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The effect of a computerized best practice alert (BPA) system in an outpatient setting on metabolic monitoring in patients on second generation antipsychotics (SGAs)

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Conflicts of Interest

No conflicts of interest have been declared.

Source of Funding

No funding has been received for this study.

SUMMARY

What is known and objective

Metabolic syndrome is a well-documented adverse effect of second generation antipsychotics (SGAs). Patients with metabolic syndrome are at an increased risk of potentially fatal cardiovascular events, including myocardial infarction and stroke. This elevated risk prompted the creation of a national guideline on metabolic monitoring for patients on SGAs in 2004. However, monitoring practices remained low at our clinic. To address this concern, a clinical decision support system was developed to alert providers of monitoring requirements. The purpose of this study is to determine the effect of the best practice alert (BPA), and to assess the impact of provider and patient characteristics on metabolic laboratory (lab) order rates.

Methods

A retrospective chart review was conducted at a large outpatient psychiatric clinic. Data were collected from all adult patients who were prescribed an SGA and triggered the BPA (indicating laboratory monitoring is needed for the patient). Data collection included a variety of patient, provider, and alert variables. The primary outcome was a composite of fasting blood glucose (FBG), hemoglobin (HbA1c), and/or fasting lipid panel (FLP) order rates. Secondary outcomes included the rate of valid response, which considered appropriate reasons for not ordering labs (i.e. monitoring already completed during recent primary care visit), as well as order rates of individual labs.

Results and Discussion

Data from 1,112 patients were collected and analyzed. Patients with a thought disorder diagnosis had significantly more labs ordered than those without. No other patient factors affected order rates. Resident psychiatrists and nurse practitioners ordered significantly more labs and had significantly more valid responses than attending psychiatrists. An active alert, which fired during medication order entry, was associated with a higher rate of lab ordering and valid response compared to a passive alert, which fired whenever a prescribing healthcare provider opened the chart.

What is new and conclusion

Prescribers may associate metabolic syndrome with schizophrenia or with use of SGAs specifically in thought disorders, even though these medications pose a risk for all indications. Higher rates of monitoring by resident physicians may have been due to spending more time with patients during the encounter and in documentation. Lastly, the active BPA was an effective tool to increase metabolic monitoring in patients taking SGAs. Continued education on the importance of regular metabolic monitoring should be implemented for all providers.

MAIN TEXT

What is known and Objective

Antipsychotic medications have been widely regarded as first-line treatment for primary thought disorders and have been shown to be effective in the management of bipolar disorder, depression with psychotic features, and post-traumatic stress disorder.[1] First-generation antipsychotics (FGAs) have been extensively used in the treatment of these disorders but are accompanied by an array of side effects. Of note, extrapyramidal symptoms can occur and be treatment limiting.[1,2] Second-generation antipsychotics (SGAs) were developed to provide equally effective treatment and were initially touted as having fewer adverse effects compared with FGAs.[3] However, SGAs are accompanied by metabolic complications including central obesity, insulin resistance, and dyslipidemia. This collection of symptoms is more broadly known as metabolic syndrome and is diagnosed when a patient has three of the five risk factors; abnormal waist circumference, triglycerides, high density lipoproteins, fasting blood glucose, and elevated blood pressure.[4] SGAs have been classified by their metabolic risk, with clozapine and olanzapine having the highest risk and aripiprazole, asenapine, lurasidone, and ziprasidone having the lowest risk.[5,6]

Metabolic syndrome increases the risk of developing serious comorbidities such as coronary artery disease, hypertension, and stroke. One study found nearly 30% of inpatients prescribed at least one SGA met criteria for metabolic syndrome.[7] In 2004, to address risks of increased metabolic adverse effects, the American Diabetes Association (ADA) and the American Psychiatric Association (APA) released a set of guidelines on metabolic monitoring in patients taking SGAs, which have not been widely implemented in psychiatric settings.[8,9] Since the release of these guidelines, steps have been taken to increase the monitoring of these laboratory (lab) values. In 2007, one study demonstrated the impact of a computerized alert system on baseline monitoring; 32% to 52% of providers were following the guidelines before implementation versus 78% to 100% of providers after implementation.[10]

These guidelines, coupled with the hope of improving monitoring practices to optimize patient care, led to the creation of a best practice alert (BPA) in our EHR. Within our institution, we previously found that only 51.2% of hospitalized patients on SGAs received a fasting blood glucose and fasting lipid panel within the past year after implementation of the alert.[8] While this finding may be an improvement from before the alert system was created, the rate of lab ordering for metabolic monitoring remained suboptimal. Further research into specific variables contributing to overall rates of metabolic monitoring would be beneficial to improve compliance with the 2004 ADA/APA guideline recommendations, as it may allow for more targeted interventions. Additionally, the use of a computerized BPA for metabolic monitoring, notably in the outpatient setting, should be evaluated in greater detail. The aim of this study is to determine how the alert is used most often (active vs. passive), who is using the alert (provider type), and for whom it is used (considering patient demographics, diagnoses, and SGA used). This will allow us to identify factors associated with statistically significant higher rates of lab ordering and thus enhance discussion with our providers to address these factors and come up with targeted interventions to improve lab ordering for all patients.

