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Prevalence of tardive dystonia

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ABSTRACT – Tardive dystonia is a rare late-onset side effect of neuroleptics. This paper presents a prevalence study of 351 inpatients conducted in our hospital. Seven patients (2%) were found to suffer from this condition. The majority were found to be young and had received neuroleptics for a variable number of years before the onset of the dystonia. In general, treatment of this condition is disappointing.

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Since 1957, tardive dyskinesia (TD) has been described in the literature as being a long-term side effect of neuroleptics (1). More recently, tardive dystonia, another tardive manifestation of neuroleptic-induced movement disorders, has been described (2, 3). Keegan & Rajput (2) reporting on one patient with drug-induced torticollis, coined the term. Burke et al. (3) described the characteristics of tardive dystonia in 42 patients and reviewed 15 cases reported in the literature up until 1982. Their criteria for diagnosing tardive dystonia were: 1) presence of chronic dystonia; 2) history of anti-psychotic drug treatment preceding or concurrent with the onset of dystonia; 3) exclusion of known causes of secondary dystonia by appropriate clinical and laboratory evaluation; 4) a negative family history of dystonia. The same authors also subdivided dystonia into: generalized dystonia, occurs in the whole body, and more common in younger individuals; segmental dystonia involves more than one body region; focal dystonia, remains confined to its site of onset. The latter two occurred in older individuals. The authors advocated that tardive dystonia was not a separate entity from TD. Following this important study, several case reports were added to the literature (4–8).

Dystonic symptoms have been reported in 1% of 97 patients assessed for movement disorders by Crane & Naranjo (9). No other prevalence studies on tardive dystonia have been reported.

This paper attempts to define the factors leading to the development of this disorder in a large number of patients.

Material and methods

All the inpatients (n = 351; 161 men and 190 women) in the adult chronic wards of Douglas Hospital (including the psychogeriatric units) were examined for drug-induced movement disorders. Tardive dystonia was identified by using the guidelines described by Burke et al. (3) and outlined above. TD was assessed using the Simpson Rating Scale for TD (10). The scale consists of 42 items divided into body areas: face (16 items), neck and trunk (7 items), and extremities (19 items). The subscales concerning tardive dystonia are distributed among the different body area scales: grimacing (item 14), retrocollis (item 18), spasmodic torticollis (item 19), torsion movements of trunk (item 20). In addition, any other item not appearing in the scale was added to items, others. The scale varies in severity from absent = 1 to very severe = 6.

After the patients were examined, all those diagnosed as exhibiting tardive dystonia were

reexamined by two psychiatrists to confirm the diagnosis. The patient was then examined by a neurologist for the presence of the Kayser-Fleischer ring and also to confirm the diagnosis. The following were also performed to exclude other conditions causing dystonia: ceruloplasmin, liver function tests and thyroid function tests. Also the patients' family members were interviewed to inquire about familial movement disorders.

Results

All the patients had normal thyroid function tests and their ceruloplasmin was within normal limits. There was no evidence of familial movement disorder as recounted by the patients and their family members.

Prevalence of tardive dystonia. Seven of the 351 assessed patients suffered from manifestations of tardive dystonia (2%): five of 161 men (3.1%) and two of 190 women (1%). This difference is not statistically significant ($\chi^2 = 1.88$).

Of the patient population, 101 were less than 50 years (43 women, 58 men). Of this group, six patients developed tardive dystonia (5.9%) as compared to one patient of 250 over the age of 50 (147 women, 103 men), constituting 0.4% of this patient population. This difference is highly significant (χ^2 = with Yates' correction = 8.6, $P < 0.005$).

Manifestations of tardive dystonia. As described in Table 1, torticollis occurred in three patients, retrocollis in four, blepharospasm in two and opisthotonus in one patient. Dystonic posturing of the arms and legs occurred in two patients.

