ABSTRACT

Many factors affect the decision to initiate pharmacotherapy for Parkinson’s disease (PD), and it is a joint decision among the patient, the physician, and the patient’s family. Drug treatment for PD should be individualized for the particular patient. If a medication switch is considered, the decision to switch medication has to be weighed carefully, because the number of treatment options is limited. Almost all of the PD drugs require titration. At each dose level, a decision must be made whether to continue increasing the dose (and risk adverse events, which are commonly dose dependent) or to live with the current treatment effect. Each decision is a trade-off for the patient. When assessing treatment outcomes, as with diagnosis, the history and examination are critical, as are discussions with the patient and family about expectations before treatment is started. This article reviews factors affecting the decision for treatment initiation, how to assess treatment response, and determining when to switch medications. The article also includes extracts from an interview with one of my patients, who describes the diagnostic process from his point of view.

sense of any asymmetry in motor signs. (Please go to www.JHASIM.com/PD2008/Tarsy to view a video showing how to perform a motor examination.)

Rigidity is also tested in all 4 limbs. To test rigidity in the legs, the patient should be reclining with the physician moving the legs passively.

Assess posture to look for stooping. Assess gait, which may reveal shortened stride length, extra short steps on turning, or reduced arm swing on 1 side. Postural instability is assessed by the pull test, in which the physician stands behind the patient, puts his or her hands on the patient's shoulders, and forcefully pulls back. A healthy patient should be able to correct falling backwards with a single step. If the patient takes 2 or 3 steps backwards to prevent falling, this is abnormal. It is important, however, to pull forcefully enough to evoke a response.

This article includes extracts from an interview with one of my patients, who describes the diagnostic process from his point of view. The interview also illustrates some of the key clinical points discovered in a patient history.

CASE STUDY: LZ

LZ is a 55-year-old man with a 5-year history of PD. He initially presented with mild resting tremor in his upper-right extremity and reduced arm swing, noticed first by his family but not the patient. He did not start pharmacologic treatment for PD until 3 years after his initial visit. He was started on the rotigotine patch, titrated to 4 mg daily. Although LZ responded well to the rotigotine patch, this formulation was discontinued due to manufacturing problems, and LZ was started on pramipexole, titrated to 4.5 mg daily.

PATIENT INTERVIEW

When I first saw Dr. Tarsy, it was primarily because of the tremor in my right hand, which had become more pronounced in the 12 to 18 months before I saw the doctor. As time went on, my gait became affected. I seemed a bit "off speed." There were also a few times when I would "lock up," particularly in closed spaces. Because my dad had PD, it was of concern to me and I wasn't getting answers from my primary care physician.

When I first saw the neurologist, these changes were getting slowly worse, but they weren't yet affect-
the initial visit. Likewise, the family’s report of response is important because family members sometimes see changes of which the patient is not aware. Also, it is important to review all ADLs at each visit, because medication may not produce improvement in all PD symptoms and signs. Tremor amplitude is notoriously unpredictable and can vary on a daily or even hourly basis (although tremor frequency tends to remain relatively constant). The clinician should strive to measure the whole spectrum of the patient’s experience.

The repeat motor examination should include all of the components mentioned previously, in addition to more global features, such as the patient’s appearance as they enter the office or facial expression.

**Patient Interview (Continued)**

I found the rotigotine patch to be very good. It reduced a lot of my symptoms. Maybe part of it was just that it gave me more confidence. I liked that I could put it on and forget about it. When I got up to 6 mg, the symptoms virtually disappeared, although only occasionally there would still be some tremor. I was on it for about 8 months and it worked the entire time—the whole 8 months. There were no breakthrough symptoms toward the end of the 24 hours, before I had to change the patch.

They discontinued the patch, so I started taking pramipexole, which I now take 1.5 mg 3 times a day. It has been moderately good. I don’t think it is as effective as the patch, in terms of my symptoms, especially the tremors, but they are still better than before I started any drug treatment. I also do better in tight spaces; I don’t lock up as much. The pramipexole has been reasonably satisfactory.

