 75% of patients in both audits, and there was a slight improvement in uptake in the second audit (see Table 2). Glucose and cholesterol levels were monitored at baseline in only 44% and 16%, respectively, of patients in the first audit, although both of these showed significant improvements by the second audit. In the first audit only four patients (16.0%) had had both random plasma glucose and fasting cholesterol levels measured, but this figure had increased to 13 patients (52.0%) by the second audit. None of the patients had had their prolactin level measured at baseline in the first audit, and only two patients had had it measured in the second audit. The proportion of patients who had had a baseline ECG performed actually decreased between the first and second audits, from 40% to 20%.

The proportion of patients in whom random plasma glucose and fasting cholesterol levels were measured 3-monthly after starting antipsychotic medication increased from 41.7% and 25%, respectively, in the first audit to 66.7% for both in the second audit. Similarly, there were substantial increases in the annual measurement of blood parameters, except for prolactin monitoring, which remained very low in both audits.

Baseline and annual monitoring rates for metabolic dysfunction and cardiovascular risk were not significantly affected by the risk profile of the antipsychotic prescribed either in 2008 or in 2010, except for the annual cholesterol monitoring rate, which was paradoxically lower for the high-risk antipsychotics than the all-antipsychotic rate in 2010 (see Figure 2).

Table 2 Proportion of patients in whom monitoring tests were carried out according to guidelines

	November 2008	January 2010
Baseline tests	(*n* = 25), *n* (%)	(*n* = 25), *n* (%)
FBC	18 (72.0)	20 (80.0)
U&Es	19 (76.0)	20 (80.0)
LFTs	20 (80.0)	20 (80.0)
RPG	11 (44.0)	13 (52.0)
Chol	4 (16.0)	14 (56.0)**
TSH	15 (60.0)	16 (64.0)
CCa	6 (24.0)	9 (36.0)
PRL	0 (0.0)	2 (8.0)
ECG	10 (40.0)	5 (20.0)
Tests in the first year	(*n* = 12), *n* (%)	(*n* = 9), *n* (%)
RPG within 6 months	5 (41.7)	6 (66.7)
3-monthly Chol checks	3 (25.0)	6 (66.7)*
Annual tests	(*n* = 16), *n* (%)	(*n* = 10), *n* (%)
FBC	10 (62.5)	8 (80.0)
U&Es	12 (75.0)	8 (80.0)
LFTs	11 (68.8)	7 (70.0)
RPG	8 (50.0)	8 (80.0)
Chol	4 (25.0)	6 (60.0)
PRL	1 (6.3)	0 (0.0)
Clozapine tests	(*n* = 2), *n* (%)	(*n* = 6), *n* (%)
FBC†	2 (100.0)	6 (100.0)
RPG‡	0 (0.0)	0 (0.0)
Chol§	0 (0.0)	0 (0.0)

* $\chi^2 = 2.143$ ($P = 0.087$), ** $\chi^2 = 7.031$ ($P = 0.007$).
† Weekly for 18 weeks, then fortnightly for 34 weeks, and monthly thereafter.
‡ One month after starting clozapine, and then again after 4 to 6 months.
§ Every 3 months after starting clozapine for the first year.

FBC, full blood count; U&Es, urea and electrolytes; LFTs, liver function tests; RPG, random plasma glucose; Chol, cholesterol; TSH, thyroid-stimulating hormone; CCa, corrected calcium; PRL, prolactin; ECG, electrocardiogram.

Measurement of appropriate FBC was achieved in all patients on clozapine therapy, most probably due to the restrictions placed on clozapine administration by the issuing authority. However, no patients had their random plasma glucose or fasting cholesterol levels measured in the first year after starting clozapine therapy as recommended.

