Tardive and idiopathic oromandibular dystonia: a clinical comparison

Eng-King Tan, Joseph Jankovic

Abstract

***Objective*—Most patients with tardive dystonia have a focal onset involving the cranial-cervical region. Because of its resemblance to idiopathic cranial dystonia, a common form of dystonia, it often poses a diagnostic problem. To compare clinical features and response to botulinum toxin (BTX) injections between patients with tardive and idiopathic oromandibular dystonia (OMD).**

***Methods*—Patients seen in a movement disorder clinic who satisfied the inclusion criteria for tardive or idiopathic OMD were studied. The clinical variables and responses to BTX between the two groups of patients were compared. In the tardive group, we also compared the clinical variables between those with oro-facial-lingual stereotypies, and those without.**

***Results*—Twenty four patients with tardive OMD and 92 with idiopathic OMD were studied. There were no differences in the demographic characteristics. Most were women, with duration of symptoms longer than 8 years. The mean duration of neuroleptic exposure was 7.1 (SD 7.9) years. Jaw closure was the most frequent subtype of OMD (tardive=41.7%, idiopathic=51.1%). Idiopathic patients were more likely to have coexistent cervical dystonia ($p<0.05$), whereas isolated OMD was significantly higher in tardive patients ($p<0.05$). Limb stereotypies, akathisia, and respiratory dyskinesia were seen only in the tardive OMD. Frequency of oro-facial-lingual stereotypy was significantly higher in the tardive than the idiopathic group (75.0% *v* 31.5%, $p<0.0001$). The peak effect of BTX was similar in both groups.**

***Conclusions*—Oro-facial-lingual stereotypies were significantly more frequent in the tardive than the idiopathic group. Presence of stereotypic movements in the limbs, akathisia, and respiratory dyskinesias in patients with OMD strongly suggests prior neuroleptic exposure. Dystonia in tardive OMD is more likely to be restricted to the oromandibular region, whereas in patients with idiopathic OMD, there is often coexistent cervical dystonia. BTX is equally effective in both groups of patients.**

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Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas, USA
E-K Tan
J Jankovic

Correspondence to:
Professor Joseph Jankovic, Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Department of Neurology 6550 Fannin, Smith 1801, Houston, Texas 77030, USA
email josephj@bcm.tmc.edu

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Tardive dystonia, a variant of tardive dyskinesia, consists of persistent dystonic movements, usually after months or years of neuroleptic exposure.[1] Its clinical characteristics have been well described.[2–7] Most of the patients have a focal onset involving the craniocervical region.[1–4 7] Oro-facial-lingual (OFL) stereotypic movements, are most typically seen in patients with tardive dyskinesia[8 9] and stereotypies and dystonia may coexist in this group of patients.[3 4 7] One recent study found the prevalence rate of tardive dystonia with tardive dyskinesia to be about 10% in a psychiatric population.[10]

Oromandibular dystonia (OMD) refers to spasms of the masticatory, facial, and lingual muscles, resulting in repetitive and sometimes sustained jaw opening, closure, deviation, or any combination of these.[11–13] Its full range may not be easily recognised.[14] The prevalence of OMD was estimated to be 68.9 cases/million persons.[15] In a survey of two movement disorders clinics, cranial dystonia (blepharospasm and OMD) was present in about 25% of 8000 patients with dystonia.[16] Because of its resemblance to tardive dystonia, idiopathic dystonia with blepharospasm and OMD may be misdiagnosed as tardive dystonia, even though there is no documented history of neuroleptic exposure.[12 17] Although there is no universal agreement, most authors believe that tardive dystonia should be considered when there is a history of neuroleptic exposure during at least 6 months before the onset of movement disorder.[4] The presence of OFL stereotypies, and akathisia in a patient with dystonia, strongly suggests the diagnosis of tardive dystonia.[4] However, there has been no direct comparison of patients with tardive or idiopathic OMD to determine which, if any, demographic or clinical characteristics differentiate these two disorders. In this study, we compared the clinical characteristics and responses to botulinum toxin (BTX) treatment, between tardive and idiopathic OMD.

