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Effect of atypical antipsychotics on body weight in geriatric psychiatric inpatients

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Abstract

Background: Studies suggest that antipsychotic-induced weight gain is not a great concern in the elderly population. This study investigated the weight change in elderly patients with various treatment duration and antipsychotics. Part 1 of the study was to determine whether atypical antipsychotics induced weight change in elderly patients. Part 2 was to determine whether certain atypical antipsychotics induced more weight change in elderly patients.

Methods: In Part 1, a retrospective chart review was done on 115 geriatric inpatients. After exclusion, patients were divided into four groups: control ($n = 17$), new treatment ($n = 18$), long-term treatment ($n = 13$), and medication switch groups ($n = 8$). In Part 2, a retrospective medication review was performed on 169 geriatric inpatients. After exclusion, patients were divided into three groups: aripiprazole ($n = 18$), olanzapine ($n = 49$), and risperidone ($n = 57$). Body weights were obtained at two different time points.

Results: No significant difference in weight change was observed among the control (1.5 kg), new treatment (0.8 kg), long-term treatment (−0.3 kg), and medication switch (1.9 kg) groups. No significant difference in weight change was observed between patients with and without dementia (0.8 and 1.1 kg, respectively). The weight change in the aripiprazole group (−2.0 kg; −2.30% from baseline) was significantly different from the weight change in the olanzapine group (0.7 kg; 1.87% from baseline; $p < 0.05$), but not from the risperidone group (−0.4 kg; −0.45% from baseline). Clinically significant weight gain (>7% increase in body weight) occurred in 14.3% of the olanzapine patients, a percentage significantly higher than the 3.5% in the risperidone group.

Conclusion: Although atypical antipsychotics were generally weight neutral in the geriatric population, aripiprazole and olanzapine were associated with significant weight loss and weight gain, respectively.

Keywords
Antipsychotic, body weight, elderly, aripiprazole, olanzapine, risperidone

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Introduction

Among the most troublesome side effects of atypical antipsychotics are weight gain and its associated metabolic side effects. The magnitude of weight gain varies with each drug within the atypical antipsychotic family. The extent of weight gain is thought to be determined, at least in part, by the drug's effect on various receptors, including serotonin, dopamine, adrenergic, histamine, and cholinergic signaling.[1] The most significant weight gain occurs with clozapine, olanzapine, and quetiapine.[2] Obesity has been associated with a number of co-morbid conditions, such as hypertension, type II diabetes, coronary heart disease, stroke, osteoarthritis, obstructive sleep apnea, and various cancers.[3,4] One survey study showed that obese patients with schizophrenia were 2.5 times more likely to miss their antipsychotics compared to non-obese patients, with distress over weight gain serving as the main reason for non-compliance.[5]

Weight gain is primarily a concern for younger patients who use atypical antipsychotics. Research suggests that the metabolic side effects of antipsychotics are not as great a concern in the elderly population. A literature review reports that