Methods

The best practice alert

The alert contains a brief explanation and reference explaining metabolic monitoring in patients on SGAs. The provider has the option to: a) order labs, b) select a reason for not ordering labs, or c) dismiss without taking any action. Lab ordering options include a) hemoglobin A1c (HbA1c), b) fasting blood glucose (FBG), and/or c) fasting lipid panel (FLP). Lab declination

options include a) screening done elsewhere, b) patient/family declined, c) medication not being taken as prescribed, or d) other (with the option to add comments).

The alert fires actively and passively if a patient is prescribed or actively on an SGA and lacks or has incomplete metabolic labs (HbA1c, FBG, & FLP) documented within the last year. The active and passive alerts include the same BPA text and are triggered for prescribers only in the adult ambulatory psychiatry clinic at Michigan Medicine. The active alert is an interruptive pop-up on order entry, whether a new start or medication renewal, whereas the passive alert only displays when the provider chooses to open the BPA section in the patient's chart. For the passive alert to fire, a patient must have an SGA on their active medication list. The passive alert is recorded to fire every time a prescriber enters a patient's chart; because it is not interruptive, multiple alerts may be recorded before the provider takes action. The BPA does not account for labs scanned in from a nonaffiliated source, hence the provider has the option to select "screening done elsewhere" as their reason for not ordering labs.

The alerts continue, even upon subsequent encounters or visits, until the prescriber addresses the alert by either a) ordering labs or b) selecting a reason labs were not ordered. Thereafter, the alert turns off for one-year. After a year, the alert will resume if the patient is still being prescribed an SGA. BPA records include the date, time, and associated encounter in which the alert was triggered. Closing out of the active alert without ordering labs or choosing an alternative response as outlined above does not suppress the BPA.

Data collection

This study was approved by Michigan Medicine's human research institutional review board. Data was pulled from the electronic health record (EHR), EPIC (Verona, WI), from 6/1/2015 to 2/28/2018. All patients 18 years or older who were prescribed an SGA by a provider in the clinic and triggered the BPA were included in the study. No patients were excluded from the study.

Data collected included a variety of patient variables (age, gender, race, ethnicity, diagnoses, medication history, visit dates), provider variables (clinician type and their response to the alert, including which labs they ordered, if any), as well as information from the BPA (time and date of firing, number of times fired, and location of BPA triggering). Patient age was reported in years, gender as male or female, race as Hispanic or Non-Hispanic, and ethnicity as White or Caucasian, Black or African American, Asian, American Indian and Alaska Native, Native

Hawaiian and Other Pacific Islander, and Other. Medication history was pulled to determine the SGA used, including aripiprazole, asenapine, brexpiprazole, cariprazine, clozapine, iloperidone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, and ziprasidone. Psychiatric and medical diagnoses were collected using a list of ICD-10 codes developed and agreed upon by the research team.

Data analysis

All patient, provider, and alert variables were analyzed to determine possible impacts on lab order rates. Patient ethnicity was broken into three subcategories: White or Caucasian, Black or African American, and Other. The latter includes patients who reported their ethnicity as Asian, American Indian and Alaska Native, Native Hawaiian and Other Pacific Islander, and Other. SGAs prescribed were broken into two subcategories based on metabolic risk: high metabolic risk SGAs (clozapine and olanzapine), and low to moderate metabolic risk (all others).[5,6] Psychiatric and medical diagnoses were further categorized to see if the potential indication or comorbid disease states including or related to metabolic syndrome influenced lab ordering.

The primary outcome is a composite of metabolic lab order rates, including FBG, HbA1c, and/or FLP, in patients prescribed SGAs who triggered the BPA. Secondary outcomes include the order rate of each individual lab and the rate of valid response to the alert, which takes into consideration that there are appropriate reasons for not ordering labs. This was called “Validity of Response” and was based on the provider’s response to the alert. Selections that were considered a valid response include “labs ordered,” “screening done elsewhere,” “patient/family declined,” and “medication not being taken as prescribed” (only if the medication was discontinued). Invalid responses include dismissed alerts and “medication not being taken as prescribed” if the prescriber further clarified the reason as either taking a low dose, taking as needed, or just started the medication. “Other” responses were manually sorted into a category based on the comment. If the provider selected “Other” without leaving a comment, the response was excluded from the analysis due to the lack of certainty whether or not the specific reason was valid.

