

Donepezil for Constipation in Lewy Body Disease: A Twelve-Month Follow-Up

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Abstract

Previously, the acetylcholinesterase inhibitor Donepezil was used in a case study to address the symptoms of constipation, obstipation, and impaction in four patients with Lewy Body diseases. In patients with both Parkinson's disease (PD) and Neurocognitive Disorder with Lewy Bodies (NCDLB), the use of Donepezil led to symptom reduction. After six months, the symptoms of the same patients were reviewed, with no loss of bowel motility nor emergence of new symptoms. After twelve months, another review of symptoms was conducted. The results indicate that Donepezil appears to be effective in reducing the symptoms of constipation, obstipation and impaction over an extended period of treatment.

Keywords: Neurocognitive disorder with lewy bodies; Parkinson's disease; Constipation; Donepezil; Acetylcholinesterase inhibitor

Introduction

Previously, the acetylcholinesterase inhibitor Donepezil was used in a case study to address the symptoms of constipation, obstipation, and impaction in four patients with Lewy Body diseases including Neurocognitive Disorder with Lewy Bodies (NSDLB) and Parkinson's Disease (PD) [1]. In that study, research was reviewed demonstrating that Lewy Bodies impede the predominantly cholinergic neurotransmitter pathways in the myenteric plexus (MP) and the colonic submucosal plexus (CSP) [2]. The consequence of Lewy Body impairment of the MP and the CSP is reduced bowel motility, leading to the symptoms of constipation, obstipation, and impaction [3-10]. Bowel immotility significantly impacts both patient quality of life and the practical aspects of care provision [11,12], complicated by the fact that in Lewy Body patients, the symptoms of constipation, obstipation and impaction appear resistant to over-the-counter medications and other conventional forms of treatment [13].

Discussion

With the intention of mitigating cholinergic impairment caused by Lewy pathology, acetylcholinesterase inhibitors (AChEIs) are prescribed to patients with NCDLB and PD [14-19]. Among the various AChEIs, Donepezil has been effective in reducing cholinergic impairment without increasing Parkinsonian symptoms or producing new symptoms [20-25]. Specific to the symptom of constipation, Donepezil has been used with nongeriatric affective patients to reduce constipation [26], and in a population diagnosed with severe bowel immotility, Donepezil increased bowel contractions 477% [27].

The mechanism through which Donepezil mitigates the symptom of constipation can be described as two-fold. Donepezil inhibits the acetylcholine-hydrolyzing enzyme acetylcholinesterase, consequently increasing acetylcholine levels, which in turn leads to a reduction of cholinergically dysfunctional symptoms [28]. Donepezil is thus

described as a specific, reversible acetylcholinesterase inhibitor [29,30]. Neuronal nicotinic acetylcholine receptors are also independently affected by Donepezil [31]. Because of this "dual action," historically Donepezil has been a drug of choice for addressing impairment of cholinergic neurotransmission [19,21,22,28,31].

In the initial study, Donepezil was administered in doses varying from 5 to 10 mg administered orally on a daily basis to four patients in various stages of NCDLB and PD, each of whom suffered from significant constipation, obstipation and/or impaction. Two of the patients had been administered Carbidopa-Levodopa for over a year to address the Parkinsonian features of their Lewy Body disease. Based on the research data, it was hoped that Donepezil would elevate cholinergic activity in the MP and CSP, countering Lewy pathology in the neurotransmitter pathways predominant in those structures, leading to increased bowel motility and reduction of the symptoms of constipation, obstipation, and impaction. Results indicated that Donepezil significantly reduced the constipation, obstipation and impaction, without an increase in existing symptoms or producing new symptoms [1]. In a follow-up study six months later, it was found that despite the progression of Lewy body symptoms in two of the patients, none of the four patients had experienced an increase in the symptoms of constipation, obstipation, or impaction, nor any new symptoms [32].

The symptom status of the four patients was reviewed again after twelve months. There was no apparent progression of Lewy Body symptoms in any of the four patients between the six months and twelve-month reviews. In one of the patients whose Lewy body symptoms had progressed at six months, doubling the dosage of Donepezil (from 5 to 10 mg orally administered daily) was associated with reduced cognitive interference (short-term memory loss and difficulty with word-finding). No other symptom changes were evident in that patient. In the remaining three patients, no symptom progression or change was apparent. None of the patients exhibited new symptoms, nor any increase in the symptoms of constipation, obstipation, or impaction.

Conclusion

It appears that Donepezil reduces constipation through the mechanism of increasing acetylcholine levels in the MP and CSP, restoring bowel motility, with consequent significant reduction of the symptoms of constipation, obstipation, and impaction [19]. It also appears that Donepezil does so without exacerbation of Parkinsonian features or producing additional symptoms. The reduction of constipation, obstipation, and impaction without exacerbation or emergence of other symptoms in all four patients over a twelve-month period suggests that the extended use of Donepezil is efficacious for treating these symptoms, including its use for patients simultaneously taking Carbidopa-Levodopa. 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. The authors declare no conflict of interest.

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