Special Article

Treatment of Parkinson's Disease in Thailand: Review of The Literature and Practical Recommendations

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The mainstay of treatment for Parkinson's Disease (PD) remains symptomatic despite the rapid expansion in knowledge of its neurodegenerative process. Therapeutic options, both medical and surgical, have been markedly improved over the past decades, resulting in better motor function, activities of daily living, and quality of life for PD patients. The principle of PD management should be individualized and the selection of treatments should aim to control symptoms as well as to prevent or delay motor complications. In Thailand, various pharmacologic and surgical options are available, including different formulations of levodopa, dopamine agonists, monoamine oxidase B inhibitor, cathechol-O-methyltransferase inhibitor, pallidotomy, and lastly deep brain stimulation. The use of dopamine agonists in early PD has a levodopa-sparing effect and reduces the incidence of motor complications. Continuous dopaminergic stimulation (CDS), which mimics physiological activation of dopaminergic receptors, has been proposed as a strategy to prevent motor complications. Based on current evidence, practical guidelines in the medical management of different types of motor complications are outlined in the present article according to what are available in Thailand. Surgical interventions should be reserved for patients with intractable motor complications after careful patient selection.

Keywords: *Parkinson's Disease, Motor complications, Deep brain stimulation*

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Parkinson's Disease (PD) is an age-related neurodegenerative disease. The prevalence of PD in Thailand has not been officially studied but the World Health Organization (WHO) estimated that PD affects approximately 700,000 people in South-East Asia[1]. The cardinal features of PD include resting tremor, rigidity, and bradykinesia, with later development of postural instability[2,3]. Nonmotor features, such as autonomic dysfunction, dementia, sleep disturbances, and depression, have recently been recognized. The main pathological features of PD are a preferential loss of dopaminergic neurons in the substantia nigra pars compacta (SNc) (Fig. 1), the presence of intracellular inclusions, called Lewy bodies in the remaining neurons, and a reduction in striatal dopamine[4,5]. Despite the increasing understanding of the neurodegenerative process underlying PD, there is still no disease-modifying treatment of proven clinically efficacy. The mainstay of PD treatments remains symptomatic. These include pharmacotherapy, such as levodopa and other dopaminergic agents (Table 1), and surgical approaches, such as deep brain stimulation (DBS). The goal of symptomatic treatments is to normalize the activity of the disturbed basal ganglia network.

In view of the rapid evolution of various therapeutic options over the recent years, several treatment guidelines have been developed in America and Europe to provide evidence-based recommendations for the management of different stages of PD[6-12]. The authors review these guidelines and focus on treatment options available in Thailand. Practical

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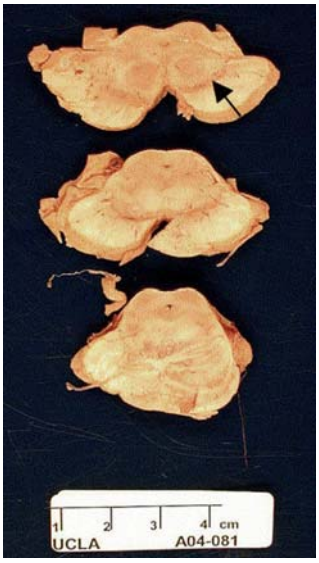

Fig. 1 Depigmentation of substantia nigra in Parkinson's disease

Table 1. Therapeutic options available in Thailand for motoric symptoms in Parkinson's disease (availability determined by the time of publication)

Levodopa
Levodopa/carbidopa
Levodopa/benserazide
Levodopa/carbidopa/entacapone
Dopamine agonists
Non-ergot derivative
Pramipexole
Piribedil
Ergot derivatives
Bromocriptine
Cathechol-*O*-methyltransferase inhibitors
Entacapone
Monoamine oxidase inhibitors
Selegiline

recommendations on the tailoring of PD medications and indications of different treatment approaches are provided to aid clinicians in their treatment decisions for patients with PD. Table 2 provides a list of therapeutic options for motoric symptoms, which are available in Thailand.