Conclusions and discussion

Our audit suggests that the use of high-visibility prompts and a low-grade educational programme improves inpatient monitoring of individuals on regular antipsychotic medication. The greatest improvements were seen in the monitoring of cholesterol and random plasma glucose levels. The former

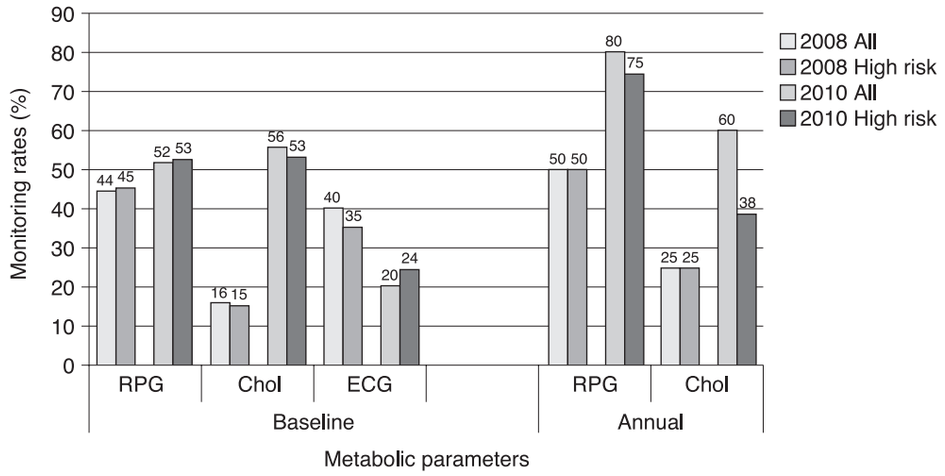

Figure 2 Change in monitoring of metabolic parameters: comparison of antipsychotics with highest risk of metabolic dysfunction with all antipsychotics.

achieved statistical significance at baseline, and almost reached statistical significance for the 3-monthly checks. It was found in the second audit that in some patients glycosylated haemoglobin had been measured rather than fasting or random plasma glucose levels. We did not consider these patients to have met the audit standard, as the diagnosis of diabetes mellitus is based upon plasma glucose levels, and glycosylated haemoglobin is more a measure of glycaemic control in patients with diagnosed diabetes, according to World Health Organization guidance.[19] However, these findings lend support to our view that there is a growing awareness among psychiatrists of the metabolic side effects of the second-generation antipsychotic medications.

The monitoring rates were not affected by the risk profile of the antipsychotics prescribed, in that the high-risk antipsychotics were not more likely to prompt greater monitoring (for metabolic dysfunction at least). This suggests that clinicians were following guidelines rather than targeting monitoring based on clinical need, perhaps reflecting the observation that it is often the junior doctors within a team who are responsible for monitoring the physical well-being of their patients.

Worryingly, seven (out of a total of 16) patients with dementia in 2008 had been prescribed antipsychotic medication. Low-dose first-generation antipsychotics were favoured in this group, generally to control the behavioural and psychological symptoms of dementia. The advice of the Committee on Safety of Medicines, which warned of a clear increase in the risk of stroke with the use of olanzapine and risperidone in elderly people with dementia, was slow to filter through to prescribing clinicians until it was made a national priority in 2009.[20,21] This may explain the relatively high rate of use of antipsychotic medications on the dementia wards in the first audit round. However, the very low rates of cardiovascular and metabolic monitoring in this patient group are a serious cause for concern. The considerable fall in antipsychotic prescribing for people with dementia between 2008 and 2010 can be explained by the closure of the ward serving this population, rather than by growing clinical awareness and consideration.

Prolactin measurement was poorly performed in both the 2008 and 2010 audits, perhaps due to the less well publicised warnings about its risks and a lack of awareness of the method of screening for hyperprolactinaemia. During the course of the first audit round it was found that one patient (who was being prescribed quetiapine) had not had their prolactin level measured for at least 2 years, despite the fact that it had been raised to more than six times the normal range in 2002, placing this patient at higher risk of osteoporosis, menstrual irregularities and sexual dysfunction.

