Diabetes medication adherence and glycemic control : patients with vs. without psychotic disorders

Sarah Elizabeth Jedele

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The University of Toledo

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Table of Contents

Introduction

Increased rates of morbidity and mortality in psychotic disorders are greatly reduced when individuals adhere to scheduled treatment plans (Liu, 2014). Side effect profiles of antipsychotic drugs play a key role in medication selection. Second generation antipsychotics (SGAs) are frequently prescribed over first generation antipsychotics (FGAs) due to fewer extrapyramidal side effects (Crossley, Constante, McGuire, & Power, 2010). SGAs increase the risk of cardiovascular disease that is associated with weight gain, diabetes mellitus type 2 (DM2), and increased lipid profiles (Tschoner et al., 2007). People who develop these side effects are presented with a dual challenge of adherence to antipsychotic (Haddad, Brain, & Scott, 2014) and anti-diabetic (Bailey & Kodack, 2011) medications.

Anti-diabetic medication adherence is variable for all individuals with DM2 (Sapkota, Brien, Greenfield, & Aslani, 2015). Adherence to anti-hyperglycemic medications in individuals with psychotic disorders, on or off atypical antipsychotic medications, compared to patients without psychotic disorders is unclear.

The purpose of this project is to identify which group is more adherent to anti-diabetic medications. After determining if one group is more adherent this project will look at whether or not the group that is more adherent has better glycemic control. The questions being answered in this review include, “Does adherence to medications for type 2 diabetes differ between individuals with vs. without psychotic disorders?” and “If there is a difference, is there a change in glycemic control?”.

Diabetes is a disease that is increasing in the United States, with a prevalence of 29.1 million in 2012 (American Diabetes Association, 2015). It is a disease that needs constant monitoring and intervention to maintain a quality of life. It is often accompanied with many comorbid

conditions including hypertension, hyperlipidemia, and obesity. A subset of individuals who are at a higher risk of developing DM2 are patients with mental illnesses. There are many factors that play a role in this increased risk. Some of these risks include the use of second generation antipsychotic medications, lifestyle habits, and increased family history (Dixon et al., 2000)

Starting a patient on anti-hyperglycemic medications varies based on lab findings and a patient's motivation to make the lifestyle changes that are necessary to decrease glycemic index. The patients who adhere to the prescribed recommendations are at an increased chance of having better glycemic control. Prescribing anti-hyperglycemic medications does not guarantee improvement in glycemic control. Patients who are less adherent to these medications are at a higher risk for morbidity and mortality (Rubin, 2005).

Key terms essential to this review include psychotic disorders and diabetic medication. For the purposes of this review the following definitions were used. Psychotic Disorder- Abnormalities in one or more of the following domains: delusions, hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms (American Psychiatric Association, 2013). Anti-Diabetic Medication- Any oral or injectable drug used to reduce glucose levels in the blood.

Methods

Data Collection

A systematic review of medication adherence to anti-hyperglycemic medication and glycemic control among patients with vs. without psychotic disorders was carried out by searching electronic databases PubMed, PsycINFO, and Google Scholar were performed up until the end of August 2016. The search terms were Diabetes Mellitus, Type 2; Antipsychotic Agents; Psychotic disorders/drug therapy; Schizophrenia; Medication Adherence; glycemic control. The electronic database search of PubMed, PsycINFO, and Google Scholar was supplemented with an extensive manual search of reference lists.

Inclusion and Exclusion Criteria

All articles were acquired from peer-reviewed journals and were written in or translated into English. The appropriateness of each report was assessed to ensure quality of the research design and reproducibility of the study. Inclusion criteria in the database searches included peer-reviewed journals; adults (18+ years) with psychotic disorders and type 2 diabetes; and adults (18+ years) with type 2 diabetes without psychotic disorders. Exclusion criteria included case reports and editorials; also excluded are languages other than English and Children (<18yrs).