Management of Early PD

Pharmacotherapy for neuroprotection

No adequate clinical trials have provided definitive evidence for pharmacologic neuroprotection. While many agents have appeared promising based on laboratory studies, the symptomatic effects of the study medications commonly confound the clinical endpoints for clinical trials. Studies in early PD have suggested that selegiline postpones the need for dopaminergic treatment by more than 6 months, and may reduce the risk of gait freezing, indicating a delay in disability progression[13]. Similarly, early treatment with rasagiline for 12 months in the TEMPO study showed less functional decline than subjects whose treatment was delayed for 6 months[14]. However, rasagiline is not currently available in Thailand. While these findings may suggest a neuroprotective effect of selegiline and rasagiline, symptomatic effects of these agents cannot be entirely excluded.

Two studies have examined the potential neuroprotective properties of pramipexole and ropinirole using b-CIT single photon emission computed tomography (SPECT)[15] and ^{18}F-dopa positron emission tomography (PET)[16] to measure dopamine markers in the brain. Patients initially treated with pramipexole demonstrated a 16% reduction in the percent of loss from baseline of striatal - CIT uptake versus a 25.5% reduction in those initially treated with levodopa during the 46-month evaluation period ($p < 0.05$). Similar results were obtained in the ropinirole study, in which patients initially treated with ropinirole demonstrated a 34% slower reduction in the striatal dopamine uptake when compared with patients initiated with levodopa ($p < 0.05$). The neuroprotective effect of dopamine agonists cannot be confirmed by these imaging studies because of the lack of placebo controls. Furthermore, the binding of these drugs with neuroimaging ligands may confound the findings.

Pharmacotherapy for symptom control

• *Dopamine agonists:* Dopamine agonists have diverse physical and chemical properties, but they share the ability to directly stimulate dopamine receptors. This contrasts with levodopa, which needs to be transformed into L-dopamine in presynaptic terminals. This D_2-like receptor agonistic activity of the dopamine agonists produces their antiparkinsonian effect. There are currently 3 dopamine agonists marketed in Thailand, 1 is ergot derivative (bromocriptine) and the other two are non-ergot derivatives (pramipexole, and piribedil).

The efficacy of dopamine agonists used as monotherapy in early PD has been demonstrated in numerous studies involving pramipexole[17],

Table 2. Lists of medications available in Thailand for motoric symptoms in Parkinson's disease (availability determined by the time of publication)

Medications (Trade name, Pharmaceutical company)	Available doses	Initial dosing	Side effects
Levodopa			
Carbidopa/levodopa (Sinemet®, M&H Manufacturing; others)	25/100 mg 25/250 mg	25/100 3 times daily	Confusion, dizziness, dry mouth, dyskinesias, hypotension, nausea, vomiting
Carbidopa/levodopa/entacapone (Stalevo®, Novartis)	25/100/200 mg (Stalevo® 100) 37.5/150/200 mg (Stalevo® 150)	25/100/200 3 times daily	Confusion, dark urine color, diarrhea, dizziness, dry mouth, dyskinesias, hypotension, nausea, vomiting
Carbidopa/levodopa (Levomet®, Unison)	25/100 mg 25/250 mg	25/100 3 times daily	Confusion, dizziness, dry mouth, dyskinesias, hypotension, nausea, vomiting
Benserazide/levodopa (Madopar®, Roche)	50/200 mg (Madopar 250 mg tab) 25/100 mg (Madopar dispersible 125 tab) 25/100 mg (Madopar HBS cap)	50/200 mg (Madopar 250 mg tab) 0.5 tab 3 times daily 25/100 mg (Madopar dispersible 125 tab) 1 tab 3 times daily 25/100 mg (Madopar HBS cap) 1 cap before bedtime	Confusion, dizziness, dry mouth, dyskinesias, hypotension, nausea, vomiting
Dopamine agonists			
Bromocriptine (Parlodel®, Novartis; Bromergon®, Sandoz)	2.5 mg	2.5 mg 3 times daily	Confusion, dizziness, edema, hallucinations, nausea, sleepiness, valvular fibrosis, vomiting
Pramipexole (Sifrol®, Boehringer Ingelheim)	0.25 mg 1 mg	0.125 mg 3 times daily	Confusion, dizziness, edema, hallucinations, nausea, pathological gambling, sleep attacks, sleepiness
Piribedil (Trivastal retard®, Servier)	50 mg	50 mg 3-5 times daily	Confusion, dizziness, edema, hallucinations, nausea, pathological gambling, sleep attacks, sleepiness
Monoamine oxidase-B inhibitors			
Selegiline (Jumex®, Sanofi-Aventis; Julab®, Biolab)	5 mg	5 mg daily in AM	Confusion, dizziness, dry mouth, hallucinations, insomnia, nausea