Methods

All sequential patients seen at the movement disorder clinic at Baylor College of Medicine over a 10 year period, diagnosed with OMD, were included. OMD was defined as dystonia of the oro-lingual-facial and masticatory muscles, leading to difficulty in swallowing, chewing, or speaking. Patients who fulfilled the following criteria were classified as tardive OMD: (1) chronic persistent dystonia of the mouth and jaw muscles for more than 1 month, (2) history of onset of dystonia during and within 3 months of active treatment with neuroleptic

drugs. Exclusion criteria for tardive OMD were: (1) presence of known causes of secondary dystonia (for example, Wilson's disease, post-traumatic, etc), and (2) no documented history of neuroleptic use. In addition, both the tardive and idiopathic groups received BTX injections with a least one follow up in our clinic. Tardive dyskinesia was predominantly manifested by stereotypic movements. Stereotypies were defined as patterned, repetitive, continuous, and coordinated movements.

All patients included in the study were examined personally by one of us (JJ). We reviewed the following information in the patients' records: demographic data, type, and duration of neuroleptic treatment, interval between initial neuroleptic exposure to dystonia onset, and age at onset, duration, and type of OMD, presence of dystonia in other body regions, presence of oro-lingual-facial dyskinesias, associated movement disorders (tremor, parkinsonism, etc), family history of movement disorders, primary diagnosis for which neuroleptic drugs were used, response to BTX measured by global rating, peak effect, and total duration of response. OMD was classified as jaw closing, jaw opening, or mixed if there was a combination of these with no clinical predominance of any of the subtypes.

Details of the assessment methods have been previously described.[18] Briefly, the severity of dystonia was rated on a 0 to 4 scale (0=no spasm; 1=mild, barely noticeable; 2=mild, without functional impairment; 3=moderate spasm, moderate functional impairment; 4=severe, incapacitating spasm). Peak effect was defined as the maximal benefit obtained from the injection. It was rated on a 0 to 4 scale (0=no effect; 1=mild improvement; 2=moderate improvement, but no change in function; 3=moderate improvement in severity and function; 4=marked improvement in severity and function). Global rating was defined as the peak effect score minus one point if the injection was associated with mild or moderate complications and two points if associated with severe or disabling complications. The total duration of improvement was defined as the entire period after the injection during which patients experienced any improvement.

The formulation and preparation of botulinum type A (BOTOX®, Allergan Pharmaceuticals, Irvine, CA, USA), the selection of muscles and the technique of injection have been previously discussed.[18 19] Only the masseters and submentalis complex (geniohyoid, digastric, mylohyoid) were injected.

The two groups with tardive and idiopathic OMD were compared for the following clinical variables: demographics, duration of symptoms and follow up, associated movement disorders (for example, dystonia, parkinsonism), family history of movement disorders, subtypes of OMD, types of oro-facial-lingual and other stereotypies, akathisias, and response to BTX injections. Dystonia is defined as muscle spasm resulting in abnormal posturing of the anatomical regions involved. Parkinsonism is defined when there are two or more of the following features: tremor, bradykinesia, rigidity and postural instability. Akathisia is defined as symptom of inner restlessness of the whole body (not just the legs), without diurnal variation and associated with signs of motor restlessness such as pacing and truncal rocking.

In the tardive group, we tabulated and analysed the following data: types of neuroleptic drugs, the duration of usage, the interval between initial onset of symptoms and use of neuroleptic drugs, and primary diagnosis for which neuroleptic drugs were prescribed. The tardive patients were further divided into two subsets, those with OFL stereotypies, and those without. The following clinical variables of these two subsets were compared: age at onset, subtype of OMD, duration of symptoms, duration of neuroleptic exposure, associated movement disorders, and stereotypies in other anatomical regions.

STATISTICAL ANALYSIS

Fischer's exact test, and unpaired *t* tests were used to compare the various variables.

Results

One hundred and sixteen patients (24 tardive, 92 idiopathic) were studied. There were no differences in the demographic characteristics between the two groups (table 1). Most were

Table 1 Demographics

	Tardive	*Idiopathic*
Total number of patients	24	92
Mean (SD) age (y)	59.1 (SD 16.1) (range 30 to 81)	60.0 (SD 12.6) (range 14 to 82)
Sex (M, F)	7 (29.2%), 17 (70.8%)	23 (25.0%), 69 (75.0%)
Mean (SD) duration of symptoms (y)	8.4 (7.6) (range 0.6 to 24)	9.9 (SD 9.1) (range 0.5 to 42)
Mean (SD) duration of follow up (y)	4.4 (3.4) (range 0.5 to 10)	5.6 (SD 7.1) (range 0.3 to 17)
Dystonia confined to orofacial muscles*	10 (41.7%)	12 (13%)
Associated movement disorders (n (%)):		
Cervical dystonia*	10 (41.7)	63 (68.5)
Blepharospasm	9 (37.5)	52 (56.5)
Limb dystonia	4 (16.7)	16 (17.4)
Spasmodic dysphonia	1 (4.2)	12 (13.0)
Tremor	5 (20.8)	17 (18.5)
Parkinsonism*	5 (20.8)	2 (2.2)
Bruxism	8 (33.3)	32 (34.8)
Family history (n (%)):		
Tremor	7 (25.9)	24 (26.8)
Parkinsonism	3 (11.1)	8 (8.7)
Dystonia	0	5 (5.4)
Bruxism	0	2 (2.2)
Blepharospasm	0	2 (2.2)

*$p<0.05$.