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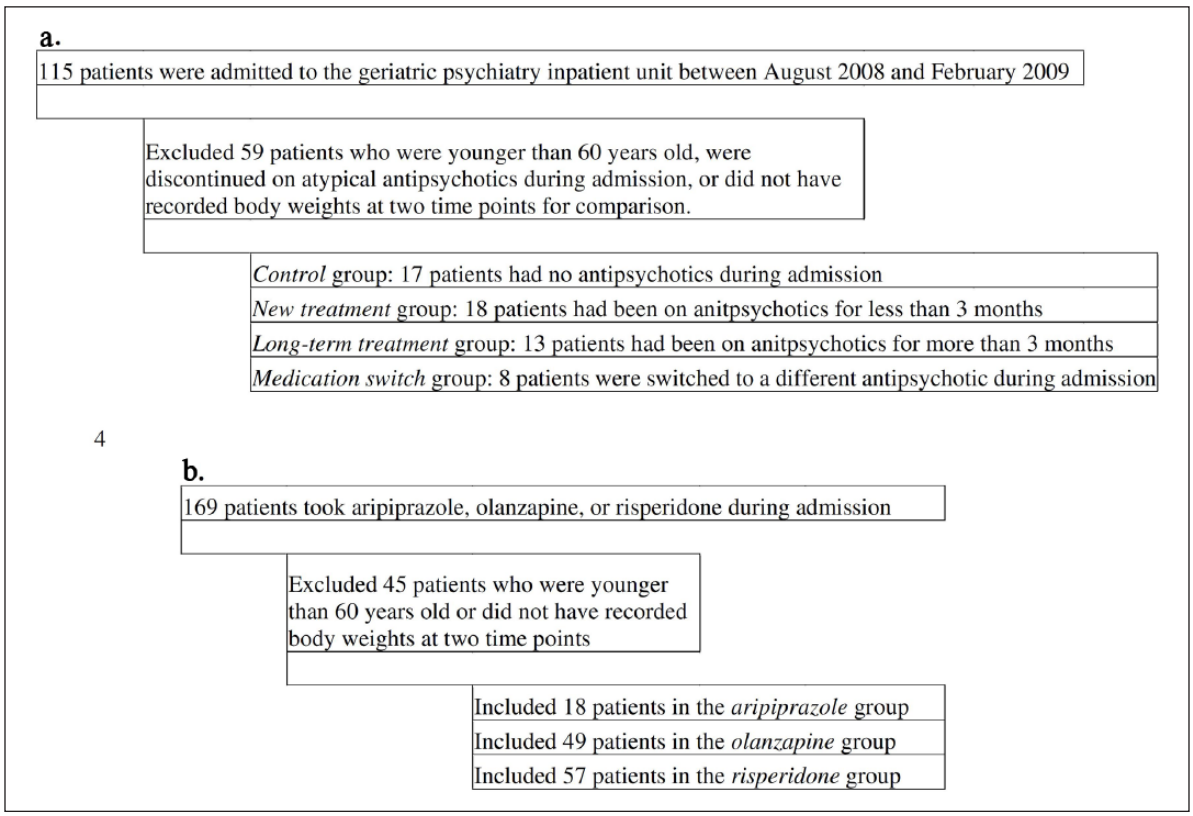

Figure 1. Patient assignment in (a) Part 1 and (b) Part 2 of the study.

atypical antipsychotics, more specifically risperidone and olanzapine, do not induce significant weight gain when used to treat schizophrenia or behavioral and psychological symptoms of dementia in the geriatric population.[6] The authors attribute this finding to the low baseline weight of many elderly patients, and the ongoing weight loss that occurred as a result of the underlying dementia. Dementia patients have been suggested to exhibit more severe wandering, purposeless activity, and inappropriate activity that increase energy expenditure and reduce intake, thereby inducing weight loss.[7] Currently, only a limited number of studies have explored the metabolic side effects of antipsychotics in the geriatric population, and the majority of them focused on the use of some older atypical antipsychotics in patients with dementia. This study comprised two parts. The first part sought to determine whether atypical antipsychotics induced weight change in elderly patients with various psychiatric diagnoses, such as dementia, psychotic disorders, bipolar affective disorders, and major depressive disorders; the second part of the study involved identifying whether or not different atypical antipsychotics induced more weight change in elderly patients.

Methods

Patients

The study was conducted using a pre-specified protocol approved by the Council of Research Ethics Board at the Royal Ottawa Mental Health Centre. In Part 1 of the study, a psychiatry resident reviewed the paper medical charts and of all patients admitted to the geriatric psychiatry inpatient unit at the Royal Ottawa Mental Health Centre between August 2008 and February 2009. A total of 115 patients were identified. Patients under 60 years of age, those discontinued on atypical antipsychotics during admission, or those without recorded body weights at two time points for comparison were excluded from the study. The remaining 56 patients were divided into four groups: (1) the *control* group, whose members had no exposure to atypical antipsychotics during the first 3 months after admission ($n=17$); (2) the *new treatment* group, whose members were started on a new atypical antipsychotic either during admission or within 3 months of admission ($n=18$); (3) the *long-term treatment* group, whose members had been on the same atypical antipsychotics for over 3 months prior to admission ($n=13$); and (4) the *medication switch* group, whose members had been switched to another atypical antipsychotic during admission ($n=8$). Figure 1(a) outlines how the patients were divided into groups. Table 1 illustrates the demographics of the patients included in Part 1 of the study.