Table 1
Demographic characteristics of tardive dystonia patients

No.	Age	Sex	Primary diagnosis	Antipsychotic drugs mg/day	Ethnic origin	Interval of exposure to anti-psychotic drugs prior to dystonia onset	Other movement disorders	Duration of dystonia (years)	Description severity of dystonia
1	26	M	schizophrenia	haloperidol 8	Italian	5 years	mild buccooral TD	5	torticollis, dystonic posturing of arms and legs
2	35	M	schizophrenia	haloperidol 60	Anglo-Saxon	13 years	respiratory TD	6	torticollis, blepharospasm
3	37	M	schizophrenia	fluphenazine 25 q 2 wks chlorpromazine 150 benztropine 4	Anglo-Saxon	6 years	-	5	retrocollis
4	38	M	schizophrenia	chlorpromazine 200	Anglo-Saxon	5 years	parkinsonian tremors in both hands, rigidity on right side	9	retrocollis, lordosis, dystonic posturing of arms and legs
5	40	M	schizophrenia	chlorpromazine 600 benztropine 4	Indian	15 years	-	4	blepharospasm
6	44	F	mental retardation	thioridazine 50 li carbonate 600	Anglo-Saxon	12 years	spasm of pharyngeal muscles, shoulder shrugging, mild buccooral TD	6	torticollis, retrocollis, opisthotonus
7	78	F	senile dementia	discontinued 2 years previously	Anglo-Saxon	13 months	moderate buccooral TD, respiratory TD	2	retrocollis

TD manifestations occurred in five of the patients and in two, there were no other movement disorders.

Severity and awareness. Six patients were acutely aware of their symptoms. They were all embarrassed and complained that it was socially unacceptable. Two patients (Nos. 4 and 6) were concerned that their movements would lead to accidents while walking in the streets and they were ridiculed by their friends and became socially isolated. Patient 4, a male, found it very difficult to have satisfactory sexual relations with his girlfriend. This patient was reported in more detail in a separate manuscript (11). The movements in patient 1 interfered with any rehabilitative attempts carried out in our hospital. The treating physicians and nurses considered the movements in patients 1, 2, 5 and 6 as being of "hysterical" nature, citing the evidence that the symptoms become more pronounced when the patient is angry or anxious.

Duration of dystonia. This varied from 13 months to 15 years after the onset of neuroleptic treatment. The dystonia continued unchanged since its appearance in five patients, despite several treatment attempts as delineated in Table 2. None of the patients was of Jewish descent and most were diagnosed as suffering from schizophrenia (see Table 1 for details).

Neuroleptic intake. Patients 1, 4, 5, 6, 7 received only one neuroleptic during their whole treatment period: haloperidol (Nos. 1 and 7), chlorpromazine (Nos. 4 and 5) and thioridazine (No. 6). Patient 2 received trifluoperazine for 90 months, then haloperidol for 14 months before the appearance of the dystonia. Patient 3 received fluphenazine enanthate 25 mg every 2 weeks and chlorpromazine 150 mg/day throughout the treatment period. The total amounts of neuroleptics, in chlorpromazine equivalent (12), varied from 20 g (No. 7) to 2232 g (No. 2) with a mean of 724 g (± SEM 276.0). None of the

Table 2
Treatment of tardive dystonia. Treatment attempts

Patient	Failed			Improved		
	Type of drug	Dose mg/day	Duration (months)	Type of drug	Dose mg/day	Duration (months)
1	Diazepam	300	3	Neuroleptics discontinued		48
2	Baclofen	90	11	–	–	–
	Lithium	900	2			
	Neuroleptics discontinued	–	60			
3	–	–	–	Benztropine discontinued		5
4	Reserpine	3	3	Baclofen	60	3
	Lecithin	60	3			
	Bromocriptine	20	4			
	Neuroleptics discontinued	–	19			
5	Neuroleptics discontinued		3			
	Benztropine discontinued		5			
6	Propranolol	40	22			
	Baclofen	60	12			
	Lithium	900	60			
	Haloperidol	10	12			
7	Neuroleptics discontinued		24			

patients had drug-free periods prior to the onset of the dystonia.

Antiparkinsonian medication was added to the treatment regimen of patients 2, 3 and 5. In addition to thioridazine, patient 6 received lithium carbonate 600 mg/day for about 3 years before the appearance of dystonia.

Treatment and outcome. Several attempts have been made to treat tardive dystonia, as outlined in Table 2. The duration of the tardive dystonia varied from 3 to 9 years from the time the first symptoms were described. All the symptoms that were first described were present at the time of the study, in five patients (Nos. 2, 3, 5, 6, 7). Patient 1 was symptom-free after discontinuation of neuroleptics for 48 months. Patient 4 improved greatly with baclofen 60 mg/day. His retrocollis improved but the parkinsonian tremors did not. Patient 5 was uncooperative and few attempts were made to treat his condition.

