Letter to the Editor

Zolpidem improves akinesia, dystonia and dyskinesia in advanced Parkinson’s disease

Dear Professor Kaye

Zolpidem, an imidazopyridine hypnotic drug acting as a selective gamma-aminobutyric acid (GABA) type A agonist, has been reported to produce significant motor improvement in patients with Parkinson’s disease (PD). However, relevant reports are scarce. We report a patient with advanced PD who had had a unilateral pallidotomy, unilateral thalamotomy and bilateral deep brain stimulation (DBS) of the subthalamic nuclei, who demonstrated an immediate improvement in akinesia, dystonia and dyskinesia after 10 mg zolpidem.

A 53-year-old man was diagnosed with PD at the age of 30 years. The initial presentation was with left hemiparkinsonism, characterized by rest tremor, bradykinesia and rigidity. He had undergone right pallidotomy in 1985 (without improvement), right thalamotomy in 1985, and bilateral deep brain stimulation (DBS) in 2001. In 2005, after adjustment of his medication and reprogramming of the DBS, he remained severely disabled (Hoehn and Yahr stage V). In addition, he also developed episodic and unpredictable dyskinesia and mild dystonia. Ten months later, he experienced an episode of severe dystonia which presented as sustained mouth-opening and head-turning to the right side. He could barely move. We administered 10 mg zolpidem at night for his insomnia. Approximately 15 min later, he was able to speak well and his dystonia resolved. He was also able to get up from the bed, and to walk with minimal aid, as well as open his mouth, chew and swallow. His dyskinesia also improved. However, improvement in motor function lasted for only 2 hours. The antidystonia and antidyksinesia effects lasted for about half a day, longer than the duration of improvement of motor function. Other hypnotics (lorazepam 2 mg) did not have such an effect. The motor score of the Unified Parkinson’s Disease Rating Scale (UPDRS-III) was performed before and after the administration of 10 mg zolpidem; a 27% improvement in the score was noted (Table 1A). There was no significant somnolence with this dose. A lower dosage of zolpidem (5 mg) was tested; although the improvement of motor performance was not satisfactory, the dosage did alleviate his dystonia and dyskinesia. Therefore, zolpidem was maintained at 5 mg three times a day and 10 mg before sleeping. Six months later, a follow-up test using 10 mg zolpidem demonstrated immediate and significant improvement (26% in UPDRS-III) 15 minutes after administration, although the baseline score was lower in the second evaluation (Table 1B).

The present observation supports a previous report that zolpidem may improve parkinsonian and dyskinesia symptoms in a subpopulation of patients with PD. It has been reported that zolpidem may also improve parkinsonian symptoms in progressive supranuclear palsy and dystonia in X-linked dystonia-parkinsonism syndrome ("Lubag"). A subhypnotic dose of zolpidem was reported to oppose dopaminergic-induced dyskinesia in PD. Our observation offers additional information. First, the patient presented here had young-onset PD and had had a unilateral pallidotomy, unilateral thalamotomy, and bilateral DBS of the subthalamic nuclei. Administration of zolpidem improved his UPDRS-III score. Second, zolpidem improved his akinesia, dyskinesia and dystonia symptoms simultaneously. The duration of the antiparkinsonian effect was much shorter than that of the antidystonia and antidyksinesia effects. The required dose for motor improvement was higher (10 mg). The reason for such a discrepancy is unknown, but this finding is consistent with a previous report that subhypnotic doses of zolpidem (2.5–5.0 mg) could oppose dopaminergic-induced dyskinesia in PD. Third, zolpidem was consistently effective irrespective of the baseline UPDRS-III score. Although the baseline UPDRS-III was better in the second test (42) than the first test (48), the improvements in motor performance after taking zolpidem were significant both in the first evaluation (27%) and in the second evaluation (26%) 6 months later.

Zolpidem, an imidazopyridine, is a nonbenzodiazepine hypnotic with a selective agonist effect for GABA type A receptors. The binding sites for zolpidem are most abundant in the output structures of the basal ganglia: the globus pallidus pars interna and substantia nigra pars reticularis.
In patients with PD, excessive thalamic inhibition leads to suppression of the cortical motor system, possibly resulting in akinesia. Increased GABAergic activities may reverse the overactivities of the subthalamic nucleus and internal pallidum and improve akinesia. Dyskinesia improved at the same time, possibly through a mechanism similar to that associated with pallidotomy. It is unclear how zolpidem benefits dystonia but GABAergic activities probably play a role.

In conclusion, zolpidem may improve parkinsonian symptoms in patients with advanced PD by modifying neuronal activity within the basal ganglia and subcortico-cortical circuits. Zolpidem also reduces complex motor complications such as dystonia and dyskinesia, for up to half a day at a very low dose. More studies are needed to clarify these multiple benefits.

References


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