Table 2. Lists of medications available in Thailand for motoric symptoms in Parkinson's disease (availability determined by the time of publication) (continue)

Medications (Trade name, Pharmaceutical company)	Available doses	Initial dosing	Side effects
Catechol-O-Methyltransferase (COMT) inhibitors			
Entacapone (Comtan®, Novartis)	200 mg	200 mg with levodopa/ carbidopa dose	Abdominal pain, constipation, dark urine color, diarrhea, dizziness, dyskinesias, nausea, vomiting
Anticholinergic agents			
Trihexyphenidyl (ACA®, Atlantic Pharma, Acamed®, Medifive)	2 mg; 5 mg	1 mg daily	Blurred vision, cognitive impairment, constipation, dilation of pupils, dizziness, drowsiness, dry mouth, hallucinations, headache, increased ocular tension, nervousness, nausea, urinary retention, vomiting, weakness

ropinirole[18] (not available in Thailand), pergolide[19], and, recently, rotigotine[20]. In the early stage, the clinical benefit from dopamine agonists is usually sufficient but when disease progresses, it becomes necessary to add levodopa, which has a better effect on symptoms. Delaying the introduction of levodopa by using a dopamine agonist postpones and reduces the occurrence of motor fluctuations seen with levodopa treatment[15,21]. Long-term follow-up studies indicated that approximately 85%, 68%, 55%, 43%, and 34% of PD patients initiated on pramipexole or ropinirole are still controlled on monotherapy at 1, 2, 3, 4 and 5 years, respectively[21,22].

There are no data to suggest that one agonist is more efficacious than another. However, an association has been reported between treatment with pergolide and the development of fibrotic valvular heart disease (Recently, pergolide has been discontinued in Thailand[23-26]. Similar findings have also been observed with bromocriptine and cabergoline, suggesting a preferential activation of 5-HT_{2B} receptor on heart valves[27]. Most published studies concluded that treatment with ergot dopamine agonists (pergolide and cabergoline in most cases), particularly at high daily doses and for periods of 6 months or longer, was associated with a substantial increased risk of newly diagnosed cardiac-valve regurgitation[23,25,28,29]. As a result, pergolide has been voluntarily withdrawn from the US market[30] and current recommendations suggest that non-ergot derivatives should be first considered when dopamine agonists are indicated.

• *Levodopa:* The efficacy of levodopa is firmly established from over 40 years of use in clinical practice. It remains the most reliable and effective treatment for PD symptoms. A recent placebo-controlled study confirmed a dose-dependent efficacy of levodopa to reduce Unified Parkinson's Disease Rating Scale (UPDRS) scores (Fig. 2)[31]. Levodopa has also been proven better at improving symptoms than dopamine agonists in numerous studies[21,22,32,33]. However, patients will develop motor complications with long-term levodopa therapy. After 5 years of treatment, about 50% of patients taking levodopa develop motor fluctuations, and 30% develop dyskinesias; these numbers may be higher in patients with young-onset PD[34,35]. Levodopa is now routinely coadministered with a decarboxylase inhibitor, either carbidopa or benserazide. They block peripheral degradation of levodopa to dopamine, allowing more levodopa to cross the blood-brain barrier. The gastric mucosa is another site of action, thus decarboxylase inhibitor also increases duodenal levodopa absorption[36,37].

