

Retrospective Review of Weight Gain with Atypical Antipsychotics at GMH and COCMHC

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Abstract

Objectives: Anti-Psychotics are a group of medications that are used to treat schizophrenia group of conditions, Mania caused by Bipolar disorder, and other conditions that can cause visual or auditory hallucinations. These hallucinations cause an individual to lose balance with reality and force their inner well being to lose self-control. The purpose of this research design is to identify the relationship between the atypical anti-psychotics and their associations with weight gain. The design is set to distinguish which of the three drugs leads to more weight gain and diabetogenic complications and added side effects in the patients at Griffin Memorial Hospital and Central Oklahoma Community Mental Health Center from 1/1/2010 to 12/31/2013.

Methods: Data from 555 patients were analyzed using a one-way ANOVA from Excel and R-version 3.0.3 statistics. Data was statistically analyzed using p tests.

Results: All of the atypical antipsychotics (Quetiapine, Olanzapine, Clozapine) led to weight gain with Risperidone having a synergistic effect. Diabetes was associated with all of the drugs and Quetiapine showed more GI complications than the other drugs and combinations ($p > 0.05$).

Conclusion: Our study suggests that atypical antipsychotics that were studied were associated with weight gain. Our findings demonstrated that no one drug was overwhelmingly led to more weight gain than the other. Adding risperidone had a synergistic effect and further enhanced weight gain. If replicated, the data may lead to clarification of the results and concluded analysis of the pharmacologic treatment plans of patients at Griffin Memorial Hospital and Central Oklahoma Mental Health Center.

Keywords: Quetiapine; Risperidone; Olanzapine; Seroquel; Antipsychotics; Weight gain

Introduction

Recent advancement in psychopharmacology and the implementation of atypical antipsychotics has made it possible for patients to have a more broad-spectrum efficacy with minimal side effect profile [1,2]. Unlike typical antipsychotics, the newer atypical drugs decrease the positive, negative and cognitive symptoms in the schizophrenia group of conditions and extrapyramidal side effects that pose with the older generation medications [3]. Atypical antipsychotics although efficacious, have shown to cause side effects, such as weight gain, that can lead to overall detrimental health effects. Increased weight gain and obesity has led to an increase in metabolic and cardiovascular complications and an increase in psychotic flare-ups due to poor compliance due via patients' efforts to avoid weight gain [4].

The purpose of this study is to analyze weight gain in patients 50 to 70 years of age at Griffin Memorial Hospital in Oklahoma (GMH) and Central Oklahoma Community Mental Health Care (COCMHC) with the different antipsychotics they are prescribed. In addition, this follow-up review will allow us to better identify which single or combination of drugs pose the most amount of weight gain and side effect profile.

Mechanism of action of atypical antipsychotics

First (typical) and second (atypical) generation antipsychotics have a propensity to bind dopamine D2 receptors in the brain. Typical antipsychotics have a higher affinity for the D2 receptors than atypical antipsychotics and therefore cause more Extrapyramidal Symptoms (EPS) and elevated prolactin levels [5]. The atypical antipsychotics, which include olanzapine (Zyprexa), quetiapine (Seroquel), and clozapine (Clozaril), have a lower affinity for D2 receptors but higher

affinity for serotonin 5-HT_{2A}, 5-HT_{2C}, 5-HT_{2E}, 5-HT₆, histamine H1, and alpha 1 receptors [6].

Atypical antipsychotics and weight gain have been studied on the basis of the receptors that these drugs target. According to various studies and articles, weight gain is directly correlated with histamine H1 and 5-HT_{2C} receptor antagonism [7-9]. Clozapine and olanzapine have the greatest antagonist effect and the most potential to cause weight gain. Quetiapine has a high affinity for H1 receptors but lower affinity for 5-HT_{2C} receptors and hypothetically causes less weight gain in comparison.

Methods

Participants: Participants were taken from the patient database at two adult mental health facilities, Griffin Memorial Hospital (GMH) and Central Oklahoma Community Mental Health Care (COCMHC). GMH also includes an inpatient and outpatient facility. To be included in our study, participants had to receive services for at least two months in either or both facilities, had to have an admission date between 1/1/2010 and 12/31/2013, and had to be between the ages of 50 and 70

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at the time of admission. This was to eliminate potential illnesses that can interfere with our results, and negate any confounding variables. Patients were selected randomly to eliminate bias. A final study roster of participants (N=555) was obtained; participants were 60% female and 40% male with a mean age at admission of 56.44 years.

