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Dental Treatment of Patients with Parkinson's Disease —Problems and Countermeasures—

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In the present paper, we discuss the problems and possible countermeasures for dental treatment of patients with Parkinson's disease. In particular, side effects of antiparkinson drugs, such as the wearing-off phenomenon, on-off phenomenon, frozen gait, psychic symptoms, oral dyskinesia, and orthostatic hypotension, are often barriers to dental treatment. We suggest that dentists should first consult with the patient's neurologist to obtain information on the patient's physical condition and possible side effects of treatment drugs.

We recommend a local anesthetic without adrenaline to avoid interactions with antiparkinson drugs. Also, macrolide antibacterial and antifungal drugs interfere with the metabolism of antiparkinson drugs in the liver and must be prescribed cautiously. Dental caregivers must avoid increasing mental stress. A preoperative electrocardiogram and another during dental treatments is recommended to monitor stress responses and to detect possible arrhythmias. We also suggest escorting the patient to prevent falls due to disturbances in posture and gait, attention to sudden involuntary movement to avoid damaging the tongue, cheek, etc., and careful management of oral care over the long-term to avoid dental caries, periodontitis, tongue coating, etc..

Key words : Parkinson's disease, Dental treatment, Side effect, L-DOPA, Antiparkinson drug

INTRODUCTION

Parkinson's disease (PD) is characterized by the degeneration of dopamine-containing neurons and the appearance of Lewy bodies in the pars compacta of the substantia nigra, as well as a marked decrease in dopamine in the corpus striatum and substantia nigra[1,2]. Onset usually occurs at 50 to 70 years of age[3]. In Japan the rate of occurrence is 50 to 100 people per 100,000[3]. Because of the rapid increase in the aging population, the number of patients with PD has also increased in recent years in Japan[4]. Recently, gene abnormalities associated with PD were reported[5]. Environmental factors might also affect the onset[6~8]. It is widely accepted that PD is due to extrapyramidal lesions and there are four main symptoms: tremor, muscle rigidity, akinesia, and difficulty maintaining posture. In addition, dysautonomia, dysbasia, psychic symptoms, and impaired cognition can occur[2] (Table. 1). The disease severity scale of Hoehn and Yahr[9], which categories the disease into five stages based on symptoms, is the most widely used in Japan (Table. 2).

The development of L-DOPA in the 1960s was a breakthrough treatment for PD[4]. Although there are many antiparkinson drugs, the drugs that exceed the benefits of L-DOPA have not yet been developed[4]. Antiparkinson drugs are classified into two groups[4,10] : dopaminergic, i. e., those directly stimulating the release of dopamine, such as L-DOPA, dopamine receptor agonists, dopamine release accelerating agents, dopamine catabolism inhibitors; and cholinergic, i. e., those that reduce cholinergic activation and increase relative dopamine activity, such as central anticholinergic drugs and the noradrenaline prodrug (Table. 3). Combinations of these drugs are often tailored according to the symptoms in individual patients[4,10]. Because radical

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treatment of PD is currently not practical, medication as symptomatic therapy is continued for a long period of time and the side effects of L-DOPA constitute a serious problem[4, 10] (Table. 4).

According to the rapid increase in the aging population, the number of elderly who undergo dental treatment has also increased in recent years in Japan[10, 11]. PD is the fourth most common neurologic disease coming after headache, cerebral apoplexy, and epilepsy[12]. PD is frequently encountered in geriatric health facilities[11, 12]. There are, however, few reports of dental treatment in patients with PD.

In the present paper, the wearing-off phenomenon, on-off phenomenon, psychic symptoms, oral

Table 1 Symptoms of Parkinson's disease

- Tremor
- Rigidity
- Bradykinesia・Akinesia
- Disturbance of the maintenance of the posture
- Gait disturbance (Dysbasia)
  - Frozen gait
  - Démarch á petit pas
  - Start hesitation
- Stiffness
- Slowness
- Muscle pain, cramps, aching
- Loss of dexterity
- Handwriting disturbance (micrographia)
- Psychiatric symptom
  - Depression
  - Nervousness
  - Hallucination
  - Delusion
  - Agitation
  - Obfuscation
- Speech distrurbance
- General fatigue, muscle weakness
- Loss of arm swing
- Mask-like-face
- Dysphagia
- Dementia
- Paresthesia
- Dysautonomia
  - Constipation
  - Drooling
  - Hidrosis
  - Oily face

From Hoehn M. M. and Yahr M. D.[9], 1967, modified.