The recording of ECGs at baseline was poor, and deteriorated further between 2008 and 2010. We re-evaluated the clinical records following this finding, and discovered that ECGs had been requested in 18 patients (out of a total of 25) in the second audit, but only performed in 5 patients. On questioning clinical staff about the poor uptake, the most common explanation cited was lack of expertise in performing ECGs. It was noted in 2010 that there had been an influx of newly trained nurses who had yet to gain clinical experience, which may partly explain the decline in ECG performance. However, part of the responsibility for monitoring lies with

the doctors who, although they were requesting the ECGs, were not ensuring that they were being carried out.

Although our intervention brought about some improvement, we consider that further work is still needed to ensure that we are not causing our patients inadvertent harm by failing to monitor the side effects of antipsychotics. In many ways the highly visible dystonic reactions of the first-generation antipsychotics have been replaced by the often undetected, and potentially fatal, adverse effect of metabolic dysfunction with the second-generation medications.

Through discussion between junior doctors, consultant psychiatrists and the pharmacists we considered further methods that may be used to improve monitoring practices for patients prescribed antipsychotics. It was agreed that a simple one-page prompt should be placed within drug cards to ensure that blood and ECG parameters have been recorded as appropriate. This approach is currently in development and will be in addition to the high-visibility ward prompts and educational programme that are used as intervention within our own audit. Furthermore, we presented the findings to a regional consortium of senior clinicians and managers in order to raise awareness of the issue in all inpatient units throughout East and West Sussex. Given the implication that it is mainly junior doctors who monitor their patients' physical health, we would support interventions that are targeted downstream, such as the implementation of a clear and succinct national policy on physical health monitoring, as has been called for by Khokhar and Tosh,[22] and increased exposure to general medical training among junior psychiatrists, as has been suggested by Dr Yasir Abbasi.[23]

The uncertainty over whose responsibility it is to oversee follow-on antipsychotic monitoring is a major obstacle to increasing physical health checks among the most vulnerable. Vasudev and Martindale have highlighted the need to incorporate primary care professionals in continuing monitoring practices for those on regular antipsychotic medication in the community.[24] To illustrate this ambiguity, it emerged through discussion with our local general practice (GP) colleagues that they are not funded to perform ECGs in patients who have been prescribed cardiotoxic medication by secondary care services. This may not be a major difficulty for those prescribed such agents by hospital-based physicians, but as community mental health teams often do not have access to ECG machines, a conflict between responsibility and delegation arises. Again, cross-specialty guidance regarding the screening of physical well-being in people with mental illness may help to improve this situation, as would integration of physical health checks into the Quality and Outcomes Framework. The move towards clinical commissioning groups that are largely overseen by GPs may provide an opportune pathway for such processes to be implemented.

Strengths and limitations

We accept that our audit was underpowered due to the small sample size, and our analysis may therefore confer a type 1 error. One particular complication that we had to contend with was the closure of a ward, which was primarily used for patients who required admission for dementia, prior to the second audit. Thus we could not include as many patients with a diagnosis of dementia in the second audit as we did in the first. However, all other demographic indicators were similar (see Table 1). We were also unable to include the other physical markers of antipsychotic adverse effects, such as blood pressure and pulse monitoring, waist circumference and weight measurement, and body mass index calculations.

Despite these limitations, we feel that our data add to a growing body of evidence for the need to improve monitoring among patients who are prescribed antipsychotic medication. Most studies investigating this subject have been performed in outpatients, as most antipsychotic prescribing and monitoring is conducted in the community. This is one of very few studies we are aware of that have been performed in admitted patients, and to our knowledge it is the only study that attempts to assess both baseline monitoring practices within inpatients and follow-on monitoring practices within the community. Furthermore, many of these studies have been conducted in data sets from at least 5 years ago. Our study provides evidence that although awareness of metabolic side effects is increasing, monitoring practices have not changed sufficiently in the intervening years.

ACKNOWLEDGEMENTS

I wish to thank Dr Gerard Bagley for supporting the audit, and Dr Arun Kishore and Dr Richard Whale for proofreading the submission.

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CONFLICTS OF INTEREST

None.

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Submitted 15 August 2011
Accepted 29 April 2013