Prevention of motor complications

A number of strategies have been developed to prevent or delay the occurrence of motor complications. Firstly, the evidence that the early use of dopamine agonists can reduce the incidence of motor

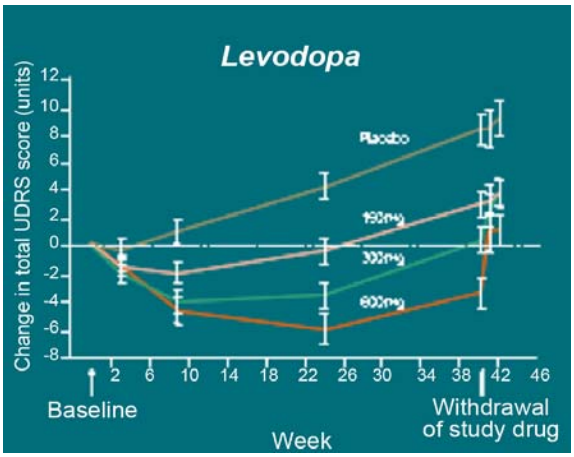

Fig. 2 ELLDOPA study: changes in total scores on the Unified Parkinson's Disease Rating Scale (UPDRS) from baseline through evaluation at week 42. Levodopa, in a dose-response pattern, significantly reduced the worsening of symptoms of PD as reflected in the change between the total score on UPDRS at baseline and that at week 42, as compared with the change in the placebo group[31] (With permission from the New England Journal of Medicine 2004; 351 (24); 2498-2508. Copyright© (2004). Massachusetts Medical Society. All right reserved)

complications (versus levodopa) has influenced most neurologists to start dopamine agonists as symptomatic monotherapy in early PD patients. Secondly, because the mechanism of levodopa-induced motor complications is probably related to the abnormal pulsatile stimulation of striatal dopamine receptors, which does not mirror the normal continuous activation of these receptors that occur physiologically[38]. The concept of continuous dopaminergic stimulation (CDS), either by using long-acting dopamine agonists or continuously delivering levodopa, has been proposed as a method of preventing motor complications[39]. Whether employing CDS therapy by continuous levodopa delivery can actually delay dyskinesias or motor fluctuations in early PD patients is unknown. A few studies are ongoing to address these questions.

Management of Late (Complicated) PD

Long-term dopaminomimetic therapy, not limited to levodopa, is often complicated by the emergence of variations of motor response in a majority of PD patients. 'Advanced disease' is defined as PD with progressive motor impairment despite levodopa therapy and an unstable medication response leading to motor complications[40]. Advanced disease typically develops after 5 years of levodopa treatment in up to 50% of PD patients[35]. Motor complications can be simply divided into motor fluctuations and dyskinesias[41]. Typically, patients may begin to experience a wearing-off (end-of-dose) effect because the motor improvement after a dose of levodopa becomes reduced in duration and Parkinsonism reappears. Subsequently, dyskinesias emerge at peak-dose levels and are classically choreiform, but they may be dystonia or myoclonus[42]. Eventually, patients may experience rapid and unpredictable fluctuations between ON and OFF periods, known as the ON-OFF phenomenon.

