Examining Anti-Dementia Drug Persistence in Alzheimer's Disease

Julia Biernot, MD[1]; Eveleen Darby, MA[2], MS; Wenyaw Chan, PhD[4]; Valory Pavlik, MD, PhD[3]; Rachelle Doody, MD, PhD[2]
[1] Illinios Neurological Institute, OSF, University of Illinois College of Medicine at Peoria, Peoria, IL
[2] Neurology and [3]Family and Community Medicine, Baylor College of Medicine, Houston, TX
[4] University of Texas Health Science Center, Houston TX

Background

- Cholinesterase inhibitors (ChI) and Memantine (Mem) are currently the only FDA approved medications for the treatment of AD.
- Medication persistence is defined as the act of continuing a treatment, or "duration of time from initiation to discontinuation" of therapy[1].
- Persistent treatment with anti-dementia medications, independently and in combination, is associated with a slower rate of cognitive and functional decline[2,3] and less likelihood of nursing home placement[4,5].
- Discontinuation of ChI has been linked to worsening of cognitive and behavioral symptoms[6].
- Persistence with ChI has been reported to be between 40 and 54%[7].
- Adherence to anti-dementia medications has been shown to be positively associated with increasing age, male gender, and higher pill burden[8].
- Individual patient characteristics that may account for discontinuation versus persistence have not been extensively studied.

Objectives

- To describe patient persistence with anti-dementia medications in an academic Alzheimer's Disease (AD) center and to determine demographic and neuropsychological patient characteristics associated with persistence.

Methods

- 1106 consecutive patients who were followed longitudinally at Baylor College of Medicine Alzheimer's Disease and Memory Disorders Center met NINCDS-ADRDA[9] criteria for Probable AD. Longitudinal data was collected in a database which was approved by the IRB. Subjects with at least one annual follow-up visit were selected.
- Cumulative anti-dementia medication use was established from a patient's time of initial symptoms[10], onward. Start and end dates of (a) medication(s) initiated prior to the new patient visit (NPV), if applicable, were recorded by a neurologist at the NPV based on information obtained from the patient, family members or pharmacy records, and review of the patient's medical record. Information on subsequent initiations and discontinuations was updated at all follow-up visits.
- If a discontinuation occurred prior or after the NPV, efforts were made to re-start medications at a subsequent clinic visit, whenever possible
- Start and stop dates for all anti-dementia medications were recorded in an electronic database. A total of 1073 patients had complete information regarding anti-dementia medication use. 33 patients were excluded from the analysis because of incomplete data.
- 5 groups of patients were examined: those who never took anti-dementia medications; those who started (a) medication(s) before the NPV and discontinued the medication(s) at least once; those who started (a) medication before or after the NPV and persisted; and those who started after the NPV and discontinued at least one time.
- Because the 5 groups had unbalanced numbers of patients, they were further subdivided into persistent (start and no discontinuation(s)) and impersistent (start and one or more discontinuation(s)) anti-dementia medication users.
- The two groups were compared based on age, sex, years of education, physician's estimate of duration of symptoms, pre-morbid IQ, preprogression rate, and Mini-Mental State Examination (MMSE). Preprogression rate was also calculated as follows: Expected MMSE score (30)-MMSE at symptom onset/ physician's estimate of duration (yrs) of symptoms at baseline. Averages of the scores for the two groups were calculated and a t test (continuous variable) or a Fisher exact test (binary variable) was done to assess for differences between groups.

Results

Table 1: 5 groups of patients based on medication usage

AD clinic patient groups	Number
Total number of patients	1073
No medications initiated	69
Start before NPV, perist	425
Start after NPV, persist	369
Start before NPV, ≥1 dicontinuation	115
Start after NPV, ≥ 1 dicontinuation	95

Table 2: Effect of demographic and neuropsychological factors on persistence

Variable	Persistent Medication Use	Total (n)	Mean	SD	95%CI	p
Age (at NPV)	Yes	794	73.62	8.60	71.76	0.29
	No	210	72.92	8.50	73.02	
Sex (M/F)	Yes	794	259/535 (0.48)			0.41
	No	210	75/135 (0.56)			
Education (yrs)	Yes	792	14.10	3.50	13.85	0.23
	No	210	13.78	3.30	13.32	
Disease duration	Yes	794	3.76	2.15	3.61	0.82
	No	210	3.80	2.13	3.51	
Estimated pre-morbid IQ	Yes	648	109.1	10.32	108.3	0.16
	No	161	107.8	9.87	106.2	
Pre-progression rate (30-mmse)/duration of symptoms at baseline	Yes	790	3.15	2.50	2.98	0.06
	No	207	3.57	2.97	3.16	
MMSE	Yes	790	20.33	6.43	19.89	0.03
	No	207	19.20	6.80	18.27	

Results

- Of 1004 patients who were treated with anti-dementia medications in an AD clinic, 54% started treatment prior to the NPV, and 46% started treatment after the NPV
- 794 patients (79%) persisted with medications, and 210 (21%) patients were impersistent
- Mini-mental status examination scores at first visit were slightly higher in persistent users (1.13±6.51, p=0.03)
- The groups were otherwise comparable with respect to age, gender, education, estimated pre-morbid IQ, pre-progression, and physician's estimate of disease duration.

Conclusion

- Persistence (79%) with anti-dementia drug treatment was higher than previously reported (40-54%)
- Contrary to prior reports, no significant difference in age or gender was found to be associated with persistence
- A trend towards higher MMSE scores in persistent users is consistent with previous findings that persistence with medications is associated with slower decline, but may also indicate that those with higher cognitive scores are more likely to persist with medications
- No other demonstrated demographic or disease characteristics explained differences in persistence
- This suggests that social factors and/or perceived side effects may have accounted for impersistence

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