Baseline metabolic monitoring of atypical antipsychotics in an inpatient setting

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ABSTRACT

Background: Atypical antipsychotic agents serve an important role in the treatment of many psychiatric disorders but have the potential to cause adverse effects, notably metabolic disturbances. These agents are known to cause increases in obesity, glucose intolerance, dyslipidemia and hypertension. In 2004, the American Diabetes Association (ADA) and the American Psychiatric Association (APA), in collaboration with other organizations, acknowledged the association between the use of atypical antipsychotics and the development of metabolic abnormalities and provided monitoring recommendations for the use of these agents. Despite these recommendations, rates of monitoring remain low.

Objective: The purpose of this study is to assess whether a pharmacist recommendation form is effective in improving baseline metabolic monitoring for patients admitted to an acute inpatient psychiatry unit who are ordered a scheduled atypical antipsychotic.

Methods: A pharmacist recommendation form with metabolic monitoring parameters was placed on the charts of patients ordered a scheduled atypical antipsychotic during a two month period. A retrospective chart review was conducted to compare the percentage of baseline monitoring ordered pre-intervention versus the intervention period. Patients ages 18 years or older who were ordered a scheduled atypical antipsychotic were included.

Results: During the intervention period, there was a significant increase in documentation for presence or absence of diabetes ($p = 0.018$) and cardiovascular disease ($p < 0.001$). A significant difference in the number of orders for hemoglobin A1c ($p = 0.007$) and lipid panels ($p < 0.001$) were noted. No other significant differences were found.

Conclusion: A pharmacist recommendation form was effective in improving the baseline monitoring of personal history of diabetes and cardiovascular disease and monitoring of hemoglobin A1c and lipid panels, but rates of other baseline monitoring parameters did not improve.

KEYWORDS

metabolic monitoring, atypical antipsychotic, pharmacist

INTRODUCTION

In 2004, the American Diabetes Association (ADA), the American Psychiatric Association (APA), the American Association of Clinical Endocrinologists (AACE), and the North American Association for the Study of Obesity (NAASO), issued a consensus statement on proper monitoring of antipsychotic drugs for adverse side effects related to obesity and diabetes.[1] Atypical antipsychotics, commonly prescribed to patients with various mental illnesses, are associated with causing metabolic disturbances such as weight gain, dyslipidemia, and diabetes. Patients with serious mental illness (SMI) have a shorter life expectancy than those without, dying on average 25 years earlier than the general population, with cardiovascular disease the leading cause of mortality.[2] Unlike typical antipsychotics, atypical antipsychotics carry a greater risk of causing metabolic abnormalities associated with cardiovascular disease. Therefore, proper monitoring is crucial to achieve optimal drug therapy results while decreasing a patient's risk of morbidity and mortality. Studies show that despite these recommendations from reputable national organizations, adherence to appropriate monitoring for metabolic disturbances as a standard of care is low.[3-5]

Atypical antipsychotic agents serve an important role in the treatment of many psychiatric disorders but have the potential to cause adverse side effects, notably metabolic disturbances. As discussed in a review by Pramyothin and Khaodhlarb, the atypical antipsychotics are known to cause increases in obesity and metabolic syndrome parameters such as glucose intolerance, dyslipidemia, and hypertension as well as abnormal glucose and lipid metabolism. The risk is even higher in younger, antipsychotic-naive populations, who are being prescribed these medications at an increasing rate.[6] In 2003, a Black Box Warning was added as a class warning to all atypical antipsychotics documenting the increased risk of hyperglycemia and diabetes. Results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Schizophrenia Trial highlighted significant changes in metabolic syndrome parameters in patients on atypical antipsychotics. This emphasizes the need for better identification of those who meet criteria for metabolic syndrome. Monitoring metabolic changes in this population is essential in order to prevent the onset of diabetes and cardiovascular disease.[7]