Table 2 Clinical characteristics

	Tardive (n=24)	*Idiopathic (n=92)*
Type of OMD (n (%):		
Jaw closure	10 (41.7)	47 (51.1)
Jaw opening	6 (25.0)	21 (22.8)
Mixed	8 (33.3)	24 (26.1)
Orofacial-lingual stereotypies (n (%):		
Total number of patients*	18 (75.0)	29 (31.5)
Facial grimacing*	7 (29.2)	7 (7.6)
Lip pursing*	9 (37.5)	16 (17.4)
Lip sucking	1 (4.2)	1 (1.1)
Lip smacking*	3 (12.5)	0
Chewing	1 (4.2)	0
Tongue protrusion*	9 (37.5)	7 (7.6)
Tongue dyskinesias (rotation, roving, etc)	3 (12.5)	4 (4.3)
Stereotypies (limb)*	5 (16.7)	0
Akathisia	1 (4.2)	0
Respiratory dyskinesia*	3 (8.3)	0

*p<0.05.

Table 3 Primary diagnosis and types of neuroleptic drugs used in tardive OMD

	Patients (%)
Diagnosis:	
Schizophrenia	6 (25.0)
Mood disorders (eg bipolar, depression)	6 (25.0)
Gastrointestinal symptoms	6 (25.0)
Personality disorders	2 (8.3)
Tic disorders	2 (8.3)
Not known	2 (8.3)
Neuroleptic drugs* (mean duration of use: 7.1 (SD 7.9) years (range 0.04 to 30):	
Haloperidol	7 (29.2)
Metoclopramide	7 (29.2)
Tthioridazine	6 (25.0)
Trifluoperazine	4 (16.7)
Trazodone	4 (16.7)
Thorazine	3 (12.5)
Perphenazine	2 (8.3)
Prochlorperazine	2 (8.3)
Thiothixene	2 (8.3)
Phentermine	1 (4.2)
Pimozide	1 (4.2)

*Patients may be on more than 1 drug.

women, with long duration of symptoms and follow up. Blepharospasm and cervical dystonia were the most common associated movement disorders in both groups. A significantly higher number of patients in the idiopathic group had cervical dystonia (p<0.05). Blepharospasm and spasmodic dysphonia were also more often seen in this group, although the difference was not significant (table 1). Tardive patients were more likely to have isolated OMD (41.7% *v* 13.0%, p<0.05).

Jaw closure was the most frequent subtype of OMD (tardive=41.7%, idiopathic=51.1%). Eighteen (75%) patients with tardive OMD, and 29 (31.5%) idiopathic patients with OMD had OFL stereotypies (p<0.0001). Lip pursing was the most common type of dyskinesia in both groups (table 2). Limb stereotypies, akathisia, and respiratory dyskinesia were seen only in tardive OMD.

The mean duration of neuroleptic usage was 7.1 (SD 7.9) years (range 0.04 to 30). The neuroleptic drugs were prescribed mainly for mood disorders, gastrointestinal disorders, and schizophrenia. Haloperidol, metoclopramide, and thioridazine made up about 80% of the responsible neuroleptic drugs (table 3). In the tardive group, those with OFL stereotypies were more likely to have jaw opening and mixed dystonia (table 4).

The average doses of BTX given to the masseter muscles (56.3 *v* 52.4 units) and submentalis muscles (29.4 *v* 28.2 units) were similar. The total duration of actions lasted about 16 weeks in both groups. There were no differences between the mean of the peak and global ratings, which was of roughly grade 3.

