Weight Change in Parkinson’s Disease patients taking Atypical Antipsychotics

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ABSTRACT

Abstract Background: Weight loss in PD is a chronic process that is observed in both early and late stages of PD. Atypical antipsychotics are drugs associated with marked weight gain. Objective: To determine body mass index (BMI) change in Parkinson’s disease (PD) before and after taking atypical antipsychotics (AA) drugs and compare against PD control and Alzheimer’s disease (AD) patients on AAs. Methods: We included PD consecutive PD subjects started on AA who had accurate weights for more than 6 months before and initiation of AA. The compared weight change in those PD subjects before and after AA use, against a control group of similarly aged matched PD subjects, and against twenty-eight AD subjects taking AA. A linear regression model was created to compare weight changes. Results: Fifty-nine PD subjects had complete data, quetiapine (n= 53) and clozapine (n=6). The mean BMI change in the period before starting AA was 0.00 kg/m2/month over 1.95 ±1.41 years. After starting AA, subjects lost 0.03 kg/m2/month (95% CI 0.62-1.21, \(P = 0.0001\)), comparing PD before AA to the same PD patients after AA. In 61 PD controls, the mean BMI loss was 0.01 kg/m2/month (95% CI 0.15-0.06, \(P = 0.007\)) comparing PD on AA vs. PD controls. The BMI change before and after starting AA drugs.

METHODS

Patients were recruited from the Baylor College of Medicine, Parkinson’s Disease Center and Movement Disorders Clinic. All patients were diagnosed as PD based on clinical criteria. We included all subjects who used AA drugs for at least 6 months who have accurate same scale weights for at least 6 months before and 6 months after initiation of the AA. Criteria for exclusion include secondary parkinsonism, ptyaloid controlled endocrine diseases such as diabetes mellitus, pyriform disease, cushing disease and polycystic ovarian syndrome; human immunodeficiency virus infection; [91], myalgic encephalomyelitis; gastrointestinal diseases except peptic ulcer or acid reflux diseases. Patients undergoing functional brain surgery for PD within 2 years of initiation of AA, or during the post-AA period were also excluded. We included all subjects prospectively seen in clinic who met the criteria. At each visit, we recorded patient weight, demographic data, Hoehn & Yahr stage, and all PD medications. The equivalent dose of L-dopa was calculated; levodopa + extended-release levodopa; 2.7 mg/kg/100 kg (COMT inhibitor used)(p<0.001), and dopamine agonists (mean±SD) 4.4 mg/kg/100 kg (21 AA have one subject had two different epochs of AA use (quetiapine and clozapine) separated by more than 2 years. Simple linear regression model was created to compare body mass index change before and after starting AA drugs.

RESULTS

We enrolled 54 PD patients, 33 (61%) male. The average age when starting AA was 71.2 ± 8.9 years (mean±SD) and the duration from the initial parkinsonian symptom to AA initiation was 11.4 years. The Hoehn & Yahr staging was 2.9 ± 0.7. (Figure 1) The PD patients were prescribed either quetiapine (87.2%) or clozapine (12.8%) depending on the severity of psychosis and other clinical factors. The indication for AA was psychosis (96.4%) and insomnia (3.6%). The average dose was 74.4 mg/day for quetiapine and 41.4 mg/day for clozapine.

Using the all weight data from the time of clinical induction (mean 6.1 years) we found that patients lost 0.6 kg/m2/year (1.8 kg/year) For the 2 years prior to initiation of AA, the mean BMI loss was also 0.6 kg/m2/year (1.8 kg/year). For the 2 years after starting AA was BMI loss was 0.4 kg/m2/year (1.2 kg/year). (NS) (Figure 2) The average equivalent doses of L-dopa for all 55 cases before and after starting AA increased form 565.1 and 818.6 mg/day, while the average doses of dopamine agonists decreased from 2.2 and 1.9 mg/day. (Figure 3) There were no documented cases on new onset diabetes mellitus.

CONCLUSIONS

AA did not cause weight gain in this population. This should not be a concern in administering these medications. Conversely they are not effective as weight gaining drugs as that expected.

Body weight gain is generally greater with AA compared to first generation antipsychotics AA have lower affinity for dopamine D2 receptors but variability have greater affinities for other neurotransmitters including serotonin (5-HT1A,2A,2C,3,7) adrenergic (a1 and a2), histamine (H1), and muscarinic acetylcholine (m1-5). Matsumura-Sakata calculated mean receptor occupancies of neurotransmitter receptors and found that H1 and mACH receptor occupancy correlated with antipsychotic-induced weight gain, while H2, mACH and 5-HT3 receptors correlated to type 2 diabetes mellitus. Although speculative, these drugs may not induce weight gain in PD simply because these brain areas also degenerate, and presumably are less functional. Other possible effects on weight include changes in dysphagia. These drugs; however have not been reported to after swallowing. Levodopa dose increased as dopamine agonists decreased. Theoretically levodopa could contribute to the weight loss by lipolytic effects, nausea or dyskinesia. To our knowledge this has never been clinically demonstrated.