



## Donepezil for Lewy Body Constipation: A Six-Month Follow-up

Lepkowsky CM\*

Independent Practice, 1143 Deer Trail Lane, Solvang, California 93463, USA

\*Corresponding author: Dr. Charles M. Lepkowsky, Independent Practice, 1143 Deer Trail Lane, Solvang, California 93463, USA, Tel: 805-688-1229, Fax: 805-686-9382; E-mail: clepkowsky@gmail.com

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### Abstract

In a previous case study, four patients at different stages of Parkinson's disease (PD) and Neurocognitive Disorder with Lewy Bodies (NCDLB) disease progression were treated with Donepezil, with the intention of mitigating Lewy body impairment of the cholinergic pathways in the myenteric plexus, increasing bowel motility, and reducing the symptom of constipation. In all four cases, the use of Donepezil was associated with significant reduction of the symptom of constipation. There was no exacerbation or instigation of other symptoms. The symptom status of the four patients was reviewed six months later. In none of the patients has there been exacerbation of the symptom of constipation, nor emergence of new symptoms. The findings suggest that Donepezil might have long-term efficacy for reducing constipation in patients with PD and NCDLB. Further research is recommended using larger numbers of subjects matched for diagnosis, age, gender, and other variables.

**Keywords:** Donepezil; Parkinson's disease; Neurocognitive disorder; Constipation

### Introduction

In a previous case study, it was hypothesized that the use of Donepezil might mitigate the symptom of constipation [1]. Research was reviewed demonstrating that (a) constipation in Parkinson's disease (PD) and Neurocognitive Disorder with Lewy Bodies (NCDLB) is the consequence of Lewy pathology in the myenteric plexus [2-8]; (b) 95% of innervation in the myenteric plexus (which controls motility in the colon) is cholinergic [9]; (c) constipation is a frequent Lewy body symptom producing difficulties for both patients and providers of care [10,11]; and (d) for patients with neurocognitive disorders, conventional constipation treatments have proven ineffective [12].

### Discussion

Because Lewy pathology impairs cholinergic function [13-17], cholinergic agonists like cholinesterase inhibitors (AChEIs) are prescribed to NCDLB and PD patients with the intention of mitigating cholinergic impairment. Data were also reviewed demonstrating that (e) among AChEIs, Donepezil has performed well [18-22]; (f) a Cochrane database systematic review found that Donepezil produced consistent reduction in neurocognitive symptoms in patients with PD and NCDLB, without exacerbation of Parkinsonian features or other side effects [23]; (g) Donepezil has reduced constipation in nongeriatric affective patients [24]; and (h) Donepezil increased cholinergically mediated bowel contractions as much as 477% in patients suffering from severe intestinal dysmotility [25].

Based on the data, four patients at different stages of PD and NCDLB disease progression were treated with 5 mg to 10 mg HS doses of Donepezil, with the intention of mitigating Lewy body impairment of the cholinergic pathways in the myenteric plexus, increasing bowel motility, and reducing the symptom of constipation. In all four cases, the use of Donepezil was associated with significant reduction of the

symptom of constipation. There was no exacerbation or instigation of other symptoms.

The symptom status of the four patients in the previous case study was reviewed six months later. In two of the four patients, there were no symptom changes. In the other two patients, there was some exacerbation of Lewy body symptoms including blunted affect, dysphoric mood, generalized anxiety, sleep disturbance (onset, median and terminal waking, REM sleep behavior disorder or RSD and/or REM sleep without atonia, or RSWA), cognitive interference (short-term memory loss and difficulty with word-finding), passive suicidal ideation, appetite suppression, and exacerbation of Parkinsonian features (motor retardation, joint and muscle pain, reduced range of motion, diminished strength and coordination, increased tremor, gait disturbances, and difficulties with balance). However, in none of the four patients has there been exacerbation of the symptom of constipation, nor emergence of new symptoms.

### Conclusion

These findings suggest that the use of Donepezil might have long-term efficacy in reducing constipation in patients with PD and NCDLB, through a mechanism that specifically mitigates Lewy body cholinergic impairment in the myenteric plexus. Further research is recommended using larger numbers of subjects matched for diagnosis, age, gender, and other variables.

### Informed Consent

Written consent was provided by each of the four patients described in the case studies to release the clinical information contained therein. Patient identifiers have been kept to a minimum.

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