In Part 2 of the study, a medical student reviewed the electronic medication records of all patients who took aripiprazole, olanzapine, or risperidone during admission to those of the geriatric psychiatry inpatient unit at the Royal Ottawa Mental Health Centre between June 2011 and June 2012. A total of 169 patients were identified. Patients under

Table 1. Demographics of the geriatric patients in Part 1 of the study.

	Control	New treatment	Long-term treatment	Medication switch
Total number	17	18	13	8
Female (%)	9 (52.9)	12 (66.7)	8 (61.5)	7 (87.5)
Male (%)	8 (47.1)	6 (33.3)	5 (38.5)	1 (12.5)
Mean age (range, SD)	77.7 (66–90, 7.0)	76.2 (69–89, 6.7)	78 (70–87, 5.9)	76.5 (65–86, 7.9)
Dementia (%)	11 (64.7)	8 (44.4)	9 (69.2)	4 (50.0)
Psychotic disorders (%)	1 (5.9)	4 (22.2)	4 (30.8)	1 (12.5)
Bipolar affective disorder (%)	3 (17.6)	2 (11.1)	2 (15.4)	1 (12.5)
Major depressive disorders or episodes (%)	7 (41.2)	8 (44.4)	5 (38.5)	4 (50.0)
Cognitive disorders not yet diagnosed (%)	2 (11.8)	4 (22.2)	2 (15.4)	2 (25.0)
On olanzapine	0 (0%)	6 (33.3%)	4 (30.8%)	5 (62.5%)
On quetiapine	0 (0%)	5 (27.8%)	5 (38.5%)	2 (25%)
On risperidone	0 (0%)	7 (38.9%)	4 (30.8%)	1 (12.5%)
Mean number of days between the two weight measurements (SD)	39 (26)	44 (28)	55 (41)	33 (19)

SD: standard deviation.

Table 2. Demographics of the geriatric patients in Part 2 of the study.

	Aripiprazole	Olanzapine	Risperidone
Total number	18	49	57
Female	13	37	34
Male	5	12	23
Mean age (range, SD)	75 (65–89, 6.4)	75 (62–91, 7.6)	78 (62–95, 7.9)
Mean number of days on the antipsychotic (range, SD)	42 (5–147, 35.6)	67 (3–318, 64.9)	50 (5–277, 49.4)
Mean number of days between the two weight measurements (SD)	40 (41)	65 (71)	40 (36)

SD: standard deviation.

60 years of age and those without recorded body weights at two time points for comparison were excluded, leaving 18 aripiprazole patients, 49 olanzapine patients, and 57 risperidone patients to be included for analysis. Figure 1(b) outlines how the patients were divided into groups. Table 2 illustrates the demographics of the patients included in Part 2 of the study.

Body weight measurement

Body weight comparisons were made from weight data recorded in the dieticians' monitoring books at two different points of time. For the *control* and *long-term* treatment groups in Part 1 of the study, body weights at the time closest to admission and closest to discharge were collected. For the *new treatment* group, body weight prior to the beginning of treatment with the new atypical antipsychotics and the body weight closest to discharge were collected for comparison. For the *medication switch* group, body weight prior to the switch of atypical antipsychotics and the body weight closest to the discharge were compared. The percentage weight change from baseline was calculated using the following formula: Weight change/baseline weight × 100%.