Table 2 The diseases severity scale of Hoehn and Yahr

Stage I :	Unilateral involvement only, unusually with minimal or no functional impairment.
Stage II :	Bilateral or midline involvement, without impairment of balance.
StageIII:	First sign of impaired righting reflex. This is evident by unsteadiness as the patient turns or is demonstrated when he is pushed from standing equilibrium with the feet together and eyes closed. Functionally the patient is somewhat restricted in his activities but may have some work potential depending upon the type of employment. Patients are physically capable of leading independent lives, and their disability is mild to moderate.
StageIV:	Fully developed, severely disabling disease; the patient is still able to walk and stand unassisted but is markedly incapacitated.
Stage V :	Confinement to bed or wheelchair unless aided.

From Hoehn M. M. and Yahr M. D.[9], 1967.

Table 3 Antiparkinson drugs

Classification	Medicine name	Brand name
Levodopa	L-dopa	Doparl
		Dopaston
Dopamine receptor agonists	Cabergoline	Cabaser
	Pergolide mesilate	Permax
	Bromocriptine mesylate	Parlodel
	Talipexole hydrochloride	Domin
Dopamine release accelerating agents	Amantadine hydrochloride	Symmetrel
Dopamine catabolism inhibitors	L-dopa・Carbidopa	Neodopaston
		Menesit
	L-dopa・Hydrochloricbenserazid	EC-Dopal
		Neo-Dopasol
		Madopar
MAO-B inhibitor	Selegiline hydrochloride	FP
Anticholinergic drug	Trihexyphenidyl hydrochloride	Artane
	Biperidine hydrochloride	Akineton
Protodrug of noradrenaline	Droxidopa	Dops

From Kagemukai N.[39], 2002, modified.

dyskinesia, dry mouth, dysphagia, and orthostatic hypotension, are considered to be barriers to dental treatments and recommendations to counter these barriers are made based on the symptoms.

1) SIDE EFFECTS OF L-DOPA

L-DOPA has many side effects in patients with PD (Table. 4). Among these symptoms, the following seven items were considered relevant to dental treatment in patients with PD.

(1) Diurnal variation

The diurnal variation of the symptoms of PD were divided into two groups, those that are symptoms of PD itself, and those that occur as side effects of anti-parkinson drugs[13] (Table. 5). In particular, the wearing-off phenomenon and on-off phenomenon are barriers to dental treatments, and are discussed here.

① Wearing-off phenomenon

The wearing-off phenomenon is when parkinsonism reappears 2 to 3 hours after the administration of L-DOPA, and is a common side effect of long-term treatment with L-DOPA[2, 10, 13]. The wearing-off phenomenon is caused by degeneration of the dopamine-containing neurons and a decline in the holding capacity of L-DOPA[2, 10, 13~15]. Neutral amino acids produced after eating compete with the metabolites of L-DOPA, thereby reducing the absorption of L-DOPA from the digestive tract and blocking passage through the blood brain barrier[16, 17], which leads to the wearing-off phenomenon.

We reported a patient with PD, for whom dental treatment was stopped due to the onset of the wearing-off phenomenon[18]. In this case, because the parkinsonism reappeared after the administration of anesthesia, it was not a big problem[18]. If the wearing-off phenomenon occurs during pulpectomy or surgical procedures, however, serious problems could occur.

Dentists should first consult the patient's neurologist to divide the daily dose of L-DOPA and increase the number of times of administration according to the symptoms. Also, adding or increasing the dose of a dopamine receptor agonist is effective. Dietetic therapy in which protein intake during breakfast and lunch is restricted as much as possible, and the required amount of daily protein is consumed at supper time is also helpful. Because the wearing-off phenomenon often occurs 2 to 3 hours after medication is taken[2, 10, 12, 13], dental treatment should be performed after a meal and within 1 to 2 hours after medication[12].

