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Tardive Dyskinesia in Elderly Psychiatric Patients: A 5-Year Study

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Objective: *The authors investigated the prevalence of tardive dyskinesia among elderly psychiatric patients who had never received neuroleptic medication before their first hospitalization.* *Method:* *The study was performed in the geriatric psychiatry unit of a university-affiliated hospital in Canada and involved all first-admission patients admitted from September 1984 through August 1989 who had never taken neuroleptic drugs. In September and October 1989, the patients who were available for follow-up were examined and given ratings on the Abnormal Involuntary Movement Scale to establish the presence or absence of tardive dyskinesia. The patients' records were reviewed for information on age, diagnosis, duration of hospitalization, neuroleptic treatment received after admission, anticholinergic drugs received, and drug-free periods.* *Results:* *Of the 162 patients who were available and whose data were analyzed, a total of 99 had been treated with neuroleptics, and 35 (35.4%) of these were found to have tardive dyskinesia. Two of the 35 also had tardive dystonia. Significantly more patients with major depression than patients with primary degenerative dementia or delusional psychosis had tardive dyskinesia.* *Conclusions:* *This study confirms the higher vulnerability of elderly psychiatric patients treated with neuroleptics to the development of tardive dyskinesia. The authors stress that caution is especially necessary when neuroleptics are prescribed for older patients with major affective disorders.*

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Tardive dyskinesia, a neuroleptic-induced movement disorder, has been reported to be more prevalent in patients whose medication is started late in their illness (1) and in newly treated elderly psychiatric patients (2–4). Thus, psychiatric patients in the geriatric age group are at risk, and there are some estimates that tardive dyskinesia may develop in a short period in almost half of neuroleptic-treated patients in this age population (4, 5). Although tardive dyskinesia may occur in a large number of elderly psychiatric patients, spontaneous dyskinesia may also occur in an average of 5% of these patients without prior neuroleptic therapy (6). Thus, when these patients are studied, it is important to provide a comparison group of patients who have never received neuroleptics in order to account for the possible appearance of spontaneous dyskinesia.

In our hospital, we have been studying the prevalence of tardive dyskinesia in newly treated elderly psychiatric patients for the past 5 years. In 1988 we reported (4) on a 2-year study that started in September 1984 and ended in August 1986 which involved 78 first-admission patients, 39 of whom received neuroleptics and 39 who never received neuroleptics. Of the patients who received neuroleptics, 16 (41.0%) developed tardive dyskinesia after a mean of 14.8 months (SD=8.3) of continuous neuroleptic therapy. This is a slightly lower proportion than that in a more recent study by Saltz et al. (5), who found that 48.9% of their subjects developed tardive dyskinesia after 48 weeks of cumulative neuroleptic exposure.

The present study extended our previous one (4). We report on the prevalence of tardive dyskinesia in patients who were treated with neuroleptics for up to 60 months (5 years) during the period from Sept. 1, 1984, to Aug. 30, 1989.

METHOD

Patients admitted for the first time to the geriatric psychiatry unit at our hospital (minimum age=65 years; catchment area=300,000 population) who had never received neuroleptics before admission—as confirmed

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by detailed medication histories obtained from the patients, relatives, and referring physicians—were evaluated for the presence of movement disorders with the Abnormal Involuntary Movement Scale (AIMS) (7). All patients who had received neuroleptics before admission were excluded from the study.

The AIMS measures the severity of tardive dyskinesia on a scale of 0 (no tardive dyskinesia) to 4 (severe tardive dyskinesia) in each of seven body areas. Because the AIMS does not measure dystonia, we also added the dystonia items of the Simpson Rating Scale (8) to the AIMS, as previously described in our tardive dystonia studies (9, 10). We followed the criteria set by Jeste and Wyatt (11) for determining the presence of tardive dyskinesia, i.e., a minimum AIMS score of 2 (mild) for one body area. We used this same criterion as the minimum in our previous studies (1, 12).

Patients admitted for the first time to our unit were also evaluated for spontaneous dyskinesia before they received any neuroleptic treatment and again during the study period, i.e., during September–October 1989.

A total of 251 patients (95 men and 156 women) who had never received neuroleptics were admitted to the hospital for the first time during the period from September 1984 through August 1989. For reexamination for the presence of tardive dyskinesia or spontaneous dyskinesia, patients were visited in their homes, nursing homes, foster homes, outpatient clinics, or inpatient unit. The examiner was blind to their neuroleptic intake since admission to the hospital. Diagnoses were made according to *DSM-III* criteria and were confirmed by two independent investigators using the Hamilton Rating Scale for Depression (13), the Mini-Mental State examination (14) for primary degenerative dementia, and the Brief Psychiatric Rating Scale (15) for delusional disorders.