In the ADA/APA consensus statement, the recommended routine monitoring frequencies for weight (body mass index), waist circumference, blood pressure, fasting plasma glucose, and fasting lipid profile were outlined.[1] Prior to these guidelines, studies examining the rates of monitoring demonstrated routine monitoring did not regularly occur.[8-11] Since the consensus statement was issued, many studies have shown recommended baseline and follow-up monitoring still remain low.[3-5] Reasons for this are likely multi-factorial, and may include explanations such as lack of awareness of metabolic risks on the part of the prescribing physician, lack of continuity of care due to patients not having primary care providers who would oversee appropriate follow-up monitoring, and the acuity of some patients who need atypical antipsychotics, as primary care concerns may get overlooked in an acute psychiatric facility. Because of this, more needs to be done to increase awareness and improve the quality of care in patients prescribed atypical antipsychotics. A previous quality improvement intervention at the University of Arizona Medical Center - South Campus sought to increase rates of monitoring. For this intervention, prescribers attended a short educational session on the association between atypical antipsychotics and risk of metabolic syndrome and were provided with a pocket reminder card that outlined recommendations. Data from this intervention showed a significant, albeit small, improvement in plasma glucose and lipid monitoring ($p = 0.007$ and 0.026, respectively) but rates were still low.[12] Therefore, it appeared that additional interventions to improve rates of baseline monitoring in this setting were needed.

The primary objective of this study was to assess whether a pharmacist recommendation form was effective in improving baseline metabolic monitoring for patients admitted to an acute inpatient psychiatry unit at an academic medical center. It was hypothesized that the percentage of monitoring parameters ordered by physicians would be relatively low in the pre-intervention period, similar to results that have been reported for other institutions. However, it was expected that the pharmacist recommendation form would increase the rate at which these monitoring parameters were ordered during the intervention period.

METHODS

This study was conducted at the University of Arizona Medical Center – South Campus. Approval from the University of Arizona Institutional Review Board was obtained prior to the commencement of the study. The study population included patients 18 years of age or older admitted to an inpatient acute behavioral health unit, with an order for a scheduled atypical antipsychotic during their admission. Patients ordered a typical antipsychotic or an atypical antipsychotic on an as needed basis only were excluded. For patients who were admitted multiple times during the study period, only the first admission during each data collection period was included.

The intervention was a pharmacist baseline metabolic monitoring recommendation form (Appendix 1) that served as a visual reminder of the recommended ADA/APA baseline monitoring parameters. The psychiatric pharmacy team checked for new orders for scheduled atypical antipsychotics on the behavioral health units on a daily basis. The recommendation form was placed on qualified patients' charts for a two-month period from January to February 2013. Prior to the intervention period, an informational group session was held with attending psychiatrists and the psychiatric nurse practitioner to inform them of recommended metabolic monitoring and the ensuing study. Psychiatry residents were educated on an individual basis. A retrospective review of charts was completed from admissions from October 1, 2012 to October 31, 2012 (pre-intervention) and from February 1, 2013 to February 28, 2013 (during intervention). For the purposes of this study, baseline orders were defined as monitoring performed within one week of an order for a scheduled

antipsychotic. Blood glucose values were considered to be fasting if obtained prior to 7am.

The primary outcome was to determine whether or not placing pharmacist recommendation forms on patient charts improved monitoring parameters ordered and documented. This was evaluated by comparing the percentage of baseline parameters recorded in the chart prior to the intervention and during the intervention. Intention-to-treat analysis was used. The descriptive variables and demographic data were analyzed by calculating summary means and standard deviations for continuous variables. Categorical variables were analyzed by calculating frequencies and percentages. Preacher chi-square test was used to compare these categorical variables.[13] The priori alpha level was set at 0.05.

RESULTS

Out of 190 patients who were ordered an atypical antipsychotic in the pre-intervention period, a total of 100 were included for analysis. Of the 190, 36 were excluded for as needed antipsychotic orders, 17 were excluded for not originating from patients on an inpatient acute behavioral health unit and 37 were excluded because the patients were admitted prior to the pre-intervention period. During the intervention period, 179 patients were ordered atypical antipsychotics for the month of February 2013. Of these, 37 were excluded for as needed antipsychotic orders, 30 were excluded for originating from non-behavioral health patients, and 24 were excluded because the patients were admitted prior to the data collection period. Eighty-eight charts remained for review. During the intervention period, the number of forms that were placed on charts was tracked. For those included in the analysis for February, 67 (78.4%) patient charts reviewed had the recommendation form placed.