Right now, some of my fine-motor coordination, in my right hand in particular, is affected. I can’t move my right hand as easily as my left. And certainly when I’m walking, I have to be conscious of the fact that I need to swing my right arm. Thankfully, I’m left-handed.

My sleep patterns were disturbed for awhile. I was falling asleep earlier than usual and waking up in the middle of the night, but that has gotten better. Other than that, I haven’t had any side effects—no nausea, no loss of appetite.

Overall, I’m better, but I see that there are now everyday activities that I have to pay attention to, whereas before I never had to think about them.

**Determining When to Switch Medications**

In LZ’s case, the decision to switch medications was determined artificially, because of the loss of availability of the initial drug. However, switching treatments may also be warranted if the signs or symptoms worsen, if there is no response to treatment, if side effects become too severe, or if mental status changes appear.

The decision to switch medication has to be weighed carefully, because the number of treatment options is limited. Clearly, worsening signs or symptoms, no response, and the emergence of mental status changes are clear criteria for switching drugs. The question of side effects as an indication for a treatment change is less clear. The clinician should assess the severity of the PD symptoms and level of patient concern. It may be better to find a way to work through or treat the adverse events, after the cause of the presumed effect is determined. For example, the dose or timing of the dose could be altered. Treatments to consider for adverse events would be an antiemetic for nausea (eg, trimethobenzamide or a nondopamine receptor blocking agent but not metoclopramide, which aggravates parkinsonism); increasing dietary salt intake or using full-length stockings for orthostatic hypotension; and medications for drowsiness (eg, methylphenidate or modafinil). In my experience, methylphenidate or modafinil are not always effective for treating somnolence due to PD medication, but several studies and general clinical experience have shown efficacy with these drugs.1-4

Mental confusion is an automatic cause for discontinuation of any PD medication. Patients do not develop tolerance to confusion or hallucinations, and even though these symptoms are always reversible with drug discontinuation or lowering the drug dose, experiencing these symptoms can be very frightening for the patient. The only exception is in a more advanced patient, where there is not the option of drug withdrawal. In those situations, antipsychotic agents such as quetiapine or clozapine can be added. These 2 drugs are not useful in treating confusion as a side effect because they only address psychotic symptoms, such as visual hallucinations and delusions. However, they may allow the patient to remain on his or her PD medication, perhaps at a lower dose.

The patient’s age can also be a factor in the decision to start or switch medication. Patients above age 70 are
at greater risk for mental confusion and psychiatric symptoms on antiparkinson medications.

**Patient Interview (Continued)**

I started on pramipexole about 6 months ago. The finger tapping in my right hand has improved noticeably. The tremor in my right hand used to be continuous but now only happens occasionally. However, I’ve developed a tremor in my left hand as well. That’s new, since I last saw Dr Tarsy. It only happens intermittently, when my hand is at rest. That’s the only change I’ve noticed, in terms of things getting worse. Overall, I am much more satisfied with my condition than I was a year ago.

**Comment:** LZ also noted occasional swelling in his right ankle, about 6 months after he started the rotigotine patch. However, he also had undergone arthroscopic surgery on his right knee. Ankle swelling can occur with dopamine agonist treatment, but it is usually bilateral. A possible explanation for the swelling in LZ’s leg is the decline in spontaneous movements of his right leg, because of PD. This was noted during the office visit—as LZ crossed his right leg over the left, it required more effort.

**Conclusions**

LZ has responded well to 2 different dopamine agonists, which bodes well for predicting his disease course and response to treatment in the future. LZ is an articulate patient who is well informed about his disease. When assessing treatment outcomes, as with diagnosis, the history and examination are critical, as are discussions with the patient and family about expectations, before treatment is started.

Almost all of the PD drugs require titration. At each dose level, a decision must be made whether to continue increasing the dose (and risk adverse events, which are commonly dose-dependent) or to be satisfied with the current treatment effect. Each decision is a trade-off for the patient.

**REFERENCES**