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Title:

Conscious sedation with midazolam intravenously for a patient with Parkinson's disease and unpredictable chorea-like dyskinesia

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## **Abstract**

Chorea-like dyskinesia, frequently occurring due to long-term levodopa medication for Parkinson's disease, causes serious problems in the precision and safety of oral surgery. However, there is no conclusive evidence to indicate whether conscious sedation with midazolam is effective against dyskinesia.

We report the first case in which levodopa-induced chorea-like dyskinesia disappeared upon intravenous administration of midazolam, under conscious sedation, in a patient with Parkinson's disease.

*Keywords:* Midazolam; Chorea-like dyskinesia; Intravenous sedation; Parkinson's disease; Basal ganglia

## **Case report**

The patient was a 70-year-old man with Parkinson's disease (height: 156.4 cm, weight: 43.2 kg). The extraction of teeth 26 and 45, and the restoration of tooth 36 were needed. He was referred to a dental anaesthesiologist by an attending oral surgeon for behavioural management, including dyskinesia control, during dental surgery.

The patient was diagnosed with Parkinson's disease at the age of 53 years, and treatment with levodopa was initiated. However, he developed severe and frequent choreic peak-dose dyskinesia, and diphasic dyskinesia of leg, arm, and neck movement, as well as on-off fluctuations and 'wearing-off' phenomenon. Enteral administration of levodopa was attempted but aborted later, while waiting for the change of hospital for rehabilitation of the remaining deficits in movement control.

The patient occasionally used to call for the nurse because of sudden and unpredictable immobility due to on-off fluctuations. The development of dyskinesia in the patient was unpredictable. He was administered a combination tablet of 25 mg carbidopa and 100 mg levodopa (Madopar<sup>TM</sup>, Chugai Pharmaceutical Ltd., Tokyo, Japan) every 4 h. It seemed ideal to perform dental surgery during the on-stage, with intravenous sedation for relieving psychological stress and preventing dyskinesia.

When the patient entered an outpatient room of our department in a wheelchair, he was in the on-stage, and dyskinesia was not observed. Aimed sedation level was set at conscious sedation for preventing aspiration, because the patient was of advanced age, exhibiting hoarseness of voice and drooling, and the treatment with irrigation was scheduled. Subsequently, midazolam (Midazolam<sup>TM</sup> injection, Sandoz K.K. Ltd., Kaminoyama, Japan) 1.5 mg was administered as an intravenous bolus, and a Ramsay's sedation score of 3 (Table 1)<sup>1</sup> was achieved. Infiltration anaesthesia was performed using 1.8 ml lidocaine (Xylocaine<sup>TM</sup> cartridge for dental use, Dentsply Sirona Ltd., Tokyo, Japan), and extraction of teeth was started. When infiltration anaesthesia was performed without pain 25 min after the first midazolam administration for restoration of tooth, chorea-like dyskinesia of the four extremities, head, and tongue was observed. Additional midazolam (1 mg bolus) treatment caused the dyskinesia to disappear within Ramsay's sedation score of 3, that is, under conscious sedation. The scheduled treatment was successfully completed. Considerable chorea-like dyskinesia of the four extremities, in the supine position, was observed when we visited the patient 1 h after the treatment.

## **Discussion**

The substantia nigra and the striatum, which are deeply involved in Parkinson's disease, are components of the basal ganglia,<sup>2,3</sup> and one of its main functions is an inhibitory regulation of motor function.<sup>4-6</sup> The excessive inhibitory effect of basal ganglia, due to the lack of dopamine in the nigrostriatal projections in Parkinson's disease, leads to decreased quantity of motion and increased muscle tone (Fig. 1).<sup>5-7</sup> Dysphagia, drooling, hoarseness of voice,<sup>8</sup> and possibility of falling due to the symptoms described above, are pre-evaluation checkpoints of the patients with Parkinson's disease, before the dental surgery.

The mechanisms of development of levodopa-induced chorea-like dyskinesia are reported to involve nigrostriatal dopaminergic denervation-induced postsynaptic supersensitivity due to long-term use of levodopa,<sup>2</sup> resulting in the increase in quantity of motion and decrease in muscle tone (Fig. 2).<sup>5-7</sup> It is highly possible that levodopa-induced dyskinesia would disappear when the patient is asleep because basal ganglia would not function in the absence of the initial command from the cerebral cortex. However, the chorea-like dyskinesia in the present case disappeared upon conscious sedation due to an additional dose of midazolam. There is a previous study on propofol-induced dyskinesia during intravenous sedation in a patient with Parkinson's disease.<sup>9</sup> Another study reported that propofol worsened involuntary movement; thereafter, propofol was replaced by midazolam for patients of Parkinson's

disease patient exhibiting poor control.<sup>10</sup> Therefore, midazolam, but not propofol, seems suitable for conscious sedation of such patients.

