Weight Change in Parkinson and Alzheimer Patients Taking Atypical Antipsychotic Drugs

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ABSTRACT

Objective:To determine body weight and body mass index(BMI) change in Parkinsons disease (PD) taking atypical antipsychotic (AA) drugs compared to PD controls and Alzheimers disease (AD) patients on AA. Background: Weight loss in PD is a chronic process that is observed in both early and late stages of PD. Atypical antipsychotic drugs are associated with marked weight gain and new onset diabetes mellitus (DM). This may result in increased cardiovascular morbidity and mortality. Methods: Sixty-six eligible consecutive PD subjects started on AA who had accurate (same scale) weights for more than 6 months prior to initiate AA and more than 6 months after, with up to 3 years when available. We compared weight change in these PD subjects before and after AA use, against a control group of sixty - one sex matched PD subjects, and against twenty - eight AD subjects taking AA. We tabulated demographic information, Hoehn and Yahr stage, UPDRS part I.2 (thought disorder), L-dopa and dopamine agonist dose equivalent and AA dosage. A linear regression model was created to compare weight change in PD subjects before and after starting AA, against PD controls, and against AD on AA adjusted for age, sex, height and observational duration. Results: Fifty - nine PD subjects had complete data. The mean actual weight and BMI loss in the period before starting AA and PD controls was less than after starting AA. (p < 0.001, pre- vs. post - AA; 0.009, PD on AA vs. PD controls). The 28 AD on AA gained weight (p < 0.001, PD on AA vs. AD on AA). There were no documented cases on new onset DM in PD subjects. Conclusions: AA did not cause weight gain in PD population. This should not be a concern when administering these medications. Conversely they are not effective as weight gaining drugs when this is desired. The different effects in PD and AD suggest uniquely altered weight homeostasis in PD, perhaps due to degeneration of histaminergic cells.

OBJECTIVE

To study weight changes in PD patients before and after starting either quetiapine or clozapine, and compare this to a control group of PD patients not taking AA, and to AD patients taking quetiapine for management of behavioral and psychological symptoms of dementia.

METHODS

Sixty–six PD patients prescribed AA were recruited from PDMDC at BCM. We included all subjects who used either quetiapine or clozapine for at least 6 months and whose weights were recorded for at least 6 - month before and after AA initiation. PD patients who presented with poorly controlled chronic diseases which affecting weight or undergoing functional brain surgery for PD were excluded. Sex, height, underlying medical diseases, Hoehn and Yahr(H&Y)stage at AA initiation, type and indication for AA usage, were recorded. (Table 1) At each visit, we recorded the patient's UPDRS I.2 (thought disorder), AA dose and PD medication doses. The average doses of - dopa, dopamine agonists and AA were calculated. Seven patients were excluded because three of them underwent deep brain stimulation, one had a revised diagnosis of drug induced parkinsonism, and three died. Fifty–nine patients were included in the analysis. We included sixty - one consecutive PD, sex-matched controls who were born between 1926 and 1944 (range for PD on AA) who met the same inclusion criteria as the AA subjects except for taking AA in our clinic from 2006-2007. Twenty -eight AD subjects taking AA (100% quetiapine) were recruited from BCM, Alzheimer's Disease and Memory Disorder Center. All eligible participants fulfilled criteria for probable AD by NINCDS-ADRDA criteria.

Table 1: Baseline demographic data of PD, AD and PD controls

	PD on AA n = 59	PD controls n = 61	P-value [a]	AD on AA n = 28	P-value [b]
Subjects					
Male	37	39	NS	7	0.001
Female	22	22		21	
Mean age at T^{AA}, yr	70.8± 9.3	65.1± 6.6	<0.0001	76.8± 6.5	0.003
Mean height at T^{AA}, m^2	2.9± 0.4	3.0± 0.4	NS	2.7± 0.4	0.004
Mean weight at T^{AA}, kg	75.3± 20.2	79.1± 14.2	NS	64.2± 13.0	0.009
Mean BMI at T^{AA}, kg/m^2	25.4±5.8	26.3± 4.2	NS	23.6± 3.1	NS
H&Y stage					
1/ 1.5	3	3			
2	9	32			
2.5	10	15			
3	27	10			
4/5	10	1			
UPDRS 1.2					
Median (1st, 3rd quartile)	3 (2,3)	0			