Discussion

Drug induced movement disorders have been described with an increasing frequency since the introduction of chlorpromazine (thorazine) in 1952.[1] This and other dopamine receptor blocking drugs, also referred to as neuroleptic drugs, can cause a wide variety of movement disorders.[1 20–22] In 1982, Burke *et al*,[2] comprehensively characterised tardive dystonia as a variant of tardive dyskinesia in 42 patients exposed to neuroleptic drugs. Since then, tardive dystonia has been widely recognised as a separate entity from tardive dyskinesia, and both can manifest at the same time.[1–4 7 10] Studies on tardive dystonia have focused on the prevalence of the anatomical areas involved, and its clinical progression.[2 3 7] The craniocervical region has been demonstrated as the most common region initially affected in patients with tardive dystonia.[1–4 7] As it is relatively common for patients and their family members to be unaware of an exposure to neuroleptic

Table 4 Tardive OMD

Patients	*With OFL stereotypies*	*Without OFL stereotypies*
No	18	6
Mean (SD) age at onset (y)	50.1 (14.9) (range 28 to 79)	52.9 (SD 12.6) (range 32 to 71)
Sex (M, F)	5 (27.8%), 13 (72.2%)	2 (33.3%), 4 (66.7%)
Mean (SD)duration of drug exposure (y)	6.7 (6.6) (range 0.04 to 20)	8.1 (11.4) (range 0.5 to 30)
Type of OMD (n (%)):		
Jaw closing	6 (33.3)	4 (66.7)
Jaw opening	5 (27.8)	1 (16.7)
Mixed	7 (38.9)	1 (16.7)
Associated movement disorders (n (%)):		
Blepharospasm	8 (44.4)	1 (16.7)
Cervical dystonia	9 (50)	1 (16.7)
Limb dystonia	3 (16.7)	1 (16.7)
Spasmodic dysphonia	1 (5.6)	0
Tremor	4 (22.2)	1 (16.7)
Parkinsonism	4 (22.2)	1 (16.7)
Bruxism*	4 (22.2)	4 (66.7)
Stereotypy (limb)	5 (27.8)	0
Respiratory dyskinesia	1 (5.6)	1 (16.7)
Akathisia	1 (5.6)	0

*p<0.05.

drugs, the presence of suggestive clinical signs that differentiates tardive dystonia from primary dystonia may help alert the physician and lead to early discontinuation of the drugs.

OMD, which refers to spasms of the masticatory, facial, and lingual muscles, resulting in jaw opening, closure, or deviation, is often misdiagnosed as temporomandibular joint syndrome, bruxism, or psychological disturbance.[23] Familiarity with its clinical presentation would enhance its diagnostic accuracy.[14] Although most cases are idiopathic, neuroleptic drugs can induce OMD.[1–4 13] The clinical appearance of patients with facial tardive dystonia may be difficult to distinguish from those with idiopathic cranial-cervical dystonia, especially if the movements do not extend to other body regions.[4] Pharmacological therapy generally is only partially effective for OMD.[24–26] Treatment with BTX has been shown to be an effective treatment for OMD[18 19 27] and tardive dystonia.[28]

In this study we compared the clinical variables and response to BTX treatment between patients with tardive and idiopathic OMD who were seen in a movement disorders clinic. Twenty four patients with tardive and 92 with idiopathic OMD were studied. There were no significant differences in age and sex. The demographics of our idiopathic group is consistent with reports in the literature.[11–13 29] Jaw closing dystonia was the most common subtype of OMD in both groups, and no significant differences in the subtypes of OMD were seen between them. This is by contrast with the presence of differentiating clinical characteristics (such as frequency of retrocollis) between tardive and idiopathic cervical dystonia.[3 7 30 31] The long duration of symptoms (mean of 8.4 years in tardive, 9.9 years in idiopathic OMD) and long follow up period (mean of 4.4 years in tardive, and 5.6 years in idiopathic OMD) in our study allowed an accurate comparison of associated dystonia in other body regions, as most patients should have shown progression to segmental or generalised dystonia, if it were to occur.[7] Patients with tardive OMD were more likely to have their dystonia confined to the oromandibular region (41.7% *v* 13.0%, $p<0.05$). The idiopathic group had significantly higher frequency of associated cervical dystonia ($p<0.05$). Blepharospasm and spasmodic dysphonia were also more commonly found in these patients, although the difference was not statistically significant. The combination of idiopathic cranial and cervical dystonia, is sometimes referred to as Meige's syndrome,[32] but the use of this eponym may not be justified as Horatio Wood had described this disorder already in 1887, 23 years before Meige. The tardive group had higher frequency of parkinsonism, but this was not surprising as drug induced parkinsonism may coexist with tardive dyskinesia.[1 33 34] Three out of the five patients with parkinsonism were drug induced. The presence of family history of movement disorders did not help to differentiate our patients.