Data: A retrospective study design was used with data received from patient's previous charts. Pre-existing condition data for diabetes mellitus and hypertension were taken from admissions forms. Prescription drug use was charted for five drugs, including four atypical antipsychotics: quetiapine, olanzapine, clozapine, and risperidone and metformin, as a secondary measure for diabetes mellitus. Data on weight gain and GI complications (most notably for nausea, vomiting, diarrhea, irritable bowel syndrome, constipation, and esophageal reflux) were also collected. This study was approved by the Oklahoma Department of Mental Health and Substance Abuse Services Institutional Review Board.

Analyses: Frequencies were obtained for all prescription drug use categories. Each participant was placed into a single category based upon the specific combination of antipsychotics he or she took while receiving mental health services. For instance, all participants taking both quetiapine and olanzapine were categorized separately from those taking olanzapine and clozapine. Means, standard deviations, and 95% confidence intervals were obtained for weight gain in each category. Proportions of patients having GI complications were also calculated. A one-way, between-subjects ANOVA comparing weight gains among the different antipsychotic categories were also run. All statistics were run in R version 3.0.3.

Results and Discussions

Out of the 555 patients included in this follow-up review, those that encountered the greatest average weight gain, 24.24 pounds, took quetiapine, followed by olanzapine, with an average weight gain of 19.59 pounds. Clozapine demonstrated a 16-pound average weight gain; however, the patient sample was small and the chance of error is high. The combination of quetiapine and olanzapine seemed to have a synergistic effect, with an average weight gain of 28.33 pounds; there was no relationship between intake and weight gain over time for the patient's that took the quetiapine-olanzapine combination. However, individual intake of either medication demonstrated a relationship with weight gain and metabolic side effects. This high average standard of deviation between single drug and combination intake illustrates a variability that exists and may indicate an error of collecting or reporting weight for some patients. Studies have shown Clozaril to cause the greatest weight gain [9], but our review was limited to three patients and therefore inconclusive for patients at GMH and COCMHC.

Of the 555 patients that were studied, 369 patients were not on any of the three drugs that were studied. These patients were on different atypical antipsychotics, such as aripiprazole (Abilify), ziprasidone (Geodon), or risperidone (Risperdal), which have been shown to cause minimal weight gain in comparison to those studied [10,16,17]. However, the patient population studied showed an average weight gain of 20.84 pounds when using either of these drugs. Out of these three atypical antipsychotics that were not studied, it has been shown that risperidone tends to lead to higher weight gain than either aripiprazole or ziprasidone [11,16].

Of the 369 patients not on quetiapine, olanzapine or clozapine, 104 patients were on risperidone strictly taken from the COCMHC database. We randomly chose patients at COCMHC and compared those only on

Risperdal to those on Risperdal combined with the medication(s) of interest. Patients only on risperidone showed a mean weight gain of 22.12 pounds, while those not on quetiapine, olanzapine, clozapine or risperidone showed an average weight gain of 20.59 pounds. However caution must be taken when interpreting these data since significant variability in the measured weight is a potential source of error. Patients who had risperidone added to their quetiapine showed a 7.78 pound weight gain over a 2 months to a 4 years span, while patients for whom risperidone was added to olanzapine showed an average gain of 5.57 pounds. There were very few patients on clozapine; therefore, the data were inconclusive in showing a relationship with risperidone. Patients on combinations of quetiapine and olanzapine with added risperidone showed a decrease in weight gain compared to patients on quetiapine and olanzapine alone. This was again inconclusive because only 15 patients were on risperidone with quetiapine and olanzapine (Table 1). With an increase in weight, there comes an increased risk of abdominal fat deposition and an increased risk of diabetes and hypertension [12-14]. Patients with pre-existing diabetes and Metformin, and hypertension were taken into account. This helped us eliminate a potential confounding factor, diabetes, for weight gain [12]. Out of the 79 patients on quetiapine, 14 were on metformin (18%). Fourteen patients were on metformin that were also on olanzapine (23%) and 1 patient was on metformin that was on clozapine (33%). Although not every patient with weight gain was on metformin, patients that were excessively obese were on metformin.

Similarly we also focused on which of the three antipsychotics were most associated with gastrointestinal symptoms, such as nausea, vomiting, diarrhea, irritable bowel syndrome, constipation, and esophageal reflux. Gastrointestinal symptoms were noted most with patients taking quetiapine, with 37 out of 79 (47%) patients complaining and being treated for gastrointestinal symptoms. 44% of the patients on Olanzapine (27/62) had G.I. complaints, and were treated accordingly.

Conclusively, quetiapine showed more patients complain of weight gain than olanzapine. Clozapine has been noted to cause weight gain [15], but the evidence was inconclusive at GMH and COCMHC for patients between 50-70 (Table 2). The combination of quetiapine and olanzapine had a synergistic effect for increase in weight. Patients on all three drugs also showed an increase, but the data were inconclusive. Evidence showed that risperidone had a synergistic effect when added to quetiapine or olanzapine. There was not much difference in diabetes prevalence amongst the quetiapine or olanzapine users (Figure 1).