Odds ratios and confidence intervals were calculated to analyze the influence of patient and provider factors on lab order and alert response rates. Lab order rates were compared using a multivariable logistic regression. Individual alert responses were modeled with univariate models. Since multiple individual alert responses fired per patient, generalized estimating

equation (GEE) logistic regressions were used to analyze alert data, accounting for intrapersonal correlation. All-pairwise post-hoc testing was performed on the alert response data with a Bonferroni correction to maintain a Family-Wise Error Rate of α=0.05, for both the p-values and the 95% confidence intervals.

Results and Discussion

Patient Demographics

There were 1,112 patients prescribed 1,276 SGAs which triggered the BPA (Table 1). The mean age was 42.6 years and 64.7% of patients were female, 86% Caucasian, and 98.2% Non-Hispanic. 94.3% of patients had a mood disorder diagnosis and 83.1% were diagnosed with an anxiety disorder. Thought disorders, in contrast, made up only 22% of the patients. Nearly half of the patients had a cardiovascular (49.6%) and/or metabolic (48.8%) diagnosis. The most commonly prescribed SGAs were quetiapine (41.8%) and aripiprazole (30.9%) (Table 2). High risk SGAs only made up 11.6% of SGAs prescribed, with under 5% of those being for clozapine.

Alert Data

We calculated the average number of alerts (± standard deviation) per patient broken down by a variety of provider and alert factors. On average, 9.3 (± 10.7) alerts fired per patient. Of these, the vast majority occurred in the general BPA section; on average, 8 (± 10.2) alerts per patient were triggered here. In contrast, an average of 1.3 (± 1.6) alerts per patient fired upon order entry. The average number of alerts per patient was relatively similar between providers, ranging from 2.6 (± 6.4) alerts per patient for attending psychiatrists to 3.2 (± 8.6) for nurse practitioners and 3.6 (± 6.4) for resident psychiatrists. Overall, 10,381 alerts fired for 1,112 patients.

Results

The analysis of the impact of patient factors on lab order rates can be reviewed in Table 3. There was only one statistically significant finding among these patient demographics; patients diagnosed with a thought disorder were significantly more likely to have labs ordered compared to patients without a thought disorder diagnosed (OR = 1.57, CI 1.12 to 2.22, p-value = 0.011).

Table 4 reports the analysis of provider and alert factors on the response to the alert. Compared to attending psychiatrists, resident psychiatrists ordered significantly more labs (OR = 1.69, adjusted CI 1.32 to 2.15, adjusted p-value = <0.001) and had significantly more valid responses

(OR = 1.54, adjusted CI 1.25 to 1.89, adjusted p-value = <0.001). Attending psychiatrists also ordered significantly fewer labs than nurse practitioners (OR = 0.64, adjusted CI 0.48 to 0.85, adjusted p-value = <0.001) and had significantly fewer valid responses (OR = 0.76, adjusted CI 0.58 to 0.99, adjusted p-value = 0.039). Significantly more labs were ordered in the enter order section than in the general BPA section (OR = 5.59, adjusted CI 4.68 to 6.69, adjusted p-value = <0.001) and there were significantly more valid responses (OR = 7.76, adjusted CI 6.46 to 9.32, adjusted p-value = <0.001).

Discussion

Patient Factors

Patients diagnosed with thought disorders were the only patient group with a statistically significant higher lab order rate than their counterparts (patients without thought disorders). This finding may indicate a misconception that metabolic monitoring is specifically required for patients diagnosed with schizophrenia, who are commonly prescribed these medications for chronic management. Many studies observing the risk of metabolic syndrome with antipsychotic use have been conducted in patients diagnosed with schizophrenia, which may enhance the perception that metabolic syndrome is a concern only in patients diagnosed with schizophrenia who are taking SGAs. By contrast, emerging data show there is no difference in risk among diagnoses.[11]