Literature Review

Medication Adherence

A few studies have been conducted comparing adherence to DM2 medications between individuals with and without psychotic disorders. One of these being a retrospective analysis of prescription claims data from Texas Medicaid between 2008-2011. This study involved a total of 18,999 patients with DM2, of these patients 1,956 were antipsychotic users. The index date of this study started on the date of the first prescription claim for an oral diabetes medication. Patients were followed for 12 months after the index date. Anti-psychotic medication users were identified as individuals who had at least two claims for anti-psychotic medication in both pre-index (6 months prior to the index date) and post-index periods. This study also calculated for differences in severity of illness between antipsychotic users and nonusers by using a caliper-matching algorithm. The two groups were matched based on their chronic disease score (CDS) in the post-index period. This method uses pharmacy claims data to determine the number of selected prescription medications used by the patient (Von Korff, Wagner, & Saunders, 1992). The results of this study revealed that adherence to oral anti-diabetics was greater among antipsychotic users at 37.2% versus nonusers at 24.0% (Desai, Adeyemi, Richards, & Lawson, 2014).

A second study is a retrospective analysis of VA patients with (N= 11,454) vs. without (N= 10,560) schizophrenia and type 2 diabetes. The data used for this study came from the VA's National Psychosis Registry from 2001 through 2003. It is noted that the patients without schizophrenia may have had other major mental disorders, such as bipolar disorder or major depression. To measure adherence, automated prescription refill records were evaluated over a 12-month period, starting with the date of the first prescription for an oral hypoglycemic.

Medication possession ratio (MPR), and objective and validated measure, was used to characterize adherence to oral hyperglycemic medications. The results of this study found that adherence to diabetes medication was better with individuals who had schizophrenia (51%) than those without this diagnosis (46%) (Kreyenbuhl et al., 2010).

A similar study was completed with 74 participants comparing those with a serious mental illness and DM2 (n=44) to those without a serious mental illness who have DM2 (n=30). Serous mental illness includes patients with a diagnosis of schizophrenia, schizoaffective, bipolar, or major depressive disorder. As a part of the methods of this study, participants with mental illnesses had to be on one or more oral or injectable hypoglycemic medications; participants without mental illnesses had to be prescribed at least one hypoglycemic medication routinely. The results of this study suggest that individuals with serious mental illnesses do not fare worse than individuals without psychiatric conditions with regard to their adherence to prescribed medications for chronic medical conditions such as type 2 diabetes (Kreyenbuhl et al., 2011).

A retrospective medical review study was completed through the Kansas City Veterans Affairs healthcare system in 2008 to compare diabetic medication adherence and glycemic control between patients with and without psychotic disorders. Glycemic control findings from this article will be discussed later in this review. The study included 124 individuals with diabetes (62 with schizophrenia or related psychotic disorder; 62 randomly selected, age-similar patients without a psychiatric illness). Adherence was calculated through an electronic refill records system that calculated a cumulative gap ratio over a 12-month period. The results of this study showed no difference in anti-diabetic medication adherence between the two groups. The mean adherence rates revealed 58 days without medication in the psychosis group and 72 days in

the non-psychiatric group. The study did find a correlation between antipsychotic and anti-diabetic medication. Patients who took at least 80% of their antipsychotic medication were significantly more likely to adhere to their anti-diabetic medication regimen (Nelson, Graham, Lindsey, Rasu, 2011).

Diabetic medication adherence in patients with psychotic disorders:

Management of a chronic illness, such as diabetes, in any patient is a very complex and challenging task. It becomes even more challenging for patients with psychotic disorders as they experience substantial health disparities including low quality health care for diabetes treatment (Chwastiak, Freudenreich, Tek, et al, 2015). A systemic review of six retrospective studies was completed of individuals with schizophrenia and diabetes to determine diabetes medication adherence. This review showed relatively low rates of adherence in adults with mental illnesses, ranging from 51%-85% (Gorczynski, Patel, Ganguli, 2014).

