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Unexpected outcome (positive or negative) including adverse drug reactions

Continuous buccolingual masticatory dyskinesia in Parkinson's disease

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Summary

Usually, levodopa-induced dyskinesia does not remain unchanged throughout the day in Parkinson's disease (PD) patients and varies according to the level of correction of PD symptomatology provided by the treatment. We observed two PD patients with unusual buccolingual masticatory movements which did not seem to fluctuate, either throughout the day during dopaminergic treatment or during a standardised levodopa challenge. After their dopaminergic treatment had been changed to a less pulsatile form of administration (ie, the use of dopamine agonist alone in the first patient and an increase in the dosage of dopamine agonist with a low dose of levodopa in the second), these abnormal movements totally disappeared in the first patient and were greatly improved in the second. These observations suggest that levodopa can have prolonged effects (several days) and induce prolonged buccolingual masticatory movements similar in type to those classically observed with dopamine receptor antagonists (neuroleptics).

BACKGROUND

In Parkinson's disease (PD), levodopa-induced dyskinesia does not usually remain constant throughout the day and varies according to the level of correction of PD symptomatology provided by the treatment.[1] We observed two PD patients with unusual buccolingual masticatory movements that were present throughout the day without any clear fluctuation in aspect or severity.

CASE PRESENTATION

Patient 1

A 74-year-old woman with PD was admitted because of chewing and masticatory difficulties that had developed over a period of 2 years (video 1). Her first PD symptoms, 15 years before, consisted of a global slowness with akinesia and rigidity of the left upper limb and were clearly improved with levodopa. After 5 years of treatment, mild to moderate wearing-off phenomena were reported. They were improved by the addition of pergolide to the levodopa treatment. At admission, she presented repetitive masticatory movements with alternating tongue protrusion and retraction, pinched lips and mandibular diduction. These movements were present on awakening and were maintained throughout the day without any clear fluctuation in severity.

Patient 2

A 65-year-old man with PD was admitted for a similar disorder. His first PD symptoms were micrographia and right upper limb akinesia, 10 years before. Initially, treatment based on levodopa and piribedil clearly improved these symptoms. Two years before the admission, he complained of mild dysarthria. Thereafter, abnormal chewing movements progressively developed. There was no clear fluctuation in PD symptoms and buccolingual masticatory dyskinesia persisted throughout the day.

INVESTIGATIONS

Neither of the patients had lesions of the mouth cavity or abnormal position of the teeth. They had never received

Table 1 Investigation of the buccolingual masticatory dyskinesia

	Levodopa challenge*						
		Before levodopa		One hour after levodopa		Treatment	
	Levodopa dose (mg)	UPDRS III	Dyskinesia	UPDRS III	Dyskinesia	At admission	Changed to a less pulsatile form of administration
Patient 1	150	33	+	12	+	Levodopa 100 mg three times a day Pergolide 1 mg three times a day†	Pergolide 1 mg three times a day†
Patient 2	200	35	+	17	+	Levodopa 150 mg three times a day Piribedil 50 mg three times a day	Levodopa 75 mg four times a day Pergolide 0.25 mg four times a day

*The standardised levodopa challenge was performed as follows: the UPDRS motor score (III) (maximal score, ie, most severe parkinsonism, 108) was measured in the morning after a 12-h withdrawal of dopaminergic treatment (ie, in the 'off' state) while the patient was in a fasting state and again 1 h after a supraliminal dose of liquid levodopa, namely the usual morning dosage of levodopa plus 50 mg (ie, in the 'on' state).
†Patient 1 also received venlafaxine (50 mg/day) for 6 years and domperidone (30 mg/day) for 1 year.
UPDRS, Unified Parkinson's Disease Rating Scale; +, presence of dyskinesia.

any neuroleptic treatment. A standardised levodopa challenge was performed in both patients. Whereas a clear improvement of PD symptoms was observed during the levodopa challenge (table 1), the buccolingual movements persisted throughout the challenge without any variation in severity or aspect (video 2). Neither patient presented dyskinesia other than buccolingual movements, either before or during the levodopa challenge.

DIFFERENTIAL DIAGNOSIS

This unusual type of levodopa-induced dyskinesia is similar to tardive dyskinesia observed in patients treated with neuroleptics.

TREATMENT

The effects of changing the dopaminergic treatment to a less pulsatile orm of administration were also assessed. In patient 1, levodopa was stopped and dopamine agonist was maintained alone. In patient 2, piribedil was replaced by pergolide. Pergolide was then increased to 0.75 mg four times a day and levodopa dosage was decreased to 75 mg four times a day.