In Part 2 of the study, body weights at the time closest to the initiation and discontinuation of atypical antipsychotics were collected. In the event that the patient had taken antipsychotics prior to admission, body weight at the time closest to admission was collected. In the event that the patient was discharged with antipsychotics, body weight closest to discharge was collected.

Data analysis

Statistical analysis was performed using the computer software GraphPad Prism version 4.00 for Windows (GraphPad Software, San Diego, CA, USA). Statistical significance was defined a priori as $p<0.05$. For dichotomous outcomes, a two-tailed Fisher's exact test was used to compare two groups, and a chi-square test was used to compare more than two groups. For continuous outcomes, a two-tailed Mann–Whitney test was used when comparing two groups, and a Kruskal–Wallis one-way analysis of variance followed by Dunn's test was used when comparing more than two groups. Because our sample sizes were relatively small and unlikely to have normal distributions, non-parametric tests (Mann–Whitney and Kruskal–Wallis) were used rather than parametric tests (Student's *t*-test and

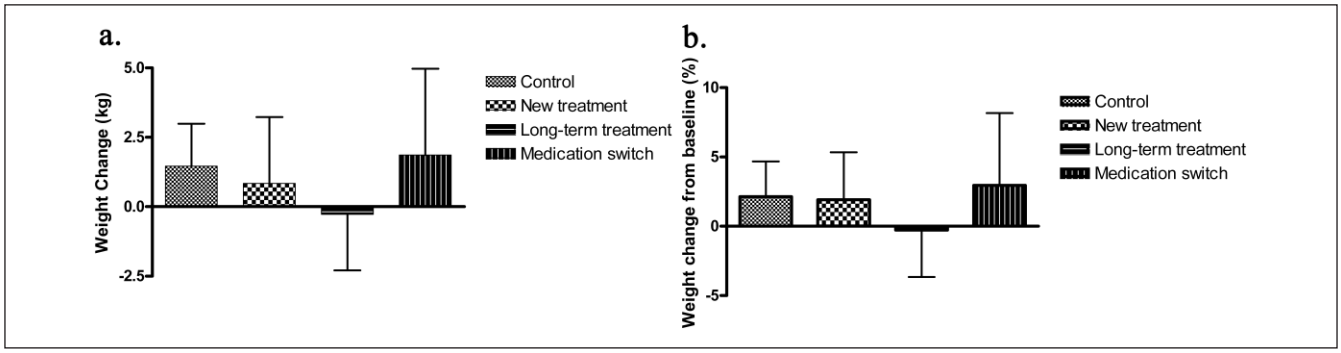

Figure 2. (a) Weight change and (b) percentage weight change from baseline in the control, treatment, long-term treatment, and medication switch groups. Data were presented as mean with 95% CI and analyzed using Kruskal–Wallis one-way analysis of variance. No statistical difference was found among the groups.

Newman–Keuls). Data were presented as a mean with a 95% confidence interval (CI) or a mean with standard deviation (SD).

A sample size calculation with continuous outcome variables, a two-tailed alpha of 5%, and a beta (or statistical power) of 80% were used.[8] A previous study on nursing home dementia patients (with a mean age of 84.4 years) showed that olanzapine treatment resulted in a weight change of −0.96 pounds (ranging from −7 to 4 pounds; SD, 1.8), whereas risperidone treatment resulted in a weight change of 3.08 pounds (ranging from −23 to 12 pounds; SD, 5.8).[9] Based on these data, a minimum of four patients was estimated to be needed per group.