Discussion

Our study indicates that tardive dystonia is not a common manifestation of the late-onset neuroleptic-induced movement disorders (2% of 351 patients). This is slightly higher than that in the only available prevalence study on the subject (9), which estimates the prevalence of this side effect at 1%. On the other hand, the prevalence of TD has been estimated at 20% (13).

Burke et al. (3) and Gimenez-Roldan et al. (7) noted that patients suffering from tardive dystonia were mainly young men. Our findings confirm these observations. This is in contrast with TD, which increases with age (14) and seems to be more common especially in older women (15).

Tardive dystonia patients seem to be more aware of their movements than patients with TD. Six of our patients suffered as a result of their movements. These movements may interfere with their rehabilitation and may cause them undue harm. In general, TD patients seem to be oblivious of their movements (16) unless they affect the trunk and limbs (17).

In our patient population, phenothiazines of different subgroups were represented: of the aliphatic group, chlorpromazine was prescribed to two patients; of the piperidine group, thioridazine was the treatment for one patient, and of the piperazine group, trifluoperazine and fluphenazine enanthate have been administered. Haloperidol was also found to contribute to tardive dystonia in two patients. Thus, no particular treatment can be accused of causing the disorder. Interestingly, antiparkinsonian medication has been used in three patients only, indicating that the contribution of these medications may be of minimal importance in the development of this side effect. In fact, Burke et al. (3) points out that some patients improved when antiparkinsonian medication was added to the treatment regimen.

Several conditions must be differentiated from tardive dystonia. These include Huntington disease, Parkinsonism, idiopathic torsion dystonia, and Wilson's disease. The latter could be ruled out by ceruloplasmin level as well as slit-lamp examination. Parkinson disease usually occurs in older patients. Idiopathic torsion dystonia usually begins in the limbs (18) and, not uncommonly, it affects the legs or trunk in the absence of face or neck movements. As seen in our patient population and in all cases reported in the literature, drug-induced tardive dystonia involves mainly the neck and face areas. In addition, neuroleptic use is not a prerequisite for the development of idiopathic torsion dystonia as it is with tardive dystonia.

Another possible differential diagnosis is idiopathic torticollis or Meige syndrome (blepharospasm-oromandibular dystonia). Perhaps the only differentiating finding between these two conditions is the preceding use of neuroleptics in tardive dystonia (3).

The relationship between TD and tardive dystonia is difficult to assess at this stage. Several case reports have indicated that both conditions may coexist (19–21) but in some patients, one may precede the other. In our patient population, three (Nos. 1, 6 and 7) showed concomitant buccooral TD. An interesting finding is the concomitant involvement of the respiratory and pharyngeal muscles in three of our patients (Nos. 2, 6 and 7) with or without buccooral TD, thus it is conceivable that respiratory disturbances in TD patients may be of dystonic nature. Respira-

tory disturbances in acute dystonia have been reported to respond to anticholinergic medication (22).

"Trick" movements have been reported with dystonias (23). In our patient population, some dystonic symptoms were controlled by leaning the head against a hard surface, e.g. a wall or a chair, or by flexing the thorax and head while extending the limbs during manual work.

The treatment of dystonias, in general, is unsatisfactory (24). Bromocriptine, a dopaminergic agent, successfully treated a patient with spasmodic torticollis (6), where it was given in high dose (20 mg b.i.d.). We attempted to replicate this finding in patient 4 without success. However, our dose may have been too low (up to 20 mg per day). Electroconvulsive therapy was effective in another patient (4). In the series described by Burke et al. (3), 68% of the patients improved with tetrabenazine, a dopamine depletor, and 39% with anticholinergics. In our series, only one patient had a complete recovery, after a period of 4 years without neuroleptics, at the expense of his continuous psychotic behaviour. In patient 3, anticholinergic medication was discontinued with dramatic temporary effect on the retrocollis. However, it recurred after 2 years while receiving benztropine. Patient 4 improved with Baclofen 60 mg but still has some residual symptoms that are not as severe as before the treatment.

In summary, tardive dystonia is a rare drug-induced movement disorder of later onset. It mainly affects younger male patients but may also affect older women. As with TD, it is usually resistant to most known drug treatment measures.

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