Effectiveness of Istradefylline for Fatigue and Quality of Life in Parkinson’s Disease Patients’ and of Their Caregivers’

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Abstract

Objectives: We evaluated efficacy and safety of istradefylline that is the first selective adenosine A2A receptor antagonist, for the treatment of non-motor symptoms and quality of life (QoL) in Parkinson’s disease (PD) patients with and QoL in their caregivers. Methods: This was a multi-sites study of 40 PD patients (female 24, male 16) who fully filled UK PD society brain bank clinical diagnostic criteria. They received istradefylline 20 mg/day for 8 weeks. We added istradefylline on the previous anti-Parkinson’s drugs. Clinical severities were evaluated by Hoehn-Yahr (H-Y) stage, unified PD rating scale (UPDRS), non-motor symptoms in PD (NMSPD), fatigue severity scale (FSS) and Euro QoL. Also, we evaluated their caregiver’s QoL by Euro QoL. Results: The scores of UPDRS part I improved from 1.3 ± 1.1 to 06 ± 0.9 (P = 0.18), part II improved from 11.9 ± 3.2 to 11.0 ± 3.1 (P = 0.17), part III improved from 34.8 ± 7.2 to 32.1 ± 8.3 (P = 0.105). There was no significant improvement or worsening of the H-Y stages. The scores of NMSPD improved from 49.9 ± 11.2 to 43.9 ± 10.6 (P = 0.08). The scores of FSS improved from 62.8 ± 7.1 to 52.3 ± 9.3 (P = 0.049). The total scores of Euro QoL in PD patients improved from 48.8 ± 14.9 to 57.2 ± 13.0 (P = 0.045). The total scores of Euro QoL in patients’ caregivers improved from 54.2 ± 11.0 to 59.8 ± 10.9 (P = 0.046). Conclusions: Our data demonstrated that istradefylline was associated with few side effects and was modestly effective for the treatment of non-motor symptoms especially fatigue that might improve QoL in PD patients as well as in their caregivers’.

Keywords
Parkinson’s Disease, Non-Motor Symptoms, Istradefylline, Fatigue, Quality of Life, Caregivers

1. Introduction

Quality of life (QoL) is an important patient- and their caregivers-reported variable that reflects the impact of disease and treatment from the patients’ perspective [1] [2]. Since Parkinson’s disease (PD) consists of wide range of complex symptoms, QoL provides valuable and comprehensive information on the patients’ and their caregivers’ health status. Some studies were found for levodopa, levodopa with added-on catechol-O-methyltransferase (COMT) inhibitors, levodopa/carbidopa gel for intestinal infusion, some dopamine agonists (ropinirole, cabergoline, pergolide), and the monoamine oxidase B (MAO-B) inhibitor [3] [4]. As a whole, these studies found a beneficial effect on patients’ QoL.

Adenosine A2A receptors are highly localized to the basal ganglia and are selectively localized on medium spiny neurons of the indirect output pathway, projecting from the striatum to the external globus pallidus, which also selectively expresses dopamine D2 receptors. The indirect pathway has been implicated in the expression of motor disability in PD. Istradefylline is the first selective adenosine A2A receptor antagonist and is effective in relieving wearing-off fluctuations of PD patients [5] [6].

We conducted an open-labeled multi-site clinical study to evaluate efficacy and safety of istradefylline for non-motor symptoms, and for PD patients’ and their caregivers’ QoL.

2. Patients and Methods

2.1. Patients

Patients (female 24, male 16; aged 44 - 80 years; Table 1) with moderate-to-severe idiopathic PD were treated with once-daily istradefylline 20 mg/day for 8 weeks. All PD patients fully filled UK PD society brain bank clinical diagnostic criteria [7]. Patients had been stable (no drug adjustments needed) on antiparkinsonian drugs for 2 weeks before enrolment. We added istradefylline on the previous antiparkinsonian drugs.

Clinical severities were evaluated by Hoehn-Yahr (H-Y) stage, unified PD rating scale (UPDRS) [8], non-motor symptoms in PD (NMSPD) [9], fatigue severity scale (FSS) [10] and Euro QoL [10]. Also, we evaluated their caregiver’s QoL by Euro QoL.