A cross-sectional, observation cohort study was completed to determine medication adherence and glucose control in patients with serious mental illnesses who also had diabetes. The study was looking at the effectiveness of collocations of primary care and mental health care. It included 365 veteran patients with type 2 diabetes and serious mental illness (SMI) seeking care from three VA medical facilities. The diagnosis for SMI included patients with schizophrenia, schizophreniform disorder, schizoaffective disorder, bipolar disorder, manic affective disorder, delusional disorder, or other nonorganic psychoses. The results of the study showed that patients with SMI and diabetes have a relatively high rate of medication adherence ($\geq$ 80%) regardless of where they received their medical care (Long, Wang, Medvedeva, et al, 2014).

Diabetic medication adherence in patients without psychotic disorders:

Research in diabetes medication adherence in patients without psychotic disorders compared to those with psychotic disorders is addressed earlier in this paper. Research identifying anti-diabetic medication adherence in general population patients (patients without psychotic disorders) is more significant in third world and developing countries.

The first article reviewed in this section includes a cross-sectional study on patients seeking anti-diabetic drug treatment and follow-up at a general hospital in Oromia Region, Ethiopia. The study was conducted by interviewing the patients visiting using a structured questionnaire and by reviewing case charts using a checklist to assess the level of adherence to anti-diabetic treatment among DM patients. These patients were followed from the dates of Jan. 24, 2014 through Feb. 7, 2014. Patients below the age of 18 years, above 80 years old, and those with obvious psychiatric problems were excluded from the study. The adjusted sample size, after considering a 5% nonresponse rate, was 271. Six variables were assessed including medication side effects, presence of glucometer, complexity of the medication regimen, monthly income, level of education, and distance from the hospital. The results of the study show that the two most significant variables that affect patient medication adherence include whether or not the medication had side effects and the distance a patient was from the hospital. Of the patients who did not experience side effects from their medications 50% were adherent and only 10% were non-adherent. Of the patients who did experience side effects from their medications only 11% were adherent and 21% were non-adherent. Non-adherence to medication was significantly different in patients who lived less than 0.5 hours from the hospital (7% non-adherence) compared to those who lived greater than 0.5 hours from the hospital (24% non-adherence) (Kassahun, Gashe, Mulisa, et al, 2016).

A second study that evaluates diabetes medication adherence in the general population includes a prospective interventional study that was carried out over a one-year period in a tertiary hospital in Kerala, India. This study included inpatients with type 2 diabetes in the general medicine department. The intervention program that was being assessed was medication therapy management (MTM). The intervention program included personal medication record, medication-related action plan, and detailed counseling. Patients with any history of mental illness were excluded. The results of this study showed that of the 104 patients included in the study the anti-diabetic medication adherence rate was 37.5% and increased to 59.5% after intervention (p-value <0.05 in a paired t-test) (Bindu Murali, Boban, Karoor Shanmughan, et al, 2016). Based on these findings anti-diabetic medication adherence in patients of the general population is significantly low.

Glycemic Control

The first article that evaluates glycemic control between patients with vs. without psychotic disorders was referenced earlier in this review, as it also compares medication adherence (Nelson, Graham, Lindsey, Rasu, 2011). Glycemic control was measured by comparing patient A1C values with the glycemic goals established by the Standards of Medical Care in Diabetes-2008. The percentage of patients who met the target A1C goal was compared between the two groups. Similar to the findings for medication adherence this study revealed no significant difference in glycemic control between the groups.

These results would not be expected based on a previous research study that looked at overall diabetes care for patients with mental illnesses, and provides supportive data that there are disparities for these patients. This national, cross-sectional study included 313, 586 non-institutionalized Veterans Health Administration patients with diabetes. Of these patients, 76,799 (25%) had mental health conditions (including depressed mood, anxiety, psychosis, manic symptoms, substance use disorders, personality disorders, and other categories). The results of the study showed that patients with diabetes and mental health conditions did not meet diabetes performance measures. The adjusted odds ratios (95% confidence interval) for these measures include 1.23 for no hemoglobin A_{1c} testing, 1.25 for no low-density lipoprotein cholesterol testing, 1.07 no eye examination done, 1.17 poor glycemic control, and 1.20 poor lipemic control. Across all of these measures there were higher disparities among the patients with psychosis, manic symptoms, substance abuse, and personality disorders (Frayne, Halanych, Miller, et al, 2005).