Provider & Alert Factors

Resident psychiatrists and nurse practitioners had statistically significant higher order and response rates compared to attending psychiatrists for every outcome. However, resident psychiatrists had an average of 3.6 alerts fire per patient, whereas attending psychiatrists averaged 2.6 alerts per patient. This may indicate that residents require more alerts before taking action. The findings on the impact of alert location, however, may be key to interpreting this discordance. When comparing lab order rates, the primary outcome, we found that labs were ordered 54.3% of the time a provider went to the order entry section, versus only 14.4% of the time that the alert was fired in the general BPA section. Similarly, the rate of valid response was 68.5% in the enter order section versus 19.6% in the general BPA section. These findings indicate when prompted by an active alert, the majority of providers responded. However, the alert that fired in the general BPA section is a passive alert, indicating it fired every time the patient's EHR was opened by a prescriber. Lower response rates here are not surprising since 1) it is likely that the prescribers entered the patient's chart on multiple occasions the day of

their visit and 2) the provider was not forced to address the alert. It is likely residents had higher lab order rates than attendings, despite attendings having fewer alerts fired, because residents enter the patient's chart multiple times, during breaks between consecutive patients, before documentation is completed and ready for attending review.

This difference in rates between the enter order and general BPA sections should be noted when analyzing provider-specific response rates. For example, provider response rates for the secondary outcome of validity of response ranged from 24.2 to 28.7%. While this appears low, analysis by location of BPA triggering showed that 68.5% of alerts fired were addressed appropriately. Due to the high volume of alerts and low order rates for the general BPA section, order rates from all locations appeared low when, in fact, the active alert was responded to appropriately more often than not. Compared to the study by Poker et al., which found an order rate of 78-81% for fasting plasma glucose and fasting lipid panels,[10] respectively, after implementation of a metabolic monitoring BPA, proper laboratory order rates were lower in our practice. This is likely due to the milieu and context. While our study and Poker et al. gathered data from outpatients, the education and involvement of dedicated staff for patient outreach likely had a positive influence in the Poker et al. study, which included a smaller number of prescribers.[10] The volume of patients in our ambulatory care setting as well as the number of prescribers makes this level of oversight challenging, but may be necessary to effect a lasting change in practice.

Limitations

Certain assumptions were made to analyze our results. For example, diagnoses were included to analyze whether the patient's psychiatric indication for the SGA as well as any potential comorbidities may have influenced lab ordering. However, there was no way to reasonably validate the indication for the SGA prescribed. Additionally, assessing lab order rates is helpful to determine barriers to provider adherence to monitoring, but does not assess whether the patient actually completed the lab order(s). Similarly, validity of response assesses whether or not the provider's response to the alert was appropriate based on the circumstances, but it cannot be concluded with certainty that the patient was properly screened and monitored. In terms of using the data to provide targeted interventions, the nature of the resident-attending relationship may have led to misguided conclusions. For example, though residents ordered labs at higher rates than attendings, this could have been in part due to the attending psychiatrist asking the resident to do so.

What is new and Conclusion

Conclusions

In conclusion, the BPA is a useful tool aiding in proper metabolic monitoring practices. This study found prescribers may associate metabolic syndrome with schizophrenia or with use of SGAs in thought disorders, even though SGAs pose risk for all indications. Additionally, resident physicians had higher rates of monitoring among their patients compared to other providers, which may have been due to having a greater level of involvement in the patient's care. Lastly, when compared to a passive alert, the active BPA was found to be an effective tool to increase metabolic monitoring in patients taking SGAs.

Implications for future practice

Though the active BPA was found to impact metabolic monitoring in this clinic, opportunities for improvement exist. Education on the importance of monitoring, with a focus on indications, as well as proper monitoring practices should be implemented for all providers. More dialogue regarding the barriers to properly monitoring patients is required to determine additional steps that should be taken to improve alert adherence.

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Tables

Table 1. Patient Demographics

Variable	Category	Summary[a]
Age		42.6 ± 15.4
Gender	Female	719 (64.7%)
	Male	393 (35.3%)
Race[b]	African American	94 (8.5%)

	Other	61 (5.5%)
	Caucasian American	956 (86.0%)
Ethnicity[c]	Hispanic or Latino	20 (1.8%)
	Non-Hispanic or Latino	1071 (98.2%)
Psychiatric Diagnosis	Mood Disorder[d]	1049 (94.3%)
	Anxiety Disorder[e]	924 (83.1%)
	Other[f]	480 (43.2%)
	Thought Disorder[g]	245 (22.0%)
Medical Diagnosis	Cardiovascular[h]	552 (49.6%)
	Metabolic[i]	543 (48.8%)
	Headache	508 (45.7%)
	Sleep	417 (37.5%)

[a]Reported as average ± standard deviation or n (%)

Missing data (n): [b]race (1), [c]ethnicity (21)

[d]Depression, bipolar disorder, other mood disorder

[e]Anxiety, obsessive compulsive disorder, acute stress disorder, post traumatic stress disorder