Demographic information for both groups is reported in Table 1. There were no significant differences between the groups in terms of baseline characteristics. However, there were significantly fewer orders for ziprasidone (see Table 2) in the intervention period versus the pre-intervention period (13 vs 3; p = 0.037). The most commonly ordered atypical antipsychotic during both study periods was risperidone. There were no orders for iloperidone or lurasidone in either study period. The measured outcomes can be found in Table 3. There were no significant differences in personal history documentation for presence or absence of obesity, dyslipidemia, or hypertension. However, there was a significant increase in documentation for presence or absence of diabetes (71% vs 86%; p = 0.018) and cardiovascular disease (46% vs. 91%; p < 0.001) between the pre-intervention and intervention groups. There were no significant differences in family history documentation for presence or absence of any of the disease states. There were also no significant differences on parameters measured such as weight, waist circumference, blood pressure, and blood glucose. There was a significant difference in the number of orders for hemoglobin A1c (7% vs. 22%; p = 0.007) and lipid panels (12% vs. 40%; p < 0.001).

Table 1. Baseline demographic and clinical characteristics*

Population Descriptors	Pre-Intervention (N=100)	Intervention (N=88)	P Value
Sex (male)	60 (60%)	43 (48.9%)	p = 0.166
Age (years)	42.42 (16.08)	43.56 (16.26)	p = 0.578
Weight (kg)	78.62 (20.18)	74.68 (21.12)	p = 0.192
BMI	26.92 (6.4)	26.5 (6.44)	p = 0.654
Systolic BP (mmHg)	126.95 (26.94)	128.17 (16.52)	p = 0.713
Diastolic BP (mmHg)	81.75 (13.59)	83.16 (13.3)	p = 0.475
Length of Stay (days)	9.29 (7.5)	11.36 (8.5)	p = 0.077
Race			
White	89 (89%)	75 (85.2%)	p = 0.933
African American	7 (7%)	8 (9.1%)	p = 0.933
Native American	1 (1%)	1 (1.1%)	p = 0.933
Other	3 (3%)	4 (4.5%)	p = 0.933
Ethnicity			
Hispanic	30 (30%)	28 (31.8%)	p = 0.938
Comorbidities			
Diabetes Mellitus	13 (13%)	9 (10.2%)	p = 0.897
Hypertension	32 (32%)	26 (29.5%)	p = 0.897
Hyperlipidemia	10 (10%)	11 (12.5%)	p = 0.897
Atypical Antipsychotic Treatment Status			
Treatment Naïve	19 (19%)	16 (18.2%)	p = 0.969
Treatment Non-Naïve	74 (74%)	64 (72.7%)	p = 0.969
Unknown	7 (7%)	8 (9.1%)	p = 0.969

*Data are reported as means (SD) or numbers (%)

Table 2. Atypical antipsychotic (AA) ordered

AA Ordered	Pre-Intervention (N=101*)	Intervention (N=89*)	P Value
aripiprazole	6 (5.9%)	8 (8.9%)	p = 0.598
asenapine	1 (0.99%)	0	---
clozapine	2 (1.98%)	2 (2.2%)	p = 0.706
olanzapine	12 (11.9%)	10 (11.2%)	p = 0.928
paliperidone	0	2 (2.2%)	---
quetiapine	23 (22.7%)	20 (22.5%)	p = 0.896
risperidone	44 (38.8%)	44 (49.4%)	p = 0.499
ziprasidone	13 (12.9%)	3 (3.4%)	**p = 0.037**

* In each data collection period, there was one patient who was discharged on two atypical antipsychotics