Conclusion

Weight gain is a serious problem in patients taking atypical antipsychotics [2,12]. Along with increased weight, we encountered that patients had an increase in the risk of cardiovascular and metabolic complications such as diabetes, hypertension, and gastrointestinal

| Antipsychotic Category | M | SD | (N) |
|--------------------------------------|-------|--------------|-----|
| Quetiapine | 24.24 | 17.81 | 79 |
| Zyprexa | 19.59 | 13.00 | 62 |
| Clozapine | 16.00 | 5.66 | 3 |
| Quetiapine and olanzapine | 28.33 | 22.72 | 28 |
| Olanzapine and clozapine | 19.00 | ^a | 7 |
| Quetiapine, olanzapine and clozapine | 19.25 | 13.15 | 6 |
| Other antipsychotics | 20.84 | 13.78 | 369 |

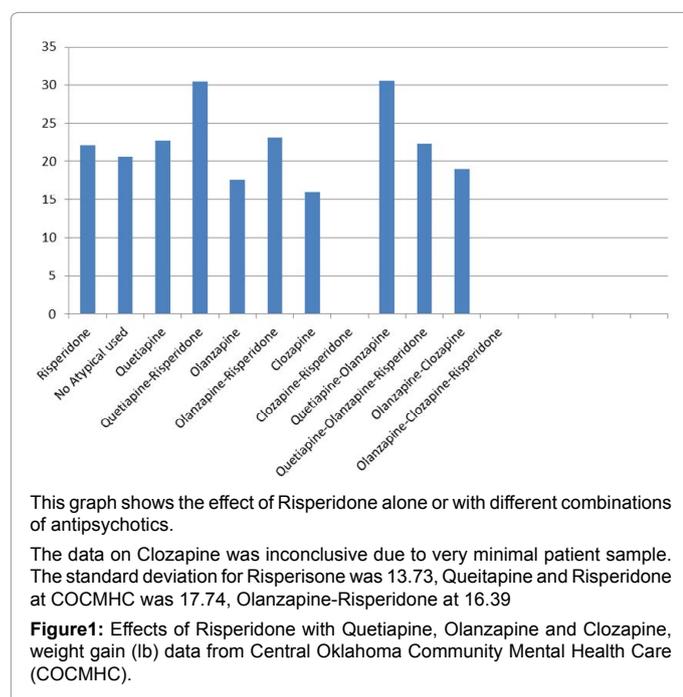
^aOne participant took both olanzapine and clozapine, preventing the calculation of a standard deviation

Table 1: Means and Standard Deviations for Weight Gain (pounds) by Antipsychotics Used.

| Drug | Total Patients on Drug | Total Patients on Metformin | Total Patients with G.I. Complaints (Nausea, Vomiting, Diarrhea, Ibs, Gerd) |
|--|------------------------|-----------------------------|---|
| Quetiapine | 79 | 14 (18%) | 37 (47%) |
| Olanzapine | 62 | 14 (22%) | 27 (44%) |
| Clozapine | 3 | 1 (33%) | 1 (33%) |
| Quetiapine-Olanzapine | 28 | 4 (14%) | 12 (43%) |
| Quetiapine-Clozapine | 1 | -- | 1 |
| Olanzapine-Clozapine | 7 | 2 (28%) | 1 (14%) |
| Quetiapine-Olanzapine-Clozapine | 6 | 3 (50%) | 2 (33%) |
| No drugs of interest, but are on other atypical antipsychotics | 369 | 52 (14%) | 100 (27%) |

This table demonstrates the relationship between patients on one Anti-Psychotic or combination with Metformin. The last column is the GI side effects associated with single antipsychotic use compared to the anti-psychotic combination use.

Table 2: Effect of Metformin and G.I. complaints on Anti-Psychotics.



manifestations. Although atypical antipsychotics are noted to cause weight gain, different drugs in the second-generation group can have different effects based on their affinity for histamine and serotonin receptors [6-9]. Our study was geared to identify all the atypical antipsychotic that cause more weight gain, what drugs are associated with more metformin intake, and which antipsychotic causes more common side effects such as gastrointestinal manifestations. Understanding that there may be errors in reporting or collecting data, we did manage to secure enough evidence to distinguish that both quetiapine and olanzapine caused weight gain in the patients of GMH and COCMHC. Adding risperidone had a synergistic effect and further enhanced weight gain. Evidently, there was not a great relationship of Metformin intake with any one or combination of anti-psychotics, it is still proved that chance of acquiring diabetes is more from the added weight gain. Studies have shown that diabetes complications have led to multiple cardiovascular manifestations, therefore, proper care needs to be taken when on antipsychotics to eliminate the potential for such adverse reactions.

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