Results

Part 1

No significant difference in weight change was observed among the *control* ($n=17$; 1.5 kg; 95% CI, −0.1 to 3.0 kg), *new treatment* ($n=18$; 0.8 kg; 95% CI, −1.6 to 3.2 kg), *long-term treatment* ($n=13$; −0.3 kg; 95% CI, −2.3 to 1.8 kg), and *medication switch* ($n=8$; 1.9 kg; 95% CI, −1.2 to 5.0 kg) groups (Figure 2(a)). Similarly, no significant difference in percentage weight change from baseline was observed among the *control* (2.13%; 95% CI, −0.41% to 4.68%), *new treatment* (1.92%; 95% CI, −1.48% to 5.32%), *long-term treatment* (−0.27%; 95% CI, −3.65% to 3.11%), and *medication switch* (2.95%; 95% CI, −2.25% to 8.11%) groups (Figure 2(b)). No significant difference in weight change was observed between patients with and without dementia ($n=32$ and 24, respectively; 0.8 and 1.1 kg, respectively; $p=0.3287$) (Figure 3(a)). Similarly, no significant difference in percentage weight change from baseline was observed between the two groups (1.35% and 2.28%, respectively; $p=0.2301$) (Figure 3(b)). Between patients with and without dementia, there was no significant difference in the percentage of patients with clinically significant weight gain (>7% increase in body weight)[2] and with clinically significant weight loss (>7% decrease in body weight)[9] (Table 3).

Part 2

The weight change in the aripiprazole group ($n=18$; −2.0 kg; 95% CI, −3.3 to −0.6 kg) differed significantly ($p<0.05$) from the weight change in the olanzapine group ($n=49$; 0.7 kg; 95% CI, −0.7 to 2.1 kg), but not from the risperidone group ($n=57$; −0.4 kg; 95% CI, −1.3 to 0.4 kg) (Figure 4(a)). A significant percentage weight loss was observed in the aripiprazole group (−2.30%; 95% CI, −3.74% to −0.87%), which was significantly different from the percentage weight loss observed for the olanzapine group (1.87%; 95% CI, −0.68% to 4.42%), but not from that of the risperidone group (−0.45%; 95% CI, −1.58% to 0.69%) (Figure 4(b)). Clinically significant weight gain occurred in 14.3% of the olanzapine patients, a percentage significantly higher than the 3.5% in the risperidone group (Table 4). Among the three antipsychotics, no significant difference was found in the number of patients with clinically significant weight loss (Table 4).

Discussion

Atypical antipsychotics generally did not cause significant weight change in the elderly patients in Part 1 of the study (Figure 2). Whether or not switching geriatric patients to another antipsychotic might be effective for weight reduction remains unclear, as our data indicated that switching antipsychotics did not cause a significant difference in weight change compared to the other groups. Similarly, a study found that switching 21 elderly patients (60–88 years of age) with schizophrenia to olanzapine did not result in significant weight change.[10]

Whether or not long-term antipsychotic treatment had a less significant effect on weight change also remains unclear, as no difference in weight change between the long-term treatment and new treatment group was found, as shown in Figure 2. However, the weight change in the long-term treatment group appeared to be less compared with that of the new treatment group. This trend was consistent with a literature analysis suggesting that weight gain in long-term atypical