Table 3. Orders for metabolic monitoring parameters

Parameter	Pre-Intervention (N=100)	Intervention (N=88)	P Value
Personal History			
Obesity	10 (10%)	8 (9%)	p = 0.974
Diabetes Mellitus	71 (71%)	76 (86%)	**p = 0.018**
Dyslipidemia	11 (11%)	10 (11%)	p = 0.879
Hypertension	82 (82%)	80 (91%)	p = 0.12
Cardiovascular Disease	46 (46%)	80 (91%)	**P < 0.001**
Family History			
Obesity	12 (12%)	0	---
Diabetes Mellitus	17 (17%)	7 (8%)	p = 0.811
Dyslipidemia	12 (12%)	0	p = 0.95
Hypertension	16 (16%)	2 (2%)	p = 0.549
Cardiovascular Disease	21 (21%)	6 (7%)	p = 0.458
Weight, Waist Circumference and Laboratory Tests			
Weight	100 (100%)	88 (100%)	---
Waist Circumference	0	0	---
Blood Pressure	100 (100%)	88 (100%)	---
Fasting Blood Glucose	39 (39%)	32 (36%)	p = 0.710
Hemoglobin A1c	7 (7%)	19 (22%)	**p = 0.007**
Lipid Panel	12 (12%)	35 (40%)	**p < 0.001**

DISCUSSION

The results of this study demonstrated a significant improvement in the rates of baseline monitoring of hemoglobin A1c and lipid panels after the initiation of a pharmacist metabolic monitoring recommendation form. However, there was a significant difference in the number of orders for ziprasidone, with fewer orders during the intervention period. This difference may have influenced the results of the study as ziprasidone is less likely to cause metabolic syndrome and, as a result, the prescriber may have ordered fewer metabolic monitoring parameters during the pre-intervention period. Although providers should be ordering monitoring despite weight neutrality of specific atypical antipsychotics, this may not always be the case. There was an improvement in the documentation of the presence or absence of personal history of diabetes and cardiovascular disease, as defined by transient ischemic attack, stroke or coronary heart disease (e.g., history of myocardial infarction, angina, arterial stenosis, or peripheral arterial disease). The presence or absence of these conditions were less frequently documented in the nursing assessment as "unable to obtain" during the intervention when compared to the pre-intervention charts. The reason for this is unclear, but it may have been due to the nurse also viewing the pharmacist recommendation form placed upon the chart.

With regard to the other monitoring parameters, no significant improvements were found. Monitoring for parameters such as weight and blood pressure are done routinely at this hospital, so as expected, these were done for almost every patient admitted for both groups and therefore, no significant change was found. Waist circumference measurements were not obtained pre-intervention and this did not change after the placement of the recommendation form. Many factors could have contributed to this, including the fact this measurement is not part of the routinely ordered measurements and there is not a designated place for its documentation in the medical chart. Each unit was provided with a measuring tape; however, at least one of the units lost their tape measure shortly after the intervention started so misplacement of tools may have been a limitation.

There are several limitations of the study that should be noted. First, it was found that 67 of 88 charts (78.4%) reviewed had the recommendation form placed on them during the data collection period. Twenty-one patient charts included in the intention-to-treat analysis did not receive a form. This may have affected the results of the study, as some prescribers may have not ordered baseline metabolic monitoring parameters because the visual reminder was not present. It is unknown why some of the charts were overlooked in the intervention, but it may be

due to difficulties with the paper chart system. Because all members of the treatment team have access to the charts and they often are taken off of the units for various reasons, they may have not been present when forms were placed. However, this gives a better estimate of the effectiveness of this type of intervention in an actual practice setting. Next, strict criteria were used for documentation of presence or absence of significant history and whether it was positive, negative, or unknown. If a parameter was not mentioned or explicitly documented in the patient chart, it was recorded as "not documented" and status listed as "unknown". This strict criteria was set as it would have been difficult to assume whether a history documented as "unknown" or "unable to assess" indicated that patients were asked about the specified criteria or not. Another potential limitation is decreased focus on non-urgent medical conditions in an acute psychiatric setting. As the focus of a psychiatric evaluation is primarily psychiatry rather than medical, this may partially explain why information pertaining to medical conditions was often incomplete or contradictory with information found elsewhere in the chart. Another limitation is the lack of a uniform place in the current chart system to document all metabolic monitoring parameters in one place. With respect to the patient population, only adults 18 years of age or older were included in the study as there are no pediatric or adolescent admissions at the study location. This may limit generalizability to a younger population. Finally, although there were no significant differences between the study groups with regard to race and ethnicity, the study population was predominately white, which may limit generalizability to minority groups.