a PD on AA vs. PD controls; b PD on AA vs. AD on AA

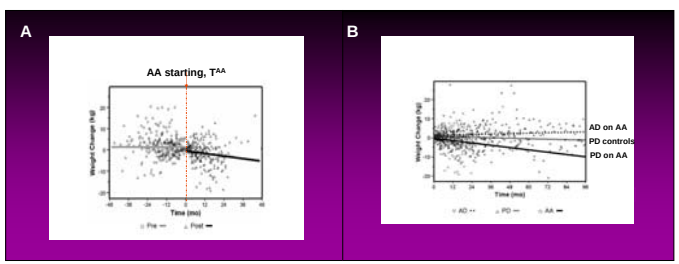
RESULTS

Patients in the PD/AA group were prescribed either quetiapine (n = 53, 89.8%)or clozapine (n = 6, 10.2%). The indication for quetiapine was psychosis (n = 46, 86.8%) and insomnia (n = 7, 13.2%); all clozapine use was for psychosis. The mean dose (mean range) of quetiapine in PD and AD was shown in Table 2. The average dose of clozapine was 44.3 (24.3-71.7) mg/day. The overall mean UPDRS part I.2 (thought disorder) improved after initiating AA. L -dopa dose increased and DA equivalents decreased after starting AA. (Table 2) The regression models comparing different groups. In the PD/AA group, the captured period before starting AA ($T^{AA} – T^{1st.wt}$,the date when we initially enrolled patients) was 1.95 ± 1.41 years. After starting AA, the actual weight and BMI was lost in pre- more than post-AA.(95% CI 0.62 to 1.21, $P < 0.0001$) (Figure 1) PD controls lost weight less than PD on AA. (95% CI 0.15 to 0.94, $P = 0.007$). AD on AA gained weight and BMI.(95% CI 0.26 to 0.83, $P < 0.0001$). (Table 2, Figure 1) There were no documented cases on new onset diabetes mellitus in any group.

Table 2: Weight and BMI correlated with quetiapine and anti-parkinson dosage in PD, AD and PD controls

	PD on AA Pre-AA	PD on AA Post-AA	(95% CI) P-value	PD controls	(95% CI) P-value	AD on AA	(95% CI) P-value
Observational period, yr	1.95± 1.41	1.44± 0.8	-	4.14± 2.71	<0.0001	1.49± 1.07	NS
Actual weight change (kg/m2/month)	0.00	-0.10	(1.92-3.62) <0.0001	-0.02	(0.38-2.67) 0.009	+0.02	(0.74-2.4) <0.000
BMI change (kg/month)	0.0	-0.03	(0.62-1.21) <0.0001	-0.01	(015-0.94) 0.007	+0.01	(0.26-0.83) <0.0001
UPDRS 1.2 (Median) (1st, 3rd interquatile range)	3 (2,3)	1 (0,3)		0			
Quetiapine (mg/d) Mean(Min.-Max.)		52.4 (12.5-196.9)				71.9 (12.5-224.3)	NS
L-dopa equiv.(mg/d) Mean (Min.-Max)	646.1 (0-2405.1)	799.0 (0-2863.3)	NS	473.7 (0-2585.2)	0.001		
D.Agonist equiv.(mg/d) Mean (Min.-Max)	2.0 (0-6.2)	1.4 (0-6.3)	NS	1.7 (0-7.4)	0.496		

Figure 1: **(A)** Weight change in PD before and after taking AA **(B)** Weight change in PD on AA, AD on AA and PD controls



CONCLUSIONS

The use of quetiapine or clozapine in PD patients was associated with significant weight loss compared to the same subjects prior to taking AA, PD controls, and AD patients taking a similar dose of AA. The exposure to these drugs clearly did not increase weight in the PD patients, which could ameliorate concerns about the possible development of insulin resistance in this patient population. AA have lower affinity for dopamine D2 receptors but are reported to have greater affinities for other neuroreceptors including serotonin (5-HT1A, 2A, 2C, 3, 6 and 7), adrenergic (α1 and α2), histamine (H1), and muscarinic acetylcholine(mACh). [1] Matsui-Sakata and colleagues found that H1 and mACh receptor occupancy correlated with antipsychotic - induced weight gain, while H1, mACh and 5 - HT2c affinity correlated with new onset type II diabetes mellitus. [2] PD subjects loose histaminergic as well as dopaminergic, and other monoaminergic neurons. [3-4] Although speculative, AA may not induce weight gain in PD simply because these brain areas also degenerate, and are presumably less affected by pharmacologic manipulation.

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