Table 4 Side effects of long-term medication with antiparkinson drigs

Symptoms of digestive organs
Arrhythmia, Anginal pain
Orthostatic hypotension
Involuntary movement
Chorea
Dyskinesia
Athetosis
Ballism
Myoclonus
Oral dyskinesia
Psychiatric symptoms
Hallucination
Delusion
Excitement, Confusion
Syndrome maline
Wearing-off phenomenon
On-off phenomenon
Frozen gait
Attenuation of effect

From Kubo, K. et al.[20], 2000, modified.

Table 5 Diuralvariation of the symptoms in the pations with PD

Medium duration response
Long duration response
End-of-dose deterioration (Wearing-off phenomenon)
Drug-resistant off period
Complicated end-of -dose effect
Random oscillation (On-off phenomenon)
Resistant fluctuators

From Nakamura Y.[13], 1997. modified.

② On-off phenomenon

The on-off phenomenon is a phenomenon in which the symptoms of PD suddenly get worse and then improve, irrespective of the time of administration of L-DOPA[2, 13]. The on-off phenomenon might occur several times a day, for a short duration[2, 13]. This symptom is observed in the severe stage of the Hoehn and Yahr scale[2, 13].

We reported a patient with PD for whom dental treatment was stopped due to a sudden onset of the on-off phenomenon[19]. Like the wearing-off phenomenon, if the on-off phenomenon appears at the time of pulpectomy or a surgical procedure, serious prob-

lems can occur.

At present, there is no effective treatment for this phenomenon. Decreasing the L-DOPA dose or administering a dopamine receptor agonist are recommended for the on-off phenomenon.

(2) Frozen gait

Frozen gait is a phenomenon in which patients cannot walk smoothly, and exhibit trembling in the feet when they attempt to pass through a narrow space (short hesitation)[2, 20]. A frozen gait might appear as a symptom of PD, or as an adverse reaction to L-DOPA[21]. This symptom is observed in the severe stage of the Hoehn and Yahr scale[2, 13].

Frozen gait is observed in approximately 29.0% of patients with PD who seek dental treatment[18].

"Kinesie paradoxale"[13, 20, 22] is recommended for a frozen gait ; that is, an obstacle is placed before the patient who cannot step forward and a series of traverse bands are drawn on the floor to help the patient walk smoothly.

(3) Psychic symptoms

Psychic symptoms occur in patients with PD and can also be side effects of antiparkinson drugs[2, 13, 23]. These symptoms are observed in the severe stage of the Hoehn and Yahr scale[2, 13]. Hallucinations account for the largest fraction of psychic symptoms, followed by delusion, agitation, and obfuscation[13]. Most hallucinations are visual and are of comparatively large objects, for example, a face, an animal, etc[13]. Other antiparkinson drugs can also cause psychic symptoms[2, 13]. Amantadine induces fine visual hallucinations, such as of an insect or a small animal[13], and anticholinergic drugs induce acute agitation and distraction[13].

One patient with PD became excited and burned his hand, and was therefore unable to initiate dental treatment[18], and another patient with PD with oral dyskinesia and depression as a side effect of L-DOPA, became neurotic because of long-term hospitalization and loneliness[24].

Dentists should consult the patient's neurologist to decrease the dose of L-DOPA and to prescribe anti-depressants.

(4) Involuntary movement

Involuntary movement is a symptom of PD[2, 13, 23], and a side effect of L-DOPA. It appears in the limbs, face, oral cavity perimeter, and trunk. Chorea, dystonia, athetosis, ballism, myoclonus, and oral dyskinesia are typical symptoms[2, 13] (Table. 4). The rate of occurrence of involuntary movement increases with long-term treatment[13].

Oral dyskinesia

In oral dyskinesia, the mouth trembles, the lips pout, the tongue protrudes, or the patients lick their lips repeatedly[2, 13, 23]. It is easy to diagnose oral dyskinesia. Generally, oral dyskinesia is induced by a spontaneous phenomenon might be a side-effect (antiparkinson drug, psychotropics) or a partial symptom of another disease, such as extrapyramidal disease[25~27]. Furthermore, occlusal disharmony and poorly-fitting dentures can induce oral dyskinesia[28]. A differential diagnosis must be performed by the patient's neurologist.

