Full Length Research Paper

Adherence to metabolic monitoring guidelines in atypical antipsychotic treated subjects: Do physicians comply?

Jesjeet Singh Gill[1]*, Tan Jin Teong[1], Lee Hong Gee[2], Tan Jing Wen[2] and Rosy Jawan[3]

[1]Department of Psychological Medicine, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia.
[2]Department of Pharmacy, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia.
[3]Department of Obstetrics and Gynecology, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia.

Since the 1990s, the arrival of the new generation of antipsychotics, the atypical antipsychotics (AAP), heralded a new era in the management on psychotic patients as they are associated with much less side effects as the older drugs. However, the psychiatric community soon realized a new problem had emerged with these drugs, namely severe metabolic side effects. Several monitoring guidelines were soon published to guide treating physicians on how to deal with this issue. This study was aimed to assess adherence to the recommended guidelines by Malaysian doctors. Data concerning metabolic monitoring over 1 year were collected from 405 subjects newly started on AAP after June 2005, when the recommended guidelines were first implemented. Results showed that almost all the recommended tests/procedures were performed in less than 50% of patients during the recommended designated times. We recommend that the guidelines, which now serve only as a "guide", be made a compulsory practice to safeguard the health of our patients.

Key words: Atypical antipsychotics, metabolic syndrome, monitoring guidelines.

INTRODUCTION

The advent of the new generation of antipsychotics, the "atypical antipsychotics (AAP)" brought new hope in the field of psychiatry as they have been found to have equal therapeutic efficacy with the older conventional "typical antipsychotics" drugs but are associated with less extra-pyramidal syndrome, tardive dyskinesia and elevated prolactin (Rafael and Rey, 2002). However, after being in the market for several years, several undesirable metabolic side effects had surfaced. Dramatic weight gain, insulin resistance, impaired glucose tolerance, dyslipidemia, or the dreaded metabolic syndrome are major metabolic adverse effects reported to be associated with AAP (Ananth et al., 2004; Haddad and Sharman, 2007). There are currently six AAP drugs approved by the US Food Drug Association which are clozapine olazapine, risperidone, quetiapine, aripiprazone and ziprasidone, with different prevalence of metabolic adverse effects. Clozapine and olazapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia. Risperidone and quetiapine are reported to have intermediate metabolic side effects while ziprasidone and aripiprazole are reported to have little or no significant occurrence of weight gain, diabetes or dyslipidemia (ADA-APA-AACE-NAASO Consensus Statement, 2004). This severe metabolic side effects associated with AAP drugs which lead to elevated risk of cardiovascular disease and increased mortality have made baseline investigations and regular metabolic parameters monitoring essential in patients on these drugs (Poulin et al., 2005).

Several guidelines have been published to address this issue. All the published monitoring guidelines agree about the importance of baseline monitoring before starting antipsychotic medication, close follow-up for the first 3 to 4 months of treatment, with subsequent ongoing

---
*Corresponding author. E-mail: jesjeet@um.edu.my. Tel: +60379492068. Fax:+60379556477.

reevaluation. There was also agreement about systematic assessment of fasting plasma glucose, fasting lipid profile, weight and height (for body mass index), waist circumference, and blood pressure (Cohn and Sernyak, 2006). One of the most often cited published guidelines is the ADA-APA guidelines which has a broad medical representation and a practical monitoring structure useful to clinicians that fulfills most of the established monitoring goals.

Various studies had been conducted to assess the monitoring of metabolic abnormalities in patients on atypical antipsychotics drugs. However, many studies found that monitoring was still poor (Motsinger et al., 2006; Taylor et al., 2004). A prospective cohort study in Northeast England that studied 83 subjects on antipsychotics revealed that none of them were monitored for their BMI and waist circumference. Although 21% of the patients were identified with the presence of weight-problem, documented evidence of lifestyle advice was found in less than 10%, and only 7% were referred for further intervention. Fifty one percent of patients' blood glucose and lipid profile were not monitored during the follow-up period and only 27% of patient had received both blood glucose and lipid profile monitoring (Mackin et al., 2007).

Another study in London to assess the adherence to Maudsley Guidelines for 60 patients started on clozapine found that at the baseline monitoring, none of the patient fasting blood glucose was monitored while only 10% of patients were monitored for random blood sugar. HbAlc and lipid levels were monitored in only 2 and 5% of patients, respectively (Gul et al., 2006).

University Malaya Medical Centre (UMMC) is a tertiary referral centre located in Kuala Lumpur, the capital of Malaysia. It has an extensive established psychiatric unit which has adopted the ADA-APA guidelines. However, there are no studies done to review if Malaysian psychiatrists adhere to the recommended guidelines. In view of this, this study was carried out to assess adherence to the recommended guidelines by doctors in University Malaya Medical Centre (UMMC).

MATERIALS AND METHODS

This study was a retrospective observational study carried out in University Malaya Medical Centre, Kuala Lumpur, Malaysia (UMMC). Approval from the Medical Center's Ethics Committee was obtained prior to the commencement of the study.