Treatment of end-of-dose wearing off

End-of-dose wearing off is the most common and usually the first sign of motor complications. The patient develops a loss of response to a dose of medication before taking the next dose, usually within four hours of the earlier dose. If they take their next dose of medication, their symptoms will improve again until the next dose begins to wear off. The problem is not generally related to drug absorption or drug interference. Treatment depends on the severity of the problem and on how dopaminergic therapy was initiated in the early stage of the disease. The predictability is somewhat reassuring to patients and this may allow simple interventions to be made. Some of the treatment options are suggested as follows (Box 1):

- *Add a catechol-O-methyltransferase (COMT) inhibitor* (Fig. 3): If the patient already takes stable doses of levodopa, this is an option. Only one selective COMT inhibitor, entacapone, is available in Thailand for clinical use. Several controlled studies demonstrated that adding COMT inhibitor is useful and has been shown to reduce "off" time by approximately 1.3 hours per day with entacapone and two to three hours per day with tolcapone (another COMT

Box 1. Treatment options of end-of-dose wearing off

1) Add a catechol-*O*-methyltransferase inhibitor (entacapone)
2) Manipulate the dose of levodopa by shortening the interval between levodopa doses
3) Add a dopamine agonist
4) Other options (less frequently used)
   - Water-soluble levodopa
   - Add selegiline

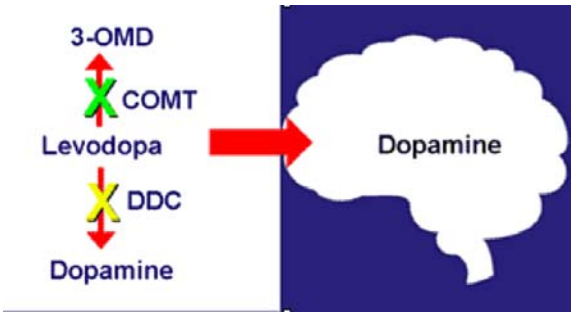

Fig. 3 Mechanism of entacapone: inhibiting peripheral catechol-*O*-methyltransferase resulting into more levodopa available in the striatum

inhibitor available in the US)[43-45]. Patients should be advised that they may develop dyskinesia within one or two days of adding COMT inhibitor and that a 20% to 30% reduction in levodopa dose may be required. Side effects of tolcapone include diarrhea occurring in 5% to 6% of patients and the possibility of developing fulminant hepatitis[46]. The introduction of levodopa/carbidopa/entacapone (LCE) offered the opportunity to simplify the dosage regimen for patients already on entacapone[47]. Patients who are stable on levodopa and entacapone given separately can be converted straight over to the equivalent dose of LCE[48]. LCE should not be cut or crushed; only one should be taken at each dose time and this agent must not be combined with additional entacapone.

• *Manipulate the dose of levodopa by shortening the interval between levodopa doses:* The next dose should be administered just before the beneficial effects from the previous dose have worn off.

• *Add a dopamine agonist:* Dopamine agonists are useful in reducing "off" time because their half-lives are longer than that of levodopa. The dose of levodopa should be maintained until a clinical response to dopamine agonist is achieved. Later, the levodopa dose can be gradually lowered. Several controlled studies confirmed the efficacy of dopamine agonist as adjunctive treatment to levodopa in reducing total daily "off" time by about 2 hours with a reduction of levodopa dose of about 19% to 25%[49-52].

• *Other options:* These options are infrequently employed to treat symptoms of wearing off. Water-soluble levodopa can be used to bridge a temporary lack of levodopa, but it can later precipitate dyskinesias[53]. Adding selegiline may mildly improve the short-duration levodopa response and increased "on" time[54].

Treatment of dyskinesia

To treat dyskinesia, the pattern of dyskinesia needs to be determined. A patient's history and PD diary are the primary source of information[55]. Once the records are reviewed, it is important for physicians to observe what patients mean by dyskinesia since they may confuse dyskinesia with tremor, "off" dystonia, or "on" dystonia. It may be worthwhile observing patients in the clinic through one to two dose cycles so that various forms of dyskinesias are witnessed and understood on both sides. Most PD patients prefer to be "on" with dyskinesia rather than to be "off". Therefore, in advanced PD patients, the balance between reductions in dyskinesia without deteriorating Parkinsonism is critical in the management. It is also important for advanced PD patients to be aware that it is often difficult to delineate a dose of medication that provides stable "on" time without inducing dyskinesia. A compromise to achieve the "balance" is probably the goal of the management. The following steps are recommended for treating patients with disabling dyskinesias (Box 2):

• *Review the patient's drug regimen:* Determine if there are any drugs that may alleviatedyskinesia without reducing the antiparkinsonian effect. Examples of options are selegiline[56] and anticholinergics[57,58].

