Use of Donepezil in Elderly Patients With Alzheimer's Disease- A Hawaii Based Study

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Abstract

Donepezil (Aricept) is a reversible acetylcholinesterase inhibitor which is indicated for the treatment of mild to moderate dementia of the Alzheimer's type. We did a retrospective analysis of 41 elderly Alzheimer's subjects of different ethnic groups including a large number of Asian and Hawaiian patients. Donepezil appears to be clinically effective in patients of different ethnicities with mild to moderate Alzheimer's disease, even at advanced age.

Introduction

Alzheimer's disease is the most common disorder causing cognitive decline. It affects approximately 4 million persons in the United States.[1] Some of the cognitive signs and symptoms of Alzheimer's disease are attributed to a deficiency of cholinergic neurotransmission.[2-5] Donepezil (Aricept), a reversible acetylcholinesterase inhibitor, is indicated for the treatment of mild to moderate dementia of the Alzheimer's type.[6,7]

Published studies have not addressed the effectiveness of donepezil in Asian and Hawaiian populations. This study was done to evaluate the effectiveness of donepezil on cognitive and functional levels in mild to moderate Alzheimer's disease among the different ethnic groups in Hawaii.

Methods

Subjects

Subjects in this study include male and female elderly of different ethnic backgrounds who were referred to the Geriatrics Consultation Clinic at Kaiser Permanente, Honolulu, Hawaii. Patients who were diagnosed as having Alzheimer's Disease were classified as mild (>19), moderate (14-19) and severe (<14) based on Folstein Mini Mental Status Examination (MMSE) scores(8). Patients who had mild to moderate Alzheimer's and who didn't have any contraindication to the use of donepezil were offered this medication. Donepezil was initiated in 41 patients.

Study Design

This is a retrospective analysis of all patients who were placed on donepezil between March 1997 and June 1998. Patients received donepezil 5 mg once daily for 1 month, after which they were increased to 10 mg once daily. MMSE and Clock Drawing Test (9) scores were evaluated at 3 month intervals. Functional and behavioral status were also assessed at 3 months intervals. Analysis was done using simple analytic methods.

Results

Out of 41 subjects who were on donepezil, 13 (32%) were males and 28(68%) were females. Eight (20%) of subjects were 65-75 years old, 23 (56%) were 76 –85 years old and 10 (24%) were >85 years old. The mean age of subjects was 80 years.

Baseline MMSE scores ranged from 14-27,with a mean of 21.5 (Fig 1). 12 subjects (29%) were assessed for at least 9 months, 11subjects (27%) for at least 6 months, 15 subjects (37%) for at least 3 months and 3 subjects (7%) for 1 month. Three subjects who were assessed for 1 month didn't have a follow up MMSE at the end of 1 month. MMSE scores improved (>2) in 12 subjects (29%). MMSE scores did not change ($\pm$2) from baseline in 15 (37%) of subjects. There were no functional or behavioral declines in the 12 subjects continuing donepezil for $\geq$ 9 months. The responses to donepezil in the 3 months ,6 months and 9 months follow up groups, are shown in Table 1. Trends of MMSE scores in the 9 month follow up group is shown in Figure 2.

Among the subjects 9 (22%) were Japanese, 9 (22%) were Chinese, 11 (26%) were Caucasian and 12 (29%) were Hawaiian. Chinese subjects had a mean change in MMSE by + 3.73 , Caucasian +1.00 , Japanese + 0.92, and Hawaiian + 0.00 at 3 months.

Out of 41 subjects (24%), 10 had side effects. (Table 2). Three subjects had agitation. Two had gross loss in weight (>10 lbs). Fifteen (35%) had clinically insignificant weight loss (<3 lbs) .

Nineteen subjects (46%) discontinued donepezil at or within 6 months (Table 3). The reasons for stopping the medication were side effects 8 (19%), family's wishes not to continue 3(7%), no cognitive improvement or cognitive decline 4 (10%) and non compliance 1(2%).