The study population was those who were 18 years old and above, and newly started on atypical antipsychotics after June 2005, when the ADA-APA consensus guidelines was first put into use. Those who were started on atypical antipsychotics as part of a clinical trial were excluded. All data were retrospectively collected using the patients medical records, the hospital's online Pharmacy Information System and the Laboratory Information System.

Data collected included demographic information of patient and the type and date the atypical antipsychotic drug was started on. In the monitoring section, data was collected concerning whether recommendations were carried out in keeping with the

recommended guideline, which was the ADA-APA, up to 12 months after antipsychotic initiation. These guidelines include 7 monitoring parameters which are medical history, family history, weight (BMI), waist circumference, blood pressure, fasting glucose and fasting lipid profile, all of which should be recorded during the baseline visit. The patient's weight should also be reassessed at 4, 8 and 12 weeks after initiation or change in atypical antipsychotic treatment and quarterly thereafter at the time of routine visits. Fasting plasma glucose, fasting lipid profile and blood pressure should be assessed every 3 months after initiation of an atypical antipsychotic drug.

RESULTS

A total of 448 patients were found to have been newly started on AAP after June 2005. However, 43 of them were then excluded because 34 patients' medical records could not be traced, and another 9 patients were participants in clinical trials. Therefore, 405 patients were included in the final analysis (clozapine n = 55, olanzapine n = 83, quetiapine n = 178, risperidone n = 72, and apriprazole n = 17).

There were 182 (44.9%) male patients and 223 (55.1%) female patients that were included in this study. In term of ethnicity, Chinese patients make up the largest portion with 215 (53.1%) patients, followed by 98 (24.2%) Malay patients, and 80 (19.8%) Indian patients. Twelve 12 (3%) patients with their ethnicities not recorded were included in this study. The sample of 405 patients had mean age of 48.80 ± 18.25 with minimum age of 18 and maximum age of 94 years.

Metabolic parameters monitoring performed by doctors were assessed from the date during which patients started on AAP treatment until 1 year thereafter. Due to the variability of the dates during which AAP was started and the duration of AAP treatment in 405 patients included in this study, the first month, second month, third month, annual or random monitoring were not applicable to certain patients in this study. For example, if a patient's duration of AAP treatment was only one month, the second month, third month, annual and random monitoring were not applicable to this patient. The number of patients applicable for baseline assessment was 405; first month = 374; second month = 347; third month = 332 and 12 months = 237.

The proportion of patients that underwent the required assessments at baseline, first month, second month, third month and at one year in accordance to the recommended ADA-APA Guidelines is shown in Table 1.

DISCUSSION

Most of the AAP were well represented in this study, with the exception of aripripazole (n = 17). This is probably due to the fact that it is a relatively new drug in the market, and its use is not yet widespread. There were about equal male and female patients in this study, which was expected as schizophrenia, the main illness where

Table 1. Proportion of patients that underwent assessments in accordance to the recommended guidelines.

Monitoring parameter	Baseline (n = 405)	1st month (n = 374)	2nd month (n = 347)	3rd month (n =332)	One year (n = 23)
Family history	143 (35.3%)				3 (1.3%)
Personal medical history	254 (62.7%)				25 (10.5%)
Weight	139 (34.3%)	35 (9.4%)	19 (5.5%)	28 (8.4%)	15 (6.3%)
Waist circumference	21 (5.2%)	4 (1.1%)	2 (0.6%)	2 (0.6%)	4 (1.75)
Blood pressure	190 (46.9%)				29 (12.2%)
Plasma glucose	201 (49.6%)				25(10.5%)
Lipid profile	51 (12.6%)				11(4.6%)

antipsychotics are used, have an equal incidence in both males and females. In terms of ethnicity, the Chinese contributed the highest percentage (53.1%) of the total patients included. It was followed by Malays and the Indians with 30.7% and 19.8%, respectively. This is not in keeping with the Malaysian population where the Malays constitute the largest portion. This was probably due to the fact that the samples were drawn from UMMC which caters to a predominantly Chinese metropolitan area.

According to ADA-APA Consensus Guidelines, family history and personal history of diabetes mellitus (DM), hypertension (HTN), dyslipidemia and cardiovascular disease (CVD), weight; waist circumference; blood pressure, plasma glucose and lipid profile need to be monitored at the baseline when patients were started on AAP treatment. In this study, less than half of the patients were monitored at the baseline for all the monitoring parameters except for personal history of diabetes, hypertension, dyslipidemia and cardiovascular disease (62.7%).

The weight of patients should have been monitored one month, two months and three months after the initiation of AAP. Besides that, patients' blood pressure, plasma glucose and lipid profile should be monitored three months after the patients started on AAP treatment while patients' family history, personal, waist circumference; blood pressure and plasma glucose need to be monitored after one year according to ADA-APA Consensus Guidelines. The continuous monitoring throughout treatment period showed a reducing trend in the percentage of patients monitored for all the monitoring parameters compared to baseline monitoring. More doctors tend to monitor patients when they started their patients on AAP treatment but the continuous monitoring was greatly reduced throughout the treatment period.