[f]Autism, intellectual disabilities, pervasive developmental disorder, dementias, other cerebral degenerations, adjustment reaction, schizotypal disorder, personality disorders, somatization disorder, mental disorders due to other conditions, physiological

malfunctions due to mental disorder

[g]Schizophrenia, schizoaffective disorder, delusional disorder, psychosis

[h]Atherosclerotic cardiovascular disease, hypertension, angina, acute and history of myocardial infarction, other ischemic heart/cerebrovascular disease, deep vein thrombosis/pulmonary embolism, pulmonary hypertension, peripheral vascular disease, heart failure, smoking

[i]Diabetes, metabolic syndrome, hyperglycemia, dyslipidemia, obesity

Table 2. Agents Prescribed

SGA Prescribed	**n (%)**
Quetiapine	465 (41.8%)
Aripiprazole	344 (30.9%)
Risperidone	126 (11.3%)
Olanzapine	123 (11.1%)
Lurasidone	106 (9.5%)
Ziprasidone	63 (5.7%)
Asenapine	15 (1.3%)
Brexpiprazole	12 (1.1%)
Paliperidone	12 (1.1%)
Clozapine	6 (0.5%)
Cariprazine	4 (0.4%)

Iloperidone	0 (0%)

Table 3. Patient Factors & Lab Order Rates[a]			
Predictor	**OR**	**CI**	**P-Value**
Age	1.01	(1.00, 1.02)	0.167
Gender (male)	0.98	(0.74, 1.29)	0.871
Race (other)	1.03	(0.51, 2.13)	0.928
Ethnicity (non-Hispanic)	1.36	(0.52, 3.39)	0.517
High risk SGA	1.09	(0.72, 1.68)	0.675
Psychiatric Diagnoses			
Thought Disorder	1.57	(1.12, 2.22)	0.011
Mood Disorder	1.16	(0.63, 2.08)	0.633
Other	1.12	(0.85, 1.47)	0.409
Anxiety Disorder	0.96	(0.66, 1.38)	0.820
Medical Diagnoses			

Sleep	1.24	(0.93, 1.67)	0.147
Headache	1.07	(0.80, 1.44)	0.639
Metabolic	1.01	(0.75, 1.35)	0.963
Cardiovascular	0.92	(0.70, 1.21)	0.546

[a]Multivariable logistic regression

Table 4. Provider & Alert Factors[a]

Outcome	Comparison	Relative Response Rates	OR	Adjusted 95% CI	Adjusted P-Value
Any Lab Ordered	**Attending Psychiatrist - Nurse Practitioner**	15.8%-19.4%	0.64	(0.48, 0.85)	<0.001
	Resident Psychiatrist - Nurse Practitioner	22.8%-19.4%	1.08	(0.86, 1.35)	>0.999
	Resident Psychiatrist - Attending Psychiatrist	22.8%-15.8%	1.69	(1.32, 2.15)	<0.001
	Enter Order - General BPA Section	54.3%-14.4%	5.59	(4.68, 6.69)	<0.001
HbA1c or FBG Ordered	**Attending Psychiatrist - Nurse Practitioner**	9.8%-12.3%	0.66	(0.51, 0.86)	<0.001
	Resident Psychiatrist - Nurse Practitioner	14.0%-12.3%	1.01	(0.83, 1.24)	>0.999

	Resident Psychiatrist - Attending Psychiatrist	14.0%-9.8%	1.53	(1.21, 1.94)	<0.001
	Enter Order - General BPA Section	33.5%- 9.0%	4.44	(3.87, 5.10)	<0.001
Lipid Panel Ordered	**Attending Psychiatrist - Nurse Practitioner**	6.0%-7.1%	0.76	(0.59, 0.98)	0.027
	Resident Psychiatrist - Nurse Practitioner	8.9%-7.1%	1.17	(0.96, 1.42)	0.177
	Resident Psychiatrist - Attending Psychiatrist	8.9%-6.0%	1.53	(1.22, 1.93)	<0.001
	Enter Order - General BPA Section	20.8%- 5.4%	4.28	(3.78, 4.84)	<0.001
Any Valid Response	**Attending Psychiatrist - Nurse Practitioner**	24.2%-24.7%	0.76	(0.58, 0.99)	0.039
	Resident Psychiatrist - Nurse Practitioner	28.7%-24.7%	1.17	(0.94, 1.45)	0.252
	Resident Psychiatrist - Attending Psychiatrist	28.7%-24.2%	1.54	(1.25, 1.89)	<0.001
	Enter Order - General BPA Section	68.5%-19.6%	7.76	(6.46, 9.32)	<0.001

[a]Univariate GEE logistic regressions with Bonferroni correction, n=10,063