OUTCOME AND FOLLOW-UP

In patient 1, PD symptoms were slightly more pronounced than before throughout the day without wearing-off phenomena. Seven days after the change in treatment, the buccolingual masticatory movements started to decrease and had completely disappeared a week later (video 3).

In patient 2, a dose of pergolide higher than 1.5 mg/day was not tolerated by the patient (confusion); attempts at reducing the levodopa dosage resulted in disabling wearing-off phenomena. In parallel with these treatment changes, buccolingual dyskinesia progressively decreased in severity and was only observed when the previous dose of levodopa wore off.

Video 1 A 74-year-old woman with chewing and masticatory difficulties that had developed over a period of 2 years.10.1136/bcr.09.2008.0910v1

Video 2 The levodopa challenge. The buccolingual movements persisted throughout the challenge without any variation in severity or aspect.10.1136/bcr.09.2008.0910v2

Video 3 Levodopa was stopped and dopamine agonist was maintained alone. The buccolingual masticatory had completely disappeared 2 weeks after.10.1136/bcr.09.2008.0910v3

DISCUSSION

These observations describe an unusual type of levodopa-induced dyskinesia that is similar to some types of tardive dyskinesia observed in patients treated with neuroleptics.[2] It consisted of repetitive buccolingual masticatory abnormal movements, which continued throughout the day without marked variation in type or severity and persisted unchanged for several days after dopaminergic treatment had been changed to a less pulsatile form of administration. The dyskinesia was, however, clearly due to the dopaminergic treatment received by these two patients. Neither patient had received any neuroleptics, drugs known to induce such movements,[2] or had suffered from dental problems, another factor that can induce buccolingual dyskinesia.[3] The main argument in favour of the dopaminergic treatment having been responsible for the genesis of this dyskinesia is its disappearance or marked improvement after the dopaminergic treatment was changed.

Facial dyskinesia has been described in PD but, as in the case of limb or other axial dyskinesia, it was described as fluctuating and was observed at a distance in time from levodopa intake and disappeared when patients were in the 'off' state.[4] As far as we are aware, such a dyskinesia has been reported once in association with choreic limb dyskinesia.[5]

The recent ELLDOPA study,[6] which found that the beneficial effects of levodopa were maintained 2 weeks after its withdrawal (the UPDRS score of patients who had been treated with levodopa did not reach that of patients who had received a placebo treatment) supports the hypothesis of a prolonged effect of levodopa in PD. There is also a considerable amount of experimental evidence that dopaminergic treatment can induce complex and prolonged cerebral changes (ie, plasticity). In animal models of PD, changes in the electrophysiological response of corticostriatal synapses[7] and in gene expression[8] have been found after levodopa treatment. In PD patients chronically treated with levodopa, structural changes of striatal medium spiny neurons have been described.[9] These changes are considered to be involved in the genesis of motor fluctuation and of dyskinesia.[10] The expression of the latter is, however, modulated at least partially by the intracerebral level of dopamine or dopamine agonist in human PD: usual dyskinesia is not present unchanged throughout the day and its presence is more or less related to the time of the last dopaminergic drug intake.[1] In our two patients, the dyskinesia did not appear to be directly influenced by intracerebral levels of dopamine or dopamine agonist. These abnormal movements might be due to a particular cerebral plasticity similar to that involved in the genesis of tardive dyskinesia induced by dopamine receptor antagonists. The rapid disappearance or improvement in these patients after the dopaminergic treatment had been changed indicates, however, a more reversible phenomenon than that usually observed in dyskinesia induced by neuroleptics. The fact that the persistent buccolingual dyskinesia switched to end-of-dose dyskinesia in patient 2 may suggest that the pathophysiology of these two types of dyskinesia is similar.

One intriguing aspect of these observations is the apparent rarity of this type of dyskinesia in PD. These two patients were elderly, suffered from a not very severe form of parkinsonism and had received a conventional dopaminergic treatment but did not have any other unusual clinical features. One hypothesis is that they may have had a particular pattern of dopaminergic denervation of the striatum, with a more severe lesion in the ventral part of this nucleus where motor control of facial muscles is located.[11] It has been suggested that dyskinesia is preferentially observed in the part of the body under the control of the most denervated part of the striatum in PD.[12]

Learning points

- Repetitive buccolingual masticatory abnormal movements could be due to the dopaminergic treatment received by patients with PD.

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Competing interests None.

Patient consent Obtained.

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