Waist circumference monitoring shows the lowest percentage of monitoring, a finding similar to a previous study (Bauer et al., 2008). Only 21 (5.2%) and 4 (1.7%) patients were monitored at the baseline and one year after the initiation of AAP treatment, respectively. This low rate indicates that doctors may not be aware of the importance of waist circumference as a strong independent predictor of cardiovascular disease (Alberti et al.,

2005). Waist circumference monitoring is important in patients with major mental illness since they are at higher risk for cardio-metabolic derangement due to genetic predisposition, developmental and environmental stressors and their lifestyles. This risk is compounded further when they receive antipsychotic medications (Hasnain et al., 2008).

In summary, the overall rate of metabolic parameters monitoring in patients prescribed with AAP drugs in UMMC was low. This concurs with the results of previous studies (Gul et al., 2006; Mackin et al., 2007; Motsinger et al., 2006; Taylor et al., 2004).

There are several possible reasons why compliance metabolic monitoring in patients on AAP treatment is poor. Medical care for patients with severe mental illness has frequently been marginalized due to the limited resources in medical care, especially in non-developed countries. Besides the belief that there is a lack of time and shortage of staff to perform these procedures, little medical knowledge or emphasis on medical needs in mental health settings form barriers to the implementation of published monitoring guidelines (Cohn and Sernyak, 2006).

Meanwhile, the issue of who is responsible for monitoring metabolic abnormalities in patients receiving AAP drugs is much debated. Cohn and Sernyak (2006) suggested that the responsibility for monitoring metabolic abnormalities in patients prescribed with AAP should come along with the prescription. They claimed that it is not necessary for psychiatrists to actually perform the monitoring tests. However, they are responsible to ensure that the task is clearly delegated if they are not going to perform the tests. The issue of liability also acts as a barrier to monitoring guidelines implementation. Some clinicians are concerned about the types of added liability are implied when monitoring tests are performed that would document the significant metabolic abnormalities such as diabetes or dyslipidemia.

Patient-related issues such as persisting symptoms such as paranoia and mania; cognitive deficits; access and affordability to medical care and non-adherence to treatment recommendations can also be barriers to implement monitoring guidelines. Furthermore, some

clinicians are resistant to change and there is a lack of familiarity with monitoring guidelines which makes the monitoring guidelines difficult to implement (Narasimhan and Bailey, 2008). Some studies also suggest that some of the psychiatrists are ignorant of metabolic dysfunctions associated with AAP drugs (Gul et al., 2006; Mackin et al., 2007).

We suggest that instead of recommending guidelines, which serves only as "guides", standardized operating procedures regarding metabolic monitoring be implemented, compelling doctors to adhere to the monitoring schedule. This ultimately is for the benefit of our patients and to safeguard their well being.

REFERENCES

ADA-APA-AACE-NAASO (American Diabetic Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association for the Study of Obesity) (2004). Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care, 27: 596-601.

Alberti KG, Zimmet PZ, Shaw J (2005). The metabolic syndrome: a new worldwide definition. Lancet, 366: 1059-1062.

Ananth J, Parameswaran S, Gunatilake (2004). Side effects of atypical antipsychotic drugs drugs. Current Pharmaceutical Design, 10: 2219-2229.

Cohn TA, Sernyak MJ (2006). Metabolic monitoring for patients treated with antipsychotic medications. Can. J. Psychiatry, 51: 492-501.

Gul M, Nihgam A, Broughton N (2006). Clinical monitoring of patients on clozapine. J. Pakistan Psychiatric Soc., 30: 90-93.

Haddad PM, Sharman SG (2007). Adverse effects of atypical antipsychotic drugs: differential risk and clinical implications. CNS Drugs, 21: 911-36.

Mackin P, Bishop DR, Watkinson HM (2007). A prospective study of monitoring practices for metabolic disease in antipsychotic-treated community psychiatric patients. BioMed. Central Psychiatry, 7: 28.

Motsinger C, Slack M, Weaver M, Reed M (2006). Physician patterns of metabolic screening for patients taking atypical antipsychotics: a retrospective database study. Primary Care Companion J. Clin. Psychiatry, 8: 220-23.

Narasimhan M, Bailey SB (2008). Schizophrenia, metabolic syndrome and antipsychotics challenges, controversies, and clinical management. Psychiatric Times, 25(3): 77-83.

Poulin MJ, Cortese L, Williams R, Wine N, McIntyre RS (2005). Atypical antipsychotics in psychiatric practice: practical implications for clinical monitoring. Can. J. Psychiatry, 50: 555-62.

Rafael ARV, Rey J (2002). Weight gain and metabolic disturbances associated with the atypical antipsychotic drugs. Professional Psychology: Research and Practice, 33(3): 341-344.

Taylor D, Young C, Esop R, Paton C, Walwyn R (2004). Testing for diabetes in hospitalized patients prescribed antipsychotic drugs. Br. J. Psychiatry. 185: 152-156.