With slight oral dyskinesia, dental treatments are difficult, but in serious cases, it is not possible to perform surgical treatments, tooth preparation, maxillomandibular registration, etc.. A decrease in the dose of antiparkinson drugs is effective, but then the patient's symptoms often get worse[25]. Dentists should consult the patient's neurologist.

Moreover, psychologic stress also induces dyskinesia[2] and so it is important to reduce psychologic stress in patients with PD. Oral dyskinesia is also improved by raising the bite with a bite plate[29].

(5) Dry mouth

Antiparkinson drugs often cause dry mouth[30, 31]. Anticholinergic drugs work on the peripheral nervous system the same as on the central nervous system[9, 30], so the secretion of saliva is reduced, leading to dry mouth. Dry mouth induces other symptoms, such as more viscous saliva, urtication, abnormal mastication, dysphagia, redness of tongue, glossdynia, dental caries, periodontitis, poorly-fitting dentures, coating of the tongue, and candidiasis due to the reduced self- cleaning and lubricant actions of saliva[32]. Although stopping the administration of these drugs is effective, it induces aggravation of parkinsonism and in almost all cases, it is impossible to completely

stop administration of these drugs[9, 10, 30]. It is difficult to treat these causes, therefore ameliorative treatment is recommended. The dental staff should hydrate the oral cavity and administer moisture-producing drugs. Oral prophylaxis is important for patients with dry mouth to prevent other symptoms, such as dental caries, periodontitis and coating of tongue, etc.

(6) Dysphagia

Fifty-eight percent of patients in stage I and 90% of patients in stages Ⅱ～Ⅳ of the Hoehn and Yahr scale have dysphagia[33]. Dysphagia is closely associated with the neural symptoms of PD and hyperphagia is observed in the early stage, reflex stage, and peristalsis stage ; most are dysfunctions of mastication, bolus formation, and sending the bolus to the esophagus. Thus, the premotor stage is extended because of akinesia[33~35]. The degree of dysphagia is in proportion to the dyskinesia[34]. In severe cases, tracheotomy is nessesary[36], but in mild cases, dietetic therapy, such as thickening the foods and rehabilitation treatment for dysphagia are recommended[36]. Because ingesting antiparkinsons drugs is difficult for patients with dysphagia, PD symptoms worsen, thereby leading to worse dysphagia. Taking medication with jelly, not with water, is recommended for dysphagic patients. Oral prophylaxis is important for the patient with dysphagia to prevent aspiration.

(7) Orthostatic hypotension

In patients with PD, orthostatic hypotension often occurs following long-term administration of L-DOPA[9]. Therefore, when raising the exam chair from a horizontal position to a sitting position, it is necessary to move the chair slowly. Also, elastic stocking on the legs is recommended to prevent orthostatic hypotension.

2) THINGS TO CONSIDER DURING DENTAL TREATMENTS

The matters to be attended to during dental treatments are as follows.

(1) Local anesthesia

In one patient with PD, elevated blood pressure was observed after injection of an adrenaline-containing local anesthetic at the time of tooth extraction[37]. In this case, it was thought that the blood pressure elevation was due to an interaction between the adrenaline in the local anesthetic and L-DOPA[37]. Selegiline hydrochloride (a MAO-B inhibitor) enhances the action of sympathomimetic drugs[38]. Moreover, in patients taking the noradrenaline prodrug droxidopa, adrenaline-containing local anesthetics can induce arrhythmia and asystole[39]. Therefore, the use of a combination of these drugs is contraindicated.

Generally, in patients with PD, local anesthetics without adrenaline are recommended.

(2) Medication

① Combined administration of macrolide antibacterial medicine and antiparkinson drugs

In patients taking a dopamine receptor stimulant (cabergoline and the methyl acid bromocriptine) and MAO-B inhibitor (selegiline hydrochloride), treatment with macrolide antibiotics suppresses metabolism of these antiparkinson drugs in the liver, and so the blood concentration of these drugs increases and the side effects worsen, such as gagging and emesis[38]. Therefore, penicillin and cephalosporin are recommended.