Following the examination of each patient, the files were reviewed to record whether the patient had received neuroleptics or not, to identify diagnosis, and to study in detail the patient's neuroleptic intake until the end of August 1989. Drug-free periods of 1 month or more were also recorded. (The chart reviews were conducted without knowledge of the patients' current tardive dyskinesia status.) Total neuroleptic time was defined as the total time that a patient received neuroleptic treatment minus the drug-free periods. Neuroleptic dosage was translated into chlorpromazine equivalents with Davis's formulas (16), except for pimozide dose, which was translated into chlorpromazine equivalents (0.5 mg equivalent to 100 mg of chlorpromazine) according to Baldessarini's method (17), and fluphenazine injection (25 mg i.m. every 2 weeks equivalent to 300 mg/day of chlorpromazine), which was calculated according to the formula of Nestoros et al. (18, 19).

RESULTS

During the 5-year period between September 1984 and August 1989, of the 251 first-admission patients who had not received neuroleptics, 64 (31 men and 33 women) died; their mean age was 79.3 years (range=66–95). Of these, 43 were diagnosed as having primary degenerative dementia, nine bipolar disorder, eight delusional disorder, and four alcoholic dementia. In addition, 25 patients (10 men and 15 women) could not be contacted for the follow-up. Their mean age was 71.5 years (range=70–85). Of these, 18 had diagnoses of major depression, six delusional disorder, and one primary degenerative dementia.

For the final analysis, 162 patients (54 men and 108 women) were available for reexamination during the months of September and October 1989. Of these, 99 (29 men and 70 women) had been prescribed neuroleptics at some point during the 5-year period covered by the study, while 63 (25 men and 38 women) had never received neuroleptics. (Anticholinergic drugs are not prescribed on a prophylactic basis in the geriatric psychiatry unit but were prescribed for some patients as needed.) The mean age of the patients who did not receive neuroleptics was 76.4 years (range=66–95). Of these, 22 had diagnoses of primary degenerative dementia, 38 major depression, one delusional disorder, and two alcoholic dementia.

Prevalence of Spontaneous Dyskinesia

Of the 251 patients admitted for the first time to our unit, 10 (six men and four women) showed evidence of spontaneous dyskinesia before any neuroleptic treatment was instituted. This constitutes 4.0% of the total patient population (6.3% of the men and 2.6% of the women). Their mean age was 77.7 years (range=70–86). Of the 10 patients with spontaneous dyskinesia, five were diagnosed as suffering from primary degenerative dementia, four from major affective disorders, and one from delusional psychosis. All of them exhibited mild bucco-oral movements. No other body areas were affected.

At follow-up, five of the patients with spontaneous dyskinesia had died. Of the other five patients, one had received neuroleptics, and her abnormal movements had disappeared. She also showed no evidence of tardive dyskinesia. Four of the patients who received no neuroleptics continued to exhibit mild bucco-oral movements. Thus, four (6.3%) of 63 patients who received no neuroleptics showed evidence of spontaneous dyskinesia at follow-up.

Prevalence of Tardive Dyskinesia

The characteristics of the patients who received neuroleptics (N=99) are presented in table 1. The patients without tardive dyskinesia were significantly older than the patients with tardive dyskinesia. The prevalence of tardive dyskinesia in the patient population was 35.4% (35 of 99). More men (13 of 29, or 44.8%) than women (22 of 70, or 31.4%) had tardive dyskinesia, but this difference was not statistically significant (χ^2=1.6, df=1). However, if we apply the criteria of Schooler and

TABLE 1. Characteristics of 99 Neuroleptic-Treated Patients With or Without Tardive Dyskinesia