• *Examine other adjunctive therapies:* If the patients are receiving sustained-release levodopa, better symptom control may be achievable if they are switched to an immediate-release preparation, particularly if dyskinesia occurs late in the day. If the COMT inhibitor is used, dose reduction may be necessary. Alternatively, a reduction in levodopa dose may be considered, but this may result in the inability to induce an "on" response in some patients. Some authors suggest the addition of a dopamine agonist coupled with a reduction in the levodopa dose may reduce dyskinesia while sustaining motor benefit.

Box 2. Treatment options of dyskinesia

1) Review the patient's drug regime to determine if there are any drugs that may alleviate dyskinesia without reducing the antiparkinsonian effect
2) Examine other adjunctive therapies
   - Switch from sustained-release to immediate-release levodopa
   - Reduction in COMT inhibitor dose
   - Reduction in levodopa dose (with the addition of dopamine agonist)
3) Add clozapine

• *Add amantadine or clozapine:* Amantadine is the only agent that suppresses dyskinesia through its action at the NMDA receptor[59-61], however, it is not available in Thailand. The antidyskinetic effect of amantadine is effective at 300mg per day, but it generally lasts about five months, with many patients experiencing a rebound in dyskinesia after drug discontinuation[60]. Alternatively, clozapine may be considered. However, it lacks definite evidence in reducing dyskinesia, and its potential toxicity, such as agranulocytosis, has limited its use[62].

Treatment of "Off" dystonia

Dystonia can be caused by levodopa or PD itself so it can occur both during the "on" and "off" state. Therefore, careful history, noting the relationship between the timing of dystonia and the timing of levodopa administration is critically important. Generally, "off" dystonia is much more common than "on" dystonia and frequently occurs in the morning, manifested as painful dystonic cramping of the toes and feet on wakening[63]. This symptom, termed early morning dystonia, probably occurs because of the wearing-off of the levodopa overnight[64]. Several treatment options are available as follows (Box 3):

• Add a bedtime dose of sustained-release levodopa or long-acting dopamine agonist to increase plasma concentrations of levodopa throughout the night and early morning[65-67].

• Have the patient take the first dose of levodopa before rising from bed. This strategy can be used with water-soluble levodopa, which has an onset of action of between 10 and 15 minutes.

Treatment of dose failures or no "On" response and delayed "On"

In some patients with advanced PD, taking a dose of levodopa may not result in any improvement in symptoms; this is known as a dose failure. If the occurrence of these symptoms is not related to a reduction in levodopa dose or appears suddenly after additional medication has been prescribed, drug interactions should be suspected. Certain medications have been reported to reduce levodopa bioavailability, including oral iron, aluminum/magnesium containing antacids, pyridoxine, and cholesterol-lowering drugs[68-70]. Recently, PD patients who received Helicobacter pylori eradication therapy showed a significant increase in levodopa absorption, which was coupled with a significant improvement of clinical disability and with a prolonged "on-time" duration[71,72]. If drug interactions are excluded, it is likely that these symptoms are due to inadequate absorption of levodopa because of an inadequate dose, slowing of gastrointestinal transit time, or competition for levodopa absorption from dietary protein[73]. Therefore, factors that delay gastric emptying may delay or blunt peak plasma levodopa levels, leading to a delay or complete failure to achieve a good clinical response[74]. The following strategies are recommended to augment levodopa absorption (Box 4):

• Withdraw anticholinergic agents

• Relieve constipation using laxatives, for example high-fiber and fruit diet and lactulose

• Instruct the patient to take the medication sufficiently in advance of meals. A high-protein meal may reduce levodopa absorption due to large neutral amino acids competing with levodopa for transfer across the intestinal mucosa and the blood-brain barrier[75,76]. If this option fails, reducing any fat intake close to the time medication is taken may be helpful.