Discussion

Based on all the articles reviewed in this section there is conflicting evidence on whether anti-diabetic medication adherence is better in patients with vs. without psychotic disorders. Compliance to anti-diabetic medications is less than ideal in both groups (Nelson, Graham, Lindsey, Rasu, 2011). The studies that compare both patients with vs. without psychotic disorders reveal a greater correlation between increased anti-diabetic medication adherence among patients with psychotic disorders. This is a useful finding as it can help providers identify what factors increase medication adherence among this patient population. Some factors identified in these studies include patients with psychotic disorders having increased continuity of care and active involvement of family members in management of care (Kreyenbuhl et al., 2010). More factors that may have a role in increased anti-hyperglycemic medication adherence in patients with psychotic disorders include having a longer days' supply of prescriptions, and improved awareness and experience in the management of chronic conditions (Desai, Adeyemi, Richards, & Lawson, 2014).

Based on the limited research comparing glycemic control between these two groups of individuals, there is inconclusive evidence of whether one group has better control than the other group. The first article in this review reports that there is no significant difference in glycemic control between the two groups. The second study reports opposite findings showing evidence that patients with diabetes and psychotic disorders have less control of their diabetes. Further investigation is needed on glycemic control between diabetic patients with vs. without psychotic disorders. The current studies in this area a scare and provide contradicting evidence.

Another area of investigation that this article review does not look at is the difference in medication adherence to other comorbid conditions in patients with vs. without psychiatric

disorders. A study was completed on antihypertensive medication adherence and blood pressure control in patients with vs. without psychiatric illnesses. This study found no significant difference between antihypertensive medication adherence, but did find a difference in blood pressure control between these groups. The psychiatric group had significantly lower frequency of blood pressure control than the non-psychiatric group (Dolder, Furtek, Lacro, et al, 2005). Further investigation of this and other comorbid conditions and identifying reasons that make one group more adherent and have better control than the other group would be beneficial for patient care.

This article review will help health care providers make informed decision about which anti-psychotic medications to start patients on. Atypical anti-psychotic medications are more commonly used due to the fewer extrapyramidal side effects, care providers often struggle with the decision to start patients on these medications with the increased risk of developing type 2 diabetes. Based on the findings in this review there is a higher chance that these patients have a higher rate of medication adherence to anti-hyperglycemic medications. Knowing this, providers can have confidence in starting and maintaining patients on atypical antipsychotics. This review offers information about factors that improve anti-diabetic medication adherence in patients with psychotic disorders. These factors are a useful tool for providers when helping patients, with or without psychotic disorders, with medication adherence.

Conclusion

This comprehensive literature review found that there may be a mild increase in anti-hyperglycemic medication adherence in patients with psychotic disorders than those without psychotic disorders. The studies reviewed suggested that anti-hyperglycemic medication adherence is less than optimal in both groups. These results can be used to guide health care providers when making decisions based on side effects of anti-psychotic medication. The results of glycemic control among these two groups are inconclusive based on limited research and conflicting evidence.

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Abstract

Objective: Conduct a systematic review to determine if diabetic medication adherence and glycemic control is different among patients with vs. without psychotic disorders. **Method**: A comprehensive search of the electronic databases PubMed, PsycINFO, and Google Scholar were performed up until the end of August 2016. The outcomes under investigation were anti-diabetic medication adherence and glycemic control in patients with psychotic disorders compared to those without psychotic disorders. **Results**: Ten studies fit the inclusion criteria. Five studies were retrospective, one was prospective, three were cross-sectional, and one was a systematic review. **Conclusion**: This comprehensive literature review found that there is an increase in anti-hyperglycemic medication adherence in patients with psychotic disorders than those without psychotic disorders. The results of which group has better glycemic control are inconclusive based on limited research and contradicting evidence.

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