	Patients With Tardive Dyskinesia						Patients Without Tardive Dyskinesia						Analysis	
	Men (N=13)		Women (N=22)		Total (N=35)		Men (N=16)		Women (N=48)		Total (N=64)		t	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	(df=97)	p
Age (years)	73.5	5.4	74.9	5.1	74.5	5.0	77.1	6.3	77.6	7.1	77.4	6.9	2.30	<0.02
Duration of hospitalization (months)	37.9	18.6	21.2	20.0	26.4	21.1	10.1	10.9	13.8	16.8	12.9	15.5	3.46	<0.001
Duration of neuroleptic treatment (months)	31.8	16.9	24.6	18.0	27.3	17.7	16.6	16.2	17.3	17.0	17.1	16.6	2.80	<0.005
Drug-free period (months)	1.8	3.3	6.0	11.3	4.4	9.3	3.4	8.2	1.2	2.8	1.8	4.8	1.86	<0.07
Total amount of neuroleptic (g)	209.9	224.6	69.5	97.8	129.5[a]	169.6	81.8	116.2	54.2	73.3	61.1[b]	85.9	2.67	<0.009
Total amount of antiparkinsonian drug (mg)	571.9	1362.4	1005.9	2207.4	842.1	1925.9	154.3	484.1	264.1	808.0	239.7	740.8	2.20	<0.03
Present neuroleptic dose (mg/day in chlorpromazine equivalents)	106.2	113.2	64.8	89.9	76.4[c]	91.5	173.7	243.0	80.7	159.4	120.7[d]	194.7	1.28	<0.20
AIMS[e] score	5.2	2.5	4.9	2.8	5.0	2.6	—	—	—	—	—	—	—	—

[a]Range=8–777 g.
[b]Range=3–467 g.
[c]Range=0–375 mg/day.
[d]Range=0–800 mg/day.
[e]Abnormal Involuntary Movement Scale.

Kane (20) for minimum manifestation of tardive dyskinesia (i.e., two areas of the body with a minimum AIMS rating of 2 or one area with a rating of 3), then the prevalence of tardive dyskinesia was 30.3% (30 of 99), and significantly more men (13 of 29, or 44.8%) than women (17 of 70, or 24.3%) exhibited tardive dyskinesia (χ^2=4.07, df=1, p<0.05).

Eleven of the patients had mild tardive dyskinesia, 21 had moderate tardive dyskinesia, and three had severe tardive dyskinesia (table 2). The bucco-oral area was affected in all 35 of these patients. In addition, six women were affected in their arms or legs. Tardive dystonia (torticollis) was present in two men; their family members did not show evidence of movement disorders. These two patients also had mild bucco-oral tardive dyskinesia. Thus, the prevalence of tardive dystonia in our patients was 2.0%, and 6.9% in the men.

Neuroleptic Intake

Patients who received neuroleptics were treated for a mean of 20.7 months (range=1–60 months). This indicates the duration of actual neuroleptic treatment, excluding drug-free periods. Patients who developed tardive dyskinesia received significantly longer neuroleptic treatment than patients without tardive dyskinesia (table 1).

Of the 99 patients who received neuroleptics, 58 received one neuroleptic: 47 received haloperidol, four received pimozide, three perphenazine, two chlorpromazine, and one each thioridazine and fluphenazine. Of the haloperidol-treated patients, 14 (29.8%) developed tardive dyskinesia. Of the pimozide-treated patients, two developed tardive dyskinesia. No tardive dyskinesia developed when the other medications were given alone. Of the remaining neuroleptic-treated patients, 31 received two neuroleptics, nine received three neuroleptics, and one received four neuroleptics.

As shown in table 1, patients with tardive dyskinesia also received significantly more total neuroleptic medication than patients without tardive dyskinesia. Men with and without tardive dyskinesia received a greater total amount of neuroleptics than women in the same groups.

Also noted in table 1, the present dose of neuroleptic drug was not significantly different for the patients with and without tardive dyskinesia. Equal proportions of patients with tardive dyskinesia (13 of 35, or 37.1%) and without tardive dyskinesia (24 of 64, or 37.5%) were not receiving neuroleptics at the time of the examination.

Duration of Neuroleptic Therapy

Of the 48 patients who received 1–12 months of continuous neuroleptic treatment, 11 (22.9%) developed tardive dyskinesia, compared to seven (50.0%) of the 14 who received neuroleptics for 13–24 months. Of the 12 patients who received neuroleptics for 25–36 months, four (33.3%) developed tardive dyskinesia, compared to eight (57.1%) of the 14 who received neuroleptics for 37–48 months. Of the 11 patients who received neuroleptics for 49–60 months, five (45.5%) developed tardive dyskinesia.

Eighteen (51.4%) of the 35 patients with tardive dyskinesia developed the side effect within the first 24 months of continuous neuroleptic therapy.

Of the 35 patients with tardive dyskinesia, 12 (34.3%) had drug-free periods, compared to 20 (31.3%) of the

64 patients without tardive dyskinesia. The mean numbers of drug-free months for the two groups were not significantly different (table 1).

Other Factors

Age. As shown in table 2, there was no indication that aging increases the chances of developing tardive dyskinesia. In fact, if we divide the patient population into 10-year age groups, we find that of the 53 patients in the age range of 65–75 years, 23 (43.4%) showed evidence of tardive dyskinesia, compared to 10 (26.3%) of the 38 in the next age group (76–85 years) (χ^2=2.79, df=1, n.s.).

