A Randomized, Double-Blind, Placebo-Controlled Study of Atomoxetine for Freezing of Gait in Parkinson's Disease

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OBJECTIVE

To evaluate the benefit of atomoxetine on freezing of gait (FoG) in Parkinson's disease (PD).

BACKGROUND

FoG is a common symptom in up to one-third of patients with longstanding or advanced PD. Various medications, surgical options and behavioral therapies have been proposed but patients often respond poorly or demonstrate inconsistent outcomes. Because a noradrenergic deficiency has been postulated to play a role in FoG, we designed a pilot study of the selective norepinephrine reuptake inhibitor atomoxetine in FoG related to PD.

DESIGN / METHODS

Five patients with FoG in PD were randomized to receive either active atomoxetine or placebo. All evaluators were blinded to treatment. Those receiving active treatment began on atomoxetine 10mg daily and the dose was escalated by 10mg increments up to 40mg over three weeks. Participants were evaluated at screening to verify eligibility, then at baseline and at two 4-week intervals, then after a two-week washout period. Scales administered were the Unified Parkinson's Disease Rating Scale (UPDRS), Gait and Balance Scale (GABS), and Clinician's Global Index of Change (CGIC). The subjects were also asked to complete the FoG Questionnaire (FOGQ) for evaluation of subjective improvement. Patients were videotaped performing tasks associated with the seven-meter step time (7MS) and the videos were rated by a blinded rater.

RESULTS

Three male patients and two female patients participated. Mean age was 65.6 ± 10.1 years. All were classified as either stage 3 or 4 on the Hoehn and Yahr (H&Y) scale and scored between 70-90 on the Schwab and England Activities of Daily Living (S-E ADL) scale. Three received active drug **(patients 2, 4 and 5)** while two received placebo (patients 1 and 3). No consistent differences in UPDRS Part I, II, or III scores were noted before or after treatment with either drug or placebo including question 14 (not shown) regarding subjective freezing. No consistent changes were noted in step number or duration on the 7MS test, in subjective improvement on the FOGQ, in GABS subscale or total scores, or in CGIC (not shown).

CONCLUSIONS

Although some patients reported subjective improvement, no consistent changes were demonstrated between atomoxetine and placebo in a small sample of PD patients with FoG. Further studies, using a large sample of subjects, may be needed to demonstrate atomoxetine's efficacy in the treatment of FoG.

TABLE 1: Patient Characteristics

Patient	Age/Sex	Diagnosed (yrs)	H&Y	S-E ADL
1	58/M	5.2	4	70
2	70/M	3.6	3	80
3	68/M	5.7	4	90
4	52/F	4.5	3	80
5	78/F	19.1	3	90

TABLE 2: Changes in GABS Scores

	Subtotal I		Subtotal II		Total I+II		Fast Walk (sec)		Timed (sec)	
Patient	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose
1	14	16	22	26	36	42	7	6	17	20
2	11	9	13	8	24	17	6	7	15	15
3	13	16	12	12	25	28	4	4	11	10
4	19	10	20	29	39	39	7	7	33	28
5	23	22	16	18	39	40	6	7	16	18

TABLE 3: Changes in 7MS Scores

	Duration (sec)		Total Steps		FoG Episodes	
Patient	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose
1	25	24	37	44	1	0
2	23	20	38	32	0	0
3	14	19	24	34	0	1
4	24	22	53	47	0	1
5	19	25	38	46	0	0

TABLE 4: Changes in UPDRS Scores

	UPDRS Part I		UPDRS Part II		UPDRS Part III	
Patient	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose
1	6	6	24	25	38	28
2	4	5	18	20	30	26
3	2	3	23	22	42	35
4	1	3	17	9	45	48
5	4	4	25	26	47	47

TABLE 5: Changes in FoGQ Scores

	Worst State		ADL Difficulty		Glued to Floor		Longest Freezing		Start Hesitation		Turn Hesitation		Total	
Patient	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose	Baseline	Max Dose
1	3	2	2	2	4	4	3	2	2	2	2	2	16	15
2	3	3	2.5	2	3.5	4	2	2	1	2	1	1	13	14
3	3	3	4	3	4	3	4	3	4	3	3	3	22	18
4	3	2	2	1	3	2	2	2	3	2	2	2	15	11
5	3	3	3	3	3	3	2	2	2	1	1	0	13	12

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