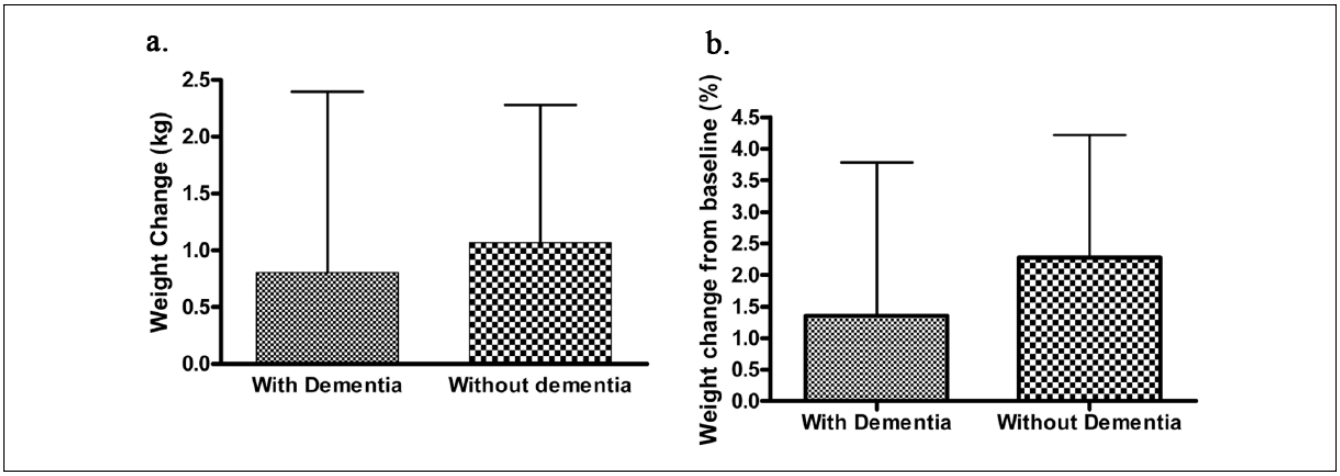

Figure 3. (a) Weight change and (b) percentage weight change from baseline in geriatric patients with dementia versus geriatric patients without dementia. Data were presented as mean with 95% CI and analyzed using two-tailed Mann–Whitney test. No statistical difference was found among the groups.

Table 3. Percentage of geriatric patients with significant weight gain (>7% from baseline) and significant weight loss (>7% from baseline) in Part 1 of the study.

	With dementia ($n=32$)	Without dementia ($n=24$)
Percentage of patients with significant weight gain	15.6%	25.0%
Percentage of patients with significant weight loss	9.4%	0%

No statistical significance versus the dementia group.
Data were analyzed using Fisher's exact test.

antipsychotic treatment was less than in short-term treatment.[11] The authors of the analysis suggested this trend could be due to weight gain reaching a plateau after 1 year of treatment. While it can be argued that many of the geriatric patients have dementia that lead to weight loss, thus offsetting the weight gain induced by antipsychotics,[6] the data presented in Figure 3 and Table 3 failed to reveal any significant difference in weight change between patients with and without dementia.

Our data add to the current debate as to whether or not atypical antipsychotic induces weight gain and metabolic side effects in the geriatric population. In a study on geriatric psychosis in an inpatient setting, 4 weeks of treatment with olanzapine resulted in increases in body weight, fasting triglycerides, and glucose levels (2.2%, 39.9%, and 8.9% from baseline, respectively).[12] The authors acknowledged that this weight gain might be secondary to improvement of psychotic symptoms, which enabled patients to eat well and restore their body weight. In comparison, the *new treatment* group in Part 1 of our study had a 1.92% increase in body weight, an amount that was not significantly different from the 2.13% increase in body weight of the control group.

In a randomized controlled trial involving 175 subjects, all 60 years of age or over with schizophrenia or schizoaffective disorder, olanzapine- and risperidone-treated patients were found to have a weight gain of 0.6 and 1.4 kg, respectively.[13] Furthermore, in a retrospective analysis of 50 nursing home patients diagnosed with dementia (with a mean age of 84.4 years), olanzapine and risperidone were associated with a weight change of 0.44 and −0.14 kg, respectively.[9] None of the patients experienced clinically significant weight gain. Overall, the weight changes in the geriatric population were much smaller than the weight changes in the younger population (4.45 kg on clozapine, 4.15 kg on olanzapine, 2.10 kg on risperidone, and 0.04 kg on ziprasidone).[14] Similarly, the weight change induced by aripiprazole, olanzapine, and risperidone in our study appeared to be trivial (−2.0, 0.7, −0.4 kg, respectively) (Figure 4(a)).