• Add domperidone: Domperidone is a prokinetic D_2 receptor antagonist, which does not cross the blood-brain barrier[77]. Therefore, the incidence of extrapyramidal symptoms is rare. In a small open study, domperidone therapy significantly reduced upper gastrointestinal symptoms and accelerated gastric emptying of a solid meal, and did not interfere with response to anti-parkinsonism treatment[78].

• Switch to water-soluble levodopa or immediate-release levodopa to help shorten the delay in "on" response. The sustained-release formulation often results in a more delayed "on" response and is generally not recommended in this particular situation.

Box 3. Treatment options of "Off" dystonia

1) Add a bedtime dose of sustained-release levodopa or long-acting dopamine agonist
2) Taking the first dose of water-soluble levodopa before rising from bed

Box 4. Treatment options of dose failures or no "On" response and delayed "On"

1) Withdraw anticholinergic agents
2) Relieve constipation
3) Instruct the patient to take the medication sufficiently in advance of meals
4) Add domperidone
5) Switch to water-soluble or immediate-release levodopa

Dissolving immediate-release levodopa in an ascorbic acid solution or fizzy drink may improve uptake from the gut.

On-Off phenomenon (unpredictable On-Off)

As PD progresses, patients may develop an unpredictable "on/off" response to medication such that motor function does not follow levodopa dosing cycles[79, 80]. The typical example is that the medication may kick in, but well before the time of the next dose, there is an abrupt "off" period (without warning), unlike the gradual "off" time that develops in the wearing-off response. There is a complete loss of predictability and, therefore, the patients will not know when they will be able to perform activities. Usually, they have severe akinetic "off" periods, accompanied by severe dyskinesias during the "on" stage.

This is one of the most difficult fluctuations to treat. Patients at this stage are very sensitive to manipulations of even small doses of levodopa. The fine-tuning of medications at this stage has to be individualized. However, sustained-release formulations are best avoided because their bioavailability is unpredictable. Other approaches to consider are as follows (Box 5):

• *Add a COMT inhibitor:* It is recommended that a COMT inhibitor be gradually titrated, for example, initially a 100 mg of entacapone to avoid disabling dyskinesias.

• *Try a different dopamine agonist if the current one is not helpful.*

• *Implement a protein redistribution diet*: Because patients at this stage have a decreased capacity to store dopamine centrally, a minor reduction in levodopa transport into the brain can lead to a dramatic reduction in striatal dopamine levels, resulting in an "off" episode[81,82]. Consuming most of the daily protein requirement during a single meal (e.g., supper) may allow better responses after the other meals of the day.

• *Consider surgical procedures such as DBS*: Both globus pallidus interna and Subthalamic nucleus (STN) are common surgical targets for DBS. However, STN has been proposed as the preferred surgical target site for treating motor complications (Fig. 4). Bilateral STN DBS has been shown to provide patients with a full range of antiparkinsonian benefits, including improvements in tremor, bradykinesia, and rigidity[83-85]. In addition, stimulation of the STN may allow levodopa doses to be lowered, thereby reducing the severity of levodopa-related dyskinesias.