Although OFL stereotypies, if they are patterned, repetitive, continuous, and coordinated, may be a result of various disorders such as autism,[35] mental retardation,[36] we have previously shown that tardive stereotypy, particularly the OFL movements, is most common in patients with tardive dyskinesia.[8] The presence of OFL stereotypies and akathisia in patients with dystonia suggests drug induced movement disorders.[3 4] Although supersensitivity of striatal dopamine receptors as a result of chronic blockage has been postulated to be a cause of tardive dyskinesia, and more recently, experimental evidence in rats suggests that oral dyskinesias may involve a functional disturbance or damage to a subpopulation of enkephalinergic neurons in the striatum,[37] it is not clear why some patients with tardive dyskinesia, develop dystonia whereas others have chiefly stereotypies.

In our study, we found a significantly greater proportion of patients with tardive dystonia manifesting OFL stereotypies compared with patients with idiopathic dystonia (75.0% *v* 31.5%, $p<0.0001$). Orofacial movements, such as facial grimacing, lip pursing, lip smacking, and tongue protrusion were significantly more often found in tardive patients ($p<0.05$). Severe tardive dyskinesia is more common in older women,[38] but no such confounding factor was present in this study as both groups were almost identical in age, and sex. Limb stereotypies, akathisia, and respiratory dyskinesia were detected only in patients with tardive OMD. Kang *et al*[3] reported OFL dyskinesias in only about 20% of their tardive dystonia patients on examination. In a more recent study, Kiriakakis *et al*[7] found that oral stereotypies were present in 30%, and akathisia in 22% of their patients with tardive dystonia. The relatively high frequency of OFL stereotypies in our study (75%) is likely due to two reasons. Firstly, all study patients were personally followed up longitudinally, thus increasing the chances of detecting stereotypies. Secondly, we only studied those with symptoms of OMD, whereas others have included all patients with tardive dystonia.

Tardive dystonia is usually disabling and persistent, and pharmacological treatment seldom results in satisfactory relief or remission of symptoms,[3] although certain medications such as tetrabenazine and clozapine have been particularly effective.[26 39] Treatment with BTX, administered by neurologists experienced in the technique, also has been demonstrated to be an effective treatment for OMD.[18 19 27] Although there may be differences in the response of the various subtypes of OMD to BTX therapy, the tardive and idiopathic patients in this study were matched in the frequency of the OMD subtype, thus allowing a fair comparison. The mean doses of BTX injected into the masseter and submentalis muscles were similar in both groups (masseters 56.3 *v* 52.4 units, submentalis 29.4 *v* 28.3 units). There was no significant difference in the total duration of action of BTX. The peak effects in both groups were excellent (2.9 *v* 3.0, 4=total abolishment of dystonia).

Among patients with tardive OMD, there were no differences in the demographics, between those with OFL stereotypies and those without. Limb stereotypies were present only in the group with OFL stereotypies. Kang *et al*[3] in their study of tardive dystonia had found no differences between those with OFL dyskinesias and those without, whereas another study[7] disclosed that those with OFL dyskinesias tended to be older at the onset of dystonia.

There are some inherent limitations in this retrospective study. Firstly, there may be a referral bias as we may be seeing the more severe cases of OMD. Secondly, documentation of all types of OFL dyskinetic movements may not be complete. Thirdly, although likely to be rare, some patients with idiopathic dystonia might have occurred coincidentally with neuroleptic use. However, all study patients have been personally evaluated, and followed up by one of us. Hence the impact of confounding factors such as inaccurate history of OFL movements, interexaminer differences, and underdocumentation of involvement of dystonia in other body regions, were reduced. The large series of idiopathic OMD enhances the statistical power of the analysis of differences with tardive patients. To our knowledge, this is the first direct clinical comparison between patients with tardive and idiopathic OMD.

In conclusion, we found a significantly higher number of patients with tardive OMD manifesting OFL stereotypies compared with idiopathic OMD. Presence of stereotypic movements in the limbs, akathisia, and respiratory dyskinesias in patients with OMD strongly suggests prior neuroleptic exposure. Patients with tardive OMD are more likely to have their dystonia confined to the oromandibular region, compared with idiopathic patients. Cervical dystonia, blepharospasm, and spasmodic dysphonia are more commonly associated with idiopathic OMD. Bruxism occurs in about a third of all patients with idiopathic or tardive OMD.[40] Treatment with BTX seems to be equally effective in idiopathic and tardive OMD.

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