Although antipsychotics appeared to be generally weight neutral in the geriatric population, aripiprazole was associated with significant weight loss in Part 2 of our study (Figure 4). The result was consistent with a meta-analysis that showed significant weight reduction among 784 schizophrenia and schizoaffective patients (with a mean age = 39.4) following the switch to aripiprazole.[10] The −2.0 kg weight change observed in our aripiprazole group was similar to the −2.55 ± 1.5 kg weight change reported in the meta-analysis. The 95% CI of weight change in the aripiprazole group (−3.3 to −0.6 kg) did not cross with the interval in the olanzapine group (−0.7 to 2.1 kg), indicative of a significant difference in size effects. Similarly, in a 26-week, double-blind, randomized-controlled trial on 317 patients (with a mean age of 38.4), the aripiprazole ($n=156$) group demonstrated a mean weight loss of 1.37 kg, while the olanzapine ($n=161$) group had a mean weight gain of 4.23 kg.[15] In addition, clinically significant weight gain was observed in 14% of the aripiprazole group, a percentage statistically different from the 37%

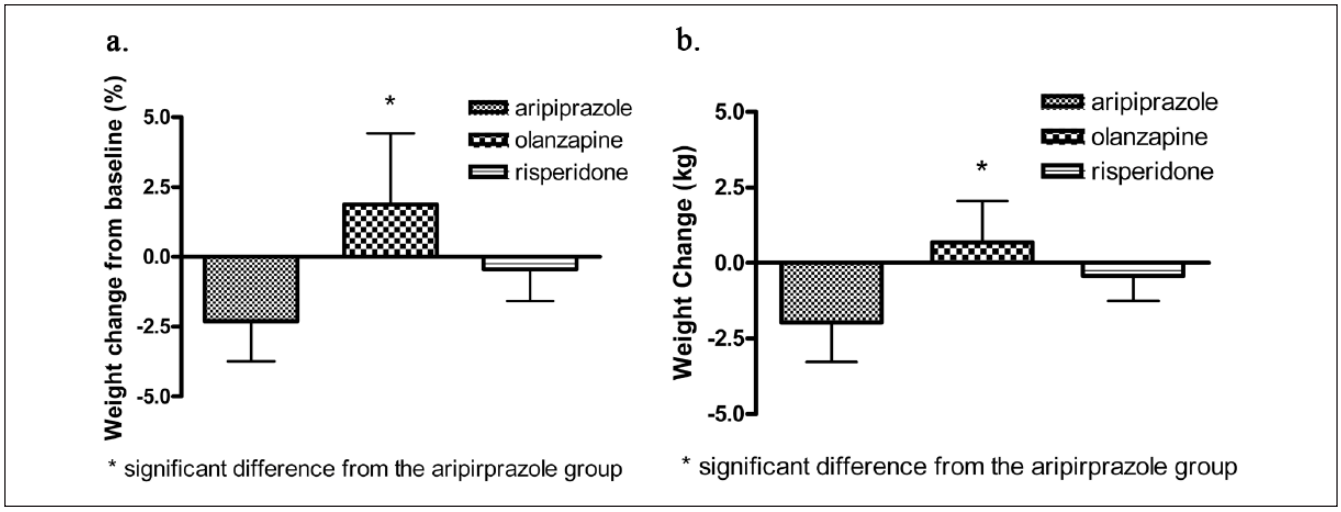

Figure 4. (a) Weight change and (b) percentage weight change from baseline in geriatric patients taking aripiprazole, olanzapine, and risperidone. Data were presented as mean with 95% CI and analyzed using Kruskal–Wallis one-way analysis of variance.

Table 4. Percentage of geriatric patients with significant weight gain (>7% from baseline) and significant weight loss (>7% from baseline) in Part 2 of the study.