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Figure 1.— Baseline MMSE score ranges in the subjects on the study

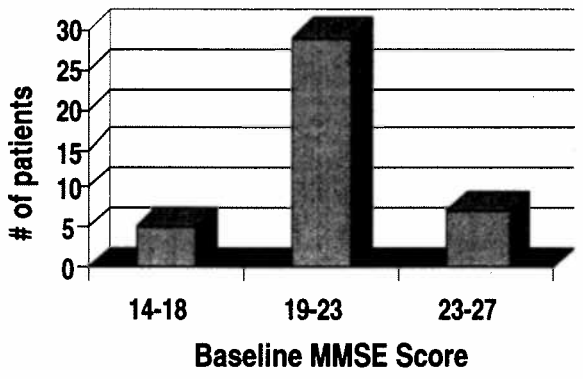

Table 1.— Responses to Donepezil

Duration of donepezil therapy	Mean Baseline MMSE score	Post intervention MMSE score
3 months- All subjects (15)	20.4 ± 3.6	21.7 ± 4.1
Responders (11)	20.8 ± 3.0	23.2 ± 3.5
Non responders(4)	19.0 ± 4.5	16.0 ± 3.7
6 months- All subjects (11)	22.3 ± 1.9	22.7 ± 4.1
Responders (8)	22.0 ± 2.1	24.5 ± 3.7
Non responders (3)	22.7 ± 1.2	19.0 ± 0.8
9 months- All subjects (12)	22.3 ± 2.9	22.2 ± 4.09
Responders (8)	22.5 ± 2.2	24.4 ± 2.5
Non responders (4)	22.0 ± 3.9	17.8 ± 2.9

Figure 2.— Trends in MMSE with Donepezil therapy over 9 months

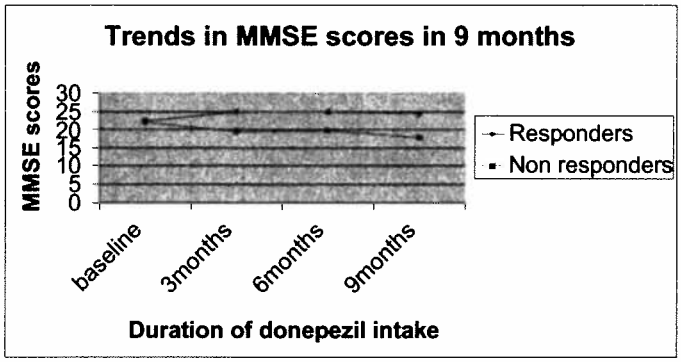

Table 2.— Side effects of Donepezil in this study

Side Effect	Number
Agitation	3
Gross Weight Loss	2
Visual Hallucination	1
Vomiting	1
Diarrhea	1
Severe Depression	1
Insomnia	1

Table 3.— Reasons for discontinuation of Donepezil treatment

Reasons	1mo	3 mo	6 mo
Due to side effects	2	3	3
Family's wishes	-	3	-
Unknown	1	1	1
No Cogn Improvement	-	2	
Cognitive Decline	-	1	1
Non-compliance	-	1	-

Discussion

To our knowledge, this is the first study which assesses and compares the effectiveness of donepezil in different ethnic groups. The results presented herein, demonstrate that donepezil appears to be clinically effective in patients of different ethnicities with mild to moderate Alzheimer's disease, even at advanced age. MMSE scores improved (> +2)or did not change (±2) from baseline in 66% of subjects in this study. Donepezil was well tolerated and continued for at least 6 months in 56% of subjects in this study.

Previously published trials utilized ADAS-cog, CIBIC plus, MMSE, CDS-SB, and IDDD to measure efficacy of donepezil.[10,11] However , the Folstein Mini Mental Status Examination is the most commonly used tool in clinical practice. This paper suggests the likely impact of donepezil on Folstein scores in patients with mild to moderate Alzheimer's disease. Age does not appear to be a factor in its effectiveness.

The limitations of this study includes its retrospective nature, different periods of follow up and the lack of a control group of untreated subjects.

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