Exposure to Anti-dementia Drugs Slows Clinical Progression of Alzheimer’s Disease (AD)


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INTRODUCTION

Recent recommendations in the management of dementia published by the American Academy of Neurology advised that cholinesterase inhibitors (ChEI) should be standard of care for treatment of mild to moderate Alzheimer’s dementia (AD). This recommendation was made based on the fact that these drugs were associated with a significantly slower rate of decline in the cognitive measures and basic activities of daily living. Treatment did not influence the rate of decline in a measure of complex activities of daily living or global dementia rating. However, differences on these latter measures associated with the persistence of use at the first visit were retained even years later. The magnitude of the treatment effect was thought to be clinically significant. Each 10% increment in the PI was associated with an increase in MMSE score 0.5 points and slowed decline by 0.09 points/year; reduced ADAS score 0.6 points and slowed decline by 0.2 points/year; slowed decline on the BPSG by 0.2 points/year; reduced BDI-CR score 0.5 points and slowed decline by 0.08 points/year; reduced CDR-SB score 0.5 points; and reduced IADL score 0.5 points. (See graphs)

RESULTS

Benefits were seen on both cognitive and functional measures. There was significantly slower decline (with, without) adjustment as the MMSE (p<0.01, p<0.05), ADAS (p<0.01, p<0.05), BPSG (p<0.01, p<0.01), and CDR-SB (p<0.01, p<0.01) were taken. Each 10% increment in the persistency index (total PI): total years of drug use divided by the total years of disease symptoms. The magnitude of the treatment effect was thought to be clinically significant. Each 10% increment in the PI was associated with an increase in MMSE score 0.5 points and slowed decline by 0.09 points/year; reduced ADAS score 0.6 points and slowed decline by 0.2 points/year; slowed decline on the BPSG by 0.2 points/year; reduced BDI-CR score 0.5 points and slowed decline by 0.08 points/year; reduced CDR-SB score 0.5 points; and reduced IADL score 0.5 points. (See graphs)

CONCLUSIONS

• Significant benefits from persistent therapy were demonstrated in AD patients followed longitudinally in a clinical practice setting.

• Benefits were found even in those with advanced disease.

• This study suggests that patients who persistently use antideementia drugs derive cognitive and functional benefits compared to those who receive less persistent therapy.

METHODS

We prospectively evaluated 401 probable AD patients followed at our center over a 20-year period, many of whom remain in active follow-up. All members of this cohort agreed to participate in a database approved by the IRB at BCM that tracks the diagnosis of probable AD as part of a longitudinal follow-up study that examines the natural history of AD. A subset of patients followed longitudinally in a clinical practice setting.

The evaluation consisted of an interview, drug therapy, education, and an important covariate and were excluded from the analysis. All patients underwent an evaluation by a neurologist and completed a standardized dementia work-up. The duration of illness was carefully estimated by the physician at the new patient visit by a standardized procedure reported on the BPMSE by 0.2 points/year; reduced PSMS score 0.2 points and slowed decline by 0.09 points/year; reduced ADAS score 0.6 points and slowed decline by 0.2 points/year; slowed decline on the BPSG by 0.2 points/year; reduced BDI-CR score 0.5 points and slowed decline by 0.08 points/year; reduced CDR-SB score 0.5 points; and reduced IADL score 0.5 points. (See graphs)

At screening 59% at the cohort had expired and 46% were alive.

To assess whether greater cumulative exposure to anti-dementia drug then first symptom until death or censoring reduces progression of AD as measured by neuropsychological testing.