Box 5. Treatment options of unpredictable On-Off

1) Gradually titrate COMT inhibitor
2) Try a different dopamine agonist if the current one is not helpful
3) Implement a protein redistribution diet
4) Consider surgical procedures, including pallidotomy, GPi DBS, and STN DBS

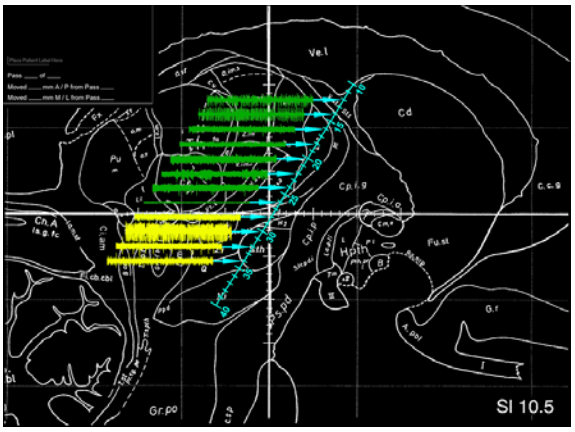

Fig. 4 Schaltenbrand atlas demonstrating microelectrode trajectory to the subthalamic nucleus

Conclusion

Due to the improvement of medical and surgical treatments for PD, there are several therapeutic options for physicians to consider for their patients. However, the most important principle in the management of PD is to customize therapy and to the needs of individual patients. The selection should be based on scientific rationale and evidence-based data. The aim should be not only to control motoric symptoms but also to prevent or delay motor complications if possible. There are no proven neuroprotective drugs, but several agents have been found to have at least levodopa-sparing effect or to reduce the risk of freezing. Surgical interventions should be reserved for patients with intractable motor complications. Because certain symptoms, for example dysarthria, dysphagia, and axial symptoms, may not respond to dopaminergic therapy, other neurochemicals may be involved and could be targets of future research. With continued research in the therapeutics of PD, it is anticipated that more pharmacologic agents and new surgical techniques will be discovered, leading to better treatments in the future.

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การรักษาโรคพาร์กินสันในประเทศไทย: วิเคราะห์ข้อมูลของการรักษาในปัจจุบันและข้อแนะนำในทางเวชปฏิบัติ

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หลักของการรักษาโรคพาร์กินสันในปัจจุบันอยู่ที่การทำให้อาการของผู้ป่วยดีขึ้นโดยเฉพาะในเรื่องของการเคลื่อนไหว ซึ่งในปัจจุบันมีการรักษาอยู่หลายวิธี ไม่ว่าจะเป็นยาในหลาย ๆ กลุ่ม ดังเช่น ยาลีโวโดปา ยาเสริมการทำงานของโดปามีน ยายับยั้งเอ็นไซม์ในการทำลายของลีโวโดปา และการผ่าตัด ได้แก่ การผ่าตัดแพลิโดโตมี (pallidotomy) หรือ การผ่าตัดแบบกระตุ้นสมองส่วนลึก (deep brain stimulation) ถึงแม้ว่าวิธีการรักษาโรคพาร์กินสันจะหลากหลาย แต่การเลือกใช้ยาในกลุ่มใดกลุ่มหนึ่ง หรือ การผ่าตัด ควรขึ้นอยู่กับอาการของผู้ป่วยในแต่ละราย โดยมีหลักของการรักษาที่จะให้เกิดการกระตุ้นของตัวรับโดปามีน (dopamine receptor) ในสมองอย่างสม่ำเสมอ (continuous dopaminergic stimulation) ซึ่งในปัจจุบันเชื่อว่า การกระตุ้นตัวรับโดปามีนอย่างสม่ำเสมอและต่อเนื่องจะส่งผลให้เกิดอาการทางการเคลื่อนไหวที่ดีขึ้นอย่างต่อเนื่อง และลด หรือ ชะลอการเกิดปัญหาในเรื่องของการตอบสนองต่อยาไม่สม่ำเสมอ ในบทความนี้ผู้นิพนธ์ ได้รวบรวมหลักของการรักษาโรคพาร์กินสันในทุกระยะ สำหรับการใช้ในเวชปฏิบัติตามหลักฐานทางวิชาการที่มีอยู่ และได้ปรับวิธีเพิ่มเติมให้เข้ากับการรักษาที่มีใช้อยู่ในประเทศไทยในปัจจุบัน