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The inhibitory regulation of the thalamus and brainstem by the basal ganglia is reported to involve gamma-aminobutyric acid (GABA).<sup>4-7</sup> The possible mechanism underlying the disappearance of dyskinesia, caused by midazolam, in the present case seems to involve the stimulation of the GABA receptors in these systems by midazolam, which rectifies the increased quantity of motion and decreased muscle tone.

### **Conclusion**

Intravenous conscious sedation with midazolam was useful for the disappearance of levodopa-induced chorea-like dyskinesia during oral surgery in a patient with Parkinson's disease exhibiting poor control.

### **Ethics statement/confirmation of patient's permission**

Ethics approval not required. The patient's written permission has been obtained.

### **Conflict of interest**

We have no conflicts of interest.

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**References:**

1) Ramsay MAE, Savege TM, Simpson BRJ, et al. Controlled sedation with alfaxalone-alphadolone. *Br Med J* 1974;2:656-9.

2) Nutt JG. Levodopa-induced dyskinesia: review, observations, and speculations. *Neurology* 1990;40(2):340-5.

3) Bastide MF, Meissner WG, Picconi B, et al. Pathophysiology of L-dopa-induced motor and non-motor complications in Parkinson's disease. *Prog Neurobiol* 2015;132:96-168.

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4) Alexander GE, Crutcher MD. Functional architecture of basal ganglia circuits: neural substrates of parallel processing. *Trends Neurosci* 1990;13(7):266-71.

5) Takakusaki K, Habaguchi T, Ohtinata-Sugimoto J, et al. Basal ganglia efferents to the brainstem centers controlling postural muscle tone and locomotion: a new concept for understanding motor disorders in basal ganglia dysfunction. *Neuroscience* 2003;119(1):293-308.

6) Takakusaki K. Motor control by the basal ganglia. *Clin Neurol (Rinshousinkeigaku)* 2009;49:325-34. (in Japanese)

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7) DeLong MR. Primate models of movement disorders of basal ganglia origin. Trends Neurosci 1990;13(7):281-5.

8) Lazarus JP, Vibha D, Handa KK, et al. A study of voice profiles and acoustic signs in patients with Parkinson's disease in North India. J Clin Neurosci. 2012;19(8):1125-9.

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9) Krauss JK, Akeyson EW, Giam P, et al. Propofol-induced dyskinesias in Parkinson's disease. Anesth Analg 1996;83(2):420-2.

10) Robb ND, Hargrave SA. Propofol infusion for conscious sedation in dentistry in patients with involuntary movement disorders--a note of caution. Anaesth Intensive Care 1997;25(4):429-30.

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Figure legend:

Fig. 1 Influence of the lack of dopamine in the nigrostriatal projections on the basal ganglia-related regulation of motor function in Parkinson's disease (modified from Takakusaki et al.<sup>5</sup>, Takakusaki<sup>6</sup>, and DeLong<sup>7</sup>)

Lack of dopamine in Parkinson's disease causes excessive inhibition of the basal ganglia-thalamocortical circuitry and the basal ganglia-brainstem tract.

The strength of each output is indicated by the width of the arrow.

Abbreviations: PPN, pedunculo pontine tegmental nucleus; PRF, pontine reticular formation; MRF, medullary reticular formation; GABA, gamma-aminobutyric acid

Fig. 2 Abnormal regulation of motor function in levodopa-induced chorea-like dyskinesia (modified from Takakusaki et al.<sup>5</sup>, Takakusaki<sup>6</sup>, and DeLong<sup>7</sup>)

The strength of each output is indicated by the width of the arrow.

Abbreviations: PPN, pedunculo pontine tegmental nucleus; PRF, pontine reticular formation; MRF, medullary reticular formation; GABA, gamma-aminobutyric acid

Table 1 Ramsay's sedation scores

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1	Patient anxious and agitated, or restless, or both
2	Patient co-operative, orientated, and tranquil
3	Patient responds to commands only
4	Asleep: patient responds briskly to a light glabellar tap or loud auditory stimulus
5	Asleep: patient responds sluggishly to a light glabellar tap or loud auditory stimulus
6	Asleep: patient does not respond to a light glabellar tap or loud auditory stimulus

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Modified from Ramsay et al.1

Fig. 1

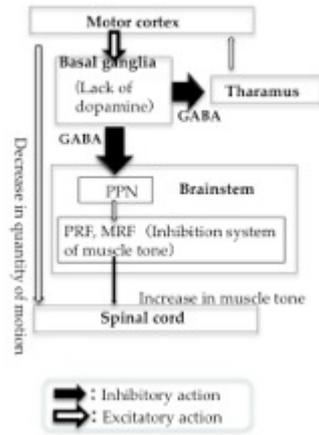


Fig. 2