Future efforts should focus on developing a metabolic monitoring form which can be incorporated as part of the medical record and can be provided to patients to allow them to be actively involved in their medical care. With expansion to an electronic medical record, a more practical route may be a metabolic monitoring panel that automatically prompts providers on the parameters/measurements that should be obtained and can allow for assessment of trends or changing values. Future research could be directed at evaluating the effect of a more integrated metabolic monitoring form or tab in an electronic medical record. The long-term impact of this intervention should also be evaluated to determine if providers continue to order metabolic monitoring parameters although no reminders are currently being placed on the patient chart.

Though providing medical care to persons with mental health diagnoses may be challenging, treatment should take into account the overall health of the patient, both mental and physical. Continued efforts should be made to appropriately monitor patients on atypical antipsychotics for changes in metabolic parameters and to increase awareness of the importance of these metabolic complications. This includes allowing for interdisciplinary teams, composed of psychiatrists, primary care physicians, specialists, nurses, pharmacists and others, to take responsibility for providing optimal care for mind and body.

CONCLUSIONS

In this study, a pharmacist's recommendation for metabolic monitoring was successful in increasing the number of baseline lipid panel and hemoglobin A1c orders for patients ordered scheduled atypical antipsychotics in an acute inpatient setting at an academic medical center. Despite some improvement, rates of monitoring for some metabolic parameters remained low; therefore, more should be done to follow the monitoring recommendations set forth in the ADA/APA consensus statement. Pharmacist intervention in this area may be an effective way to increase metabolic monitoring and thereby improve patient outcomes.

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APPENDIX 1. PHARMACIST BASELINE METABOLIC MONITORING RECOMMENDATIONS

This form should not be part of the medical record.

Your patient is on or has been initiated on the following atypical antipsychotic:

- ☐ aripiprazole (Abilify®)
- ☐ asenapine (Saphris®)
- ☐ clozapine (Clozaril®)
- ☐ iloperidone (Fanapt®)
- ☐ lurasidone (Latuda®)
- ☐ olanzapine (Zyprexa®)
- ☐ paliperidone (Invega®)
- ☐ quetiapine (Seroquel®)
- ☐ risperidone (Risperdal®)
- ☐ ziprasidone (Geodon®)

Per ADA/APA guidelines, the following monitoring parameters/labs are recommended when a new atypical antipsychotic is started:

- Personal AND Family History of (please note the presence or absence of:)
  - Obesity
  - Diabetes
  - Dyslipidemia
  - Hypertension
  - Cardiovascular Disease
- Weight
- Fasting Plasma Glucose
- Waist Circumference
- Hemoglobin A1c
- Blood Pressure
- Fasting Lipid Profile

For patients continuing previous atypical antipsychotic therapy, please refer to the following table for monitoring parameters/labs:

Metabolic Monitoring Recommendations Based on the APA/ADA Guidelines

	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually
Personal/Family History	X					X
Weight (BMI)	X	X	X	X	X	
Waist Circumference	X					X
Blood Pressure	X			X		X
Fasting Plasma Glucose	X			X		X
Fasting Lipid Profile	X			X		*

American Diabetes Association; American Psychiatric Association; American Association of Clinical Endocrinologists; North American Association for the Study of Obesity: Consensus development conference on antipsychotics drugs and obesity and diabetes. *Diabetes Care.* 2004;27:596-601.

If you have any questions, please contact:

Name:_____ Extension:_____

*Fasting Lipid Profile should be monitored every five years unless significant abnormalities are present. If present, the lipid panel should be monitored annually.