② Combined administration of antifungal drug and antiparkinson agents

Generally, anticholinergic drugs induce dry mouth and thrush. In patients taking the dopamine receptor stimulant (cabergoline and methyl acid bromocriptine) and MAO-B inhibitor (selegiline hydrochloride), iatraconazole (antifungal drug) suppresses metabolism in the liver of these antiparkinson drugs, and so the blood concentration of these drugs and the side effects, such as gagging and emesis, are increased[38]. In these cases, minonazole and amphotericin B are recommended.

(3) Notes for treating patients

① Avoid psychologic stress

In one patient with PD taking L-DOPA, although the blood pressure was generally stable, fear of the tooth extraction increased blood pressure occurred after administration of local anesthesia, even though a local anesthetic without adrenaline was used[37]. In this case, catecholamines were secreted because of

the mental stress due to the fear of dental treatment and elevation of blood pressure occurred by the interaction of endogenous adrenaline and L-DOPA[37]. Also, in another patient with PD, ventricular premature beats worsened due to psychologic stress during dental treatments[40]. Mizuno suggested that arrhythmia was related to the sudden death of the patient with PD who took L-DOPA[41].

Dental treatments often induce mental stress. Because mental stress can induce arrhythmia[42], we suggest that in treating patients with PD, dentists should take an electrocardiogram preoperatively and during dental treatments.

Almost all patients with PD have slow movements[9]. Therefore, it is possible that fast-paced movements of the dental staff increase the psychologic stress of the patient, which leads to increased parkinsonism symptoms. Therefore, the dentist and dental staff should keep pace with the patients.

② Escort the patients

Patients with PD are apt to fall down because of disturbances in the maintenance of the posture and acceleration of gait[9, 18]. Clearing the passage to avoid frozen gait is recommended. If frozen gait does occur, "Kinesie paradoxale"[13, 20, 22] is recommended. Dentists and dental staff should escort these patients to prevent their falling down between the waiting room and dental chair.

③ Pay attention to sudden involuntary movement

Involuntary movement often occurs in patients with PD[9]. In addition, because the patient can exhibit sudden involuntary movements, it is important to take care not to damage the tongue, cheek, and labium oris. Holding the tongue with a tongue depressor and holding the lower jaw with fingers to reduce oral dyskinesia, in particular, makes it easy to perform oral care and stabilize the patient against sudden involuntary movements.

(4) Manage oral care

In almost all patients with PD, eating takes a long time because of slow movement and rigidity. Patients are therefore unwilling to perform their oral cleaning because of fatigue. The patients also have difficulties performing their oral cleaning as the disease progresses. Therefore, the incidence of dental caries, periodontitis, coating of tongue, etc., increases.

It is difficult for the patients with PD to brush their teeth and rinse their mouth because of oral dyskinesia and other involuntary movements. Specifically, they cannot skillfully brush their teeth and move the toothbrush with the necessary quick and short steps because of involuntary movements, thereby leading to poor oral care.

The mean time required to handle dentures in patients with PD is significantly longer than in other aged patients[43]. In severe cases, patients cannot insert or remove their dentures by themselves[43].

The dental staff should provide instruction in the methods of oral care to the patients family or health-care workers to manage their oral care over the long-term.

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パーキンソン病患者の歯科治療
—問題点とその対策—

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キーワード：パーキンソン病，歯科治療，副作用，L-DOPA，抗パーキンソン病薬

パーキンソン病患者の歯科治療時の問題点とその対策について考察した．特に問題は，Wearing-off現象，On-off現象，すくみ足，精神症状，不随意運動，オーラルジスキネジア，起立性低血圧などのL-DOPA製剤の副作用である．歯科治療開始前には必ず主治医との連携を図り，全身状態および服用中の抗パーキンソン病薬およびその副作用の発現状況を把握すべきである．

パーキンソン病患者の歯科治療時には，抗パーキンソン病薬との相互作用を避けるためエピネフリン非含有の局所麻酔剤を使用した方がよい．マクロライド系抗菌剤や抗真菌剤の中には抗パーキンソン病薬の代謝を阻害するものがある．また，歯科スタッフは患者に精神的ストレスを加えないように配慮し，精神的ストレスに起因する不整脈等の発現に備え，歯科治療中，心電図および血圧測定による全身管理を行うべきである．

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