Antiparkinsonian medication. Patients with tardive dyskinesia received significantly more antiparkinsonian drugs than patients without tardive dyskinesia, as shown in table 1. Of the 35 patients with tardive dyskinesia, 19 (54.3%) received antiparkinsonian drugs, compared to 20 (31.3%) of the 64 patients without tardive dyskinesia (χ^2=4.11, df=1, p<0.05, with Yates' correction). Two of the men with tardive dyskinesia, two of the men without tardive dyskinesia, and one woman without tardive dyskinesia received amantadine as their antiparkinsonian agent.

Diagnosis. Of the 99 patients receiving neuroleptics, 49 were diagnosed as suffering from primary degenerative dementia. Of these, 12 (24.5%) were found to have tardive dyskinesia, compared to 12 (60.0%) of 20 with the diagnosis of major depression, a statistically significant difference (χ^2=6.41, df=1, p<0.03, with Yates' correction). This difference is still significant if Schooler and Kane's criteria are applied (11, or 22.4%, of the 49 patients with dementia and 10, or 50.0%, of the 20 with major depression; χ^2=3.87, df=1, p<0.05, with Yates' correction). This difference was not due to a longer duration of neuroleptic treatment (for dementia patients, mean=26.3 months, SD=17.4, range=2–53 months; for depressed patients, mean=22.1 months, SD=15.0, range=8–60 months) or to the total amount of neuroleptic treatment in either diagnostic category (for dementia patients, mean=94.8 g, SD=44.1; for depressed patients, mean=67.6 g, SD=27.7).

Of the 23 patients with delusional (paranoid) disorder, six (26.1%) developed tardive dyskinesia. The difference between the proportion of patients with delusional (paranoid) disorder and the proportion with major depression (60.0%) who developed tardive dyskinesia was statistically significant (χ^2=4.97, df=1, p< 0.05). Of the seven patients with alcoholic dementia, five (71.4%) developed tardive dyskinesia.

Other medications. Of the 35 patients with tardive dyskinesia, 12 (34.3%) received no concomitant medications, compared to 42 (65.6%) of the 64 patients without tardive dyskinesia. Antidepressants were prescribed for 16 (45.7%) of the patients with tardive dyskinesia, compared to nine (14.1%) of the patients without tardive dyskinesia. Antihypertensives (mainly diuretics and methyldopa) were prescribed for five patients with tardive dyskinesia (14.3%) and three patients without tardive dyskinesia (4.7%). Antidiabetics were prescribed for three patients with tardive dyskinesia (8.6%), compared to two patients without tardive dyskinesia (3.1%). Digoxin was prescribed for three patients with tardive dyskinesia (8.6%) and four patients without tardive dyskinesia (6.3%). Levothyroxine sodium was prescribed for two patients with tardive dyskinesia (5.7%) and one patient without tardive dyskinesia (1.6%). Lorazepam was prescribed for 10 patients with tardive dyskinesia (28.6%) and 19 patients without tardive dyskinesia (29.7%).

TABLE 2. Distribution of 99 Neuroleptic-Treated Patients by Age Group

Item	Age (years)				
	65–70	71–75	76–80	81–85	86 or Older
Patients with tardive dyskinesia					
Mild					
Men	0	0	2	0	0
Women	3	3	2	0	1
Moderate					
Men	4	3	1	1	0
Women	2	6	3	1	0
Severe					
Men	2	0	0	0	0
Women	0	0	1	0	0
Patients with tardive dyskinesia as a percentage of all patients in age group					
Men	60.0	37.5	60.0	20.0	0.0
Women	33.3	45.0	35.3	9.1	14.3
Patients without tardive dyskinesia					
Men	4	5	2	4	1
Women	10	11	11	10	6
All patients					
Men	10	8	5	5	1
Women	15	20	17	11	7

DISCUSSION

The prevalence of tardive dyskinesia in an elderly population recruited over 5 years, treated continuously with neuroleptics for a mean of 20.7 months (range= 1–60 months), was 35.4%. On the other hand, of 63 patients who received no neuroleptics, four (6.3%) showed spontaneous dyskinesia. These findings are compatible with those in the published studies of comparable patient populations (2, 3, 5).