	Aripiprazole ($n=18$)	Olanzapine ($n=49$)	Risperidone ($n=57$)
Percentage of patients with significant weight gain	0%	14.3%*	3.5%
Percentage of patients with significant weight loss	5.6%	8.2%	5.3%

*Significant difference versus the risperidone group.
Data were analyzed using Fisher's exact test.

observed in the olanzapine group ($p<0.001$). The difference in weight change was believed to be the result of the difference in the antipsychotic pharmacology. Olanzapine has a significant affinity for the H1 histamine and M1 muscarinic cholinergic receptors, both of which can induce hunger, satiety, and sedation; meanwhile, aripiprazole has only a low-to-moderate affinity for these receptors.[15] It is important to note that weight gain and no weight change were also reported in the younger population who took aripiprazole.[4,16]

Table 4 reveals that 14.3% of patients given olanzapine experienced clinically significant weight gain. This percentage was significantly higher than the 3.5% of risperidone patients who demonstrated a clinically significant weight gain. These percentages are similar to those of a previous study, in which 14.8% of geriatric patients given olanzapine and 5.1% of geriatric patients given risperidone experienced clinically significant weight gain.[13] Therefore, clinicians should carefully monitor the body weight of geriatric patients on olanzapine.

Our study faced several limitations. First of all, despite our initial attempt to review specific metabolic side effects of atypical antipsychotics, such as the lipid profile and body mass index, only body weights were available as primary outcomes for all patients. Due to the retrospective nature of our chart review, lab values were not consistently recorded at the time of admission. Despite being statistically insignificant, the number of days between weight measurement and duration of antipsychotics appeared to be variable in different groups. Second, this study had a relatively small sample size that lowered the statistical power, especially in our secondary outcomes and subgroups. For example, we observed about 10% difference in percentage of patients with significant weight gain in the dementia versus non-dementia groups (Tables 3 and 4), but were unable to find statistical significance. The distributions of male and female patients were not equal in our study. We should consider repeating the study on these secondary outcomes and subgroups with a larger sample size. Third, all our patients were psychiatric inpatients in one center that limited the generalizability of our findings. We did not examine the inter-reliability of our findings. Fourth, we did not examine medications other than antipsychotic medications that the patients might be taking, such as antidepressants, which may be responsible for increasing or decreasing their weights. Their prior-to-admission conditions, psychiatric diagnoses, and medical co-morbidities could also affect their weight change, but our study did not record these information. In addition, patients with no recorded weights were excluded that could lead to selection bias. These patients might have more severe mental disorders and thus refused to have their weights measured.

Many atypical antipsychotic studies to date have only examined geriatric patients with dementia.[17–20] However, in a real clinical setting, antipsychotic use is not limited to dementia. Another one of this study's strengths was that rather than dividing groups into only treatment and control groups, we examined a *long-term treatment* group and *medication switch* groups, which are often seen in clinical settings.

Conclusion

It is important not to assume that all atypical antipsychotics cause non-significant weight gain in the geriatric populations. Clinicians should carefully monitor the body weight of geriatric patients on aripiprazole since our data showed that its use was associated with significant weight loss. Our study is retrospective and is thus hypothesis-generating at best. The sample size calculation with continuous outcome variables can be used with a two-tailed alpha of 5%, a beta of 80%,[8] and the current data on the weight change associated with aripiprazole (−2.0 kg; SD, 2.7 kg) and olanzapine (0.7 kg; SD, 4.8 kg). As such, a minimum of 50 elderly patients will be needed per group as a means to conduct a prospective trial. Because weight change is a cause of medication non-compliance,[5] addressing this issue in the elderly population is important.

Although studies on the efficacy of aripiprazole on elderly patients have previously been performed,[21] their primary endpoints were not weight change. It is also unclear as to whether antipsychotic-induced weight loss is beneficial or harmful to the elderly. In a study that estimated the impact of antipsychotic-induced weight gain on the mortality rate of from 5209 respondents, a "U-shaped" association between the body mass index and mortality rate was found.[22] We encourage researchers to conduct prospective trials to confirm whether aripiprazole causes weight loss in the geriatric population and to assess whether this effect is beneficial.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval for this study was obtained from the Royal Ottawa Mental Health Centre Council of Research Ethics Board. It does not have an approval number.

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Informed consent

This is a retrospective chart review that cannot require patients' informed consent. All patients' information are anonymized.

Trial registration

This is a retrospective review that does not require a trial registration number.

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