2.2. Statistical Analysis

Two-tail t test or Mann-Whitney test was used to compare the clinical values at the base line and 8 weeks after (Statistical package for Mac version 2, Esumi Co, Tokyo). The results were presented as mean values ± standard error of the mean (SEM). A P value < 0.05 was considered as statistically significant.

3. Results

Patients had PD for 7.82 ± 3.00 years and were prescribed antiparkinsonian drugs that were calculated into levodopa equivalent doses as 604 ± 214 mg/day.

The scores of UPDRS part I improved from 1.3 ± 1.1 to 0.6 ± 0.9 (P = 0.18), part II improved from 11.9 ± 3.2 to 11.0 ± 3.1 (P = 0.17), part III improved from 34.8 ± 7.2 to 32.1 ± 8.3 (P = 0.105). There was no significant improvement or worsening of the H-Y stages. The scores of NMSPD improved from 49.9 ± 11.2 to 43.9 ± 10.6 (P = 0.085, Figure 1). The total scores of FSS significantly improved from 62.8 ± 7.1 to 52.3 ± 9.3 (P = 0.049, Figure 2). The total scores of Euro QoL in PD patients significantly improved from 48.8 ± 14.9 to 57.2 ± 13.0 (P = 0.045, Figure 3). The total scores of Euro QoL in patients’ caregivers significantly improved from 54.2 ± 11.0 to 59.8 ± 10.9 (P = 0.046, Figure 4).

4. Discussions

PD is relatively common neurodegenerative disorder and accurate diagnosis and individualized assessment of

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<th>Table 1. Baseline characteristics of patients.</th>
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<td>Age, years</td>
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Figure 1. Non motor scale changes from baseline. The scores of non motor scale for Parkinson’s disease (NMSPD) improved from 49.9 ± 11.2 to 43.9 ± 10.6 (P = 0.08).

Figure 2. Severity of fatigue changes from baseline. The total scores of fatigue severity scale (FSS) significantly improved from 62.8 ± 7.1 to 52.3 ± 9.3 (P = 0.049).

Figure 3. Patients’ QoL changes from baseline. The total scores of Euro QoL in PD patients significantly improved from 48.8 ± 14.9 to 57.2 ± 13.0 (P = 0.045).
the risks and benefits of available antiparkinsonian medications should guide treatment for PD patients. Levodopa still remains the gold standard for the treatment of motor symptoms of PD, but dopamine agonists, COMT inhibitors and MAO B inhibitors have also provide more continuous oral delivery of dopaminergic stimulation to improve motor outcomes [11]. Despite all of the therapeutic advances achieved within the last 20 years, PD continues to be a progressive disorder with severe disability caused by motor and non-motor symptoms. Istradefylline is a newly developed selective adenosine A2A receptor antagonist [9]. Istradefylline has been reported to be effective for wearing-off fluctuations of PD patients, however, istradefylline might also be effective for non-motor symptoms, and the results of our study supported this. In addition, istradefylline was effective for PD patients’ fatigue and QOL, and also for their caregivers’ QoL.

Fatigue is the most troubling but least elucidated syndrome in PD [10]. Fatigue can be distinguished from depression, and although depression in PD has some relationship with motor syndromes, fatigue does not. While PD patients’ anhednia or anxiety also cause trouble for patients’ caregivers, fatigue has been reported as the most troublesome non-motor symptom for patients’ caregivers [12]. We presented a possibility that Istradefylline might improve PD patients’ fatigue, but mechanism of improvement remains uncertain. Several points could be raised for this. A recent randomized, double-blind, placebo-controlled trial conducted in 373 patients with fluctuating PD showed a significant reduction in OFF time after taking Istradefylline [13]. Since motor fluctuations in PD induced patients’ non-motor symptoms such as fatigue or anxiety, removing or alleviating motor fluctuations may improve non-motor symptoms. As was reported before fatigue had close relations with patients’ and also their caregivers’ QoL, thus Istradefylline may improve their QoL.

5. Conclusion
Although there may be limitation from small size of sample, the main finding that emerges from this study is that administration of Istradefylline was associated with few side effects and was modestly effective for the treatment of non-motor symptoms especially fatigue, and that might also improve PD patients’ QoL as well as in their care givers’ QoL.

References