Although for many years one of the few consistent research findings has been that the prevalence of tardive dyskinesia increases with age, relatively few studies have been devoted to those patients who receive neuroleptics for the first time after age 65. Crane and Smeets (2) found that tardive dyskinesia developed in 39% of 39 patients (median age=74 years, range=63–89) who were followed for a period up to 28 months. Lieberman et al. (3) found that tardive dyskinesia developed in

16.5% of 79 elderly patients who were treated with neuroleptics for 18 months (mean age=85.5 years, range=65–99). Finally, Saltz et al. (5) found that tardive dyskinesia developed in 49% of 84 patients treated with neuroleptics for a mean of 16.7 weeks (mean age=76.6 years, range=57–96). The mean prevalence of tardive dyskinesia in these studies is 34.2%, which is close to the 35.4% in our present study.

Women have been overrepresented in all the studies dealing with elderly psychiatric patients, but we found the prevalence of tardive dyskinesia to be nonsignificantly higher in the men than in the women, if the more liberal Jeste and Wyatt criteria (11) are applied. And, if the Schooler and Kane criteria (20) are applied, tardive dyskinesia appears to have been significantly more prevalent in the men than in the women. Tardive dyskinesia was found to be equally distributed in both sexes in a recent study of a similar patient population (5).

Our study is the first to indicate the prevalence of tardive dystonia in an elderly psychiatric population. We found that tardive dystonia was present in 2% of the treated patients. This corresponds to findings in our previous studies (9, 10), where tardive dystonia occurred in 2% of a younger population.

Spontaneous dyskinesia was found in 4% of our patient population, corresponding to the weighted mean of 4% in the most recent reviews on the subject (6, 11, 21, 22). At the end of the 5-year period we studied, four (6.3%) of 63 patients who never received neuroleptics exhibited spontaneous dyskinesia. None of the 63 patients had developed *de novo* spontaneous dyskinesia or tardive dyskinesia when reexamined.

In our study, we found that patients with tardive dyskinesia stayed longer in the hospital, were treated with neuroleptics for a longer period, and received a larger mean total amount of neuroleptics than patients without tardive dyskinesia. Some studies dealing with younger subjects have identified duration of neuroleptic treatment as a factor in the development of tardive dyskinesia (23–25), whereas others have not (26, 27). It is possible that for our patients with tardive dyskinesia, the larger amounts of neuroleptic medication reflect the longer duration of treatment with these medications.

In some studies (12, 25), drug-free periods have been found to be a factor in the development of tardive dyskinesia, but this was not true in our study.

We were also unable to confirm that the prevalence of tardive dyskinesia increased with age. We found that the younger patients (65–75 years) had a higher but not statistically significant prevalence of tardive dyskinesia than the older patients (76–85 years): 43.4% and 26.3%, respectively. This is consistent with the findings reported recently in a patient group similar to ours, in which aging was not found to contribute to a higher prevalence of tardive dyskinesia (5).

We never prescribe prophylactic antiparkinsonian drugs for our patients. Whenever acute extrapyramidal side effects develop, we prefer to reduce the neuroleptic dosage as a first choice, rather than giving antiparkinsonian drugs. Even so, we found that patients with tardive dyskinesia received significantly more antiparkinsonian drugs than patients without tardive dyskinesia, indicating that acute extrapyramidal side effects may develop more in patients with tardive dyskinesia than in those without tardive dyskinesia. A possible reason for the greater amounts of antiparkinsonian drugs received by patients with tardive dyskinesia is that these patients received larger amounts of neuroleptics.

Our study confirms the finding that more patients with affective disorders than patients without affective disorders have tardive dyskinesia. Several studies (28–31) have indicated that patients with affective disorders (particularly depressed patients) are more prone to develop tardive dyskinesia than patients in other diagnostic categories. Our study indicates that this holds true even in an elderly psychiatric population. We found that tardive dyskinesia was more prevalent among depressed patients (60.0%) than among patients with primary degenerative dementia (24.5%) or delusional (paranoid) disorder (26.1%). This higher prevalence of tardive dyskinesia in depressed patients does not reflect the duration or total amount of neuroleptic treatment, and it is difficult at present to speculate on the reason for the higher prevalence in these patients.

In summary, tardive dyskinesia developed in 35.4% of elderly psychiatric patients who received neuroleptics for up to 60 months. We found that gender was not a factor in the development of tardive dyskinesia in this aged population. Patients with tardive dyskinesia, however, received neuroleptics for longer periods and in larger amounts than patients without tardive dyskinesia. They also received more antiparkinsonian drugs, indicating that acute extrapyramidal side effects may be precursors of the development of tardive dyskinesia. More patients with affective disorders than patients in other diagnostic categories developed tardive dyskinesia; thus, clinicians should be cautious when prescribing neuroleptics for these patients.

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