SHOULD AD APPROVED MEDICATIONS BE USED IN ADVANCED DEMENTIA? YES

Michael D. Geschwind, USA

One of the ever present questions for physicians who care for patients with advanced dementia is when or if to stop treatment(s). When are treatments no longer of benefit? In answering this question, we must determine whom we are benefiting – the patient, the family/caregivers, or both. This also must be weighed against the cost of these medicines to the healthcare system and society. In the United States, only donepezil and memantine are approved by the US Food & Drug Administration for treatment of moderate to severe dementia. In the UK, one study suggested that it was not cost-effective to prescribe donepezil in advanced dementia, but this does not tell the whole story.

Studies have shown that the major cost for caring for patients with dementia occurs in the last few months and years of life. Although much of this caring occurs from inpatient hospitalization for treatment of conditions associated with end of life issues, much of the burden, in time and behavior management is on caregivers. Although AD-approved medications were largely approved for their cognitive benefits, there are also benefits in terms of improved behavior, reduced caregiver burden, longer time to requiring nursing care, delayed time to nursing home placement and others. One large study, however, showed that persistent treatment with acetylcholinesterase inhibitors or memantine slowed progression AD in multiple cognitive, functional, and global outcome measures, even in those with advanced disease. In a sub-analysis of a placebo-controlled trial of donepezil in moderate to severe AD, donepezil lead to significant improvement in several behaviors including, depression/dysphoria, anxiety, irritability and apathy/indifference. A study of memantine or placebo added to donepezil in moderate to severe AD showed that memantine added to donepezil led improvement on measures of cognition, activities of daily living, global outcome, and behavior. Memantine has also been shown to decrease caregiver burden in moderate to severe AD, in part by improving patient's behavior and thereby decreasing the amount of time the caregiver needs to spend caring for the patient. AD-approved therapies, particularly combination therapy, have been shown in several studies to delay disease progression, even in advanced AD. Importantly, making a patient less agitated or irritable through AD-approved medications might lead to improved quality of life for the patient, something which might not be easily measured by a patient scale due to their dementia, as well as for the caregiver. Regarding the cognitive effects of these medicines, the argument might be made that improving someone with moderate to severe dementia by a few points on the MMSE might not be clinically meaningful, on the other hand, allowing a patient to interact slightly more with their loved ones, might have a positive impact well beyond the few points changed on MMSE.

Importantly, randomized controlled trials, while certainly informative, do not always give a real-world clinical picture, as they only enroll highly-selected patients and follow them only for months. Long-term observational controlled studies (LTOCs), however, study patients in the real-world over years, and thus may provide perhaps more realistic, practical data. LTOCs often have shown AD-combination therapy to be superior to AD-monotherapy, which in turn is superior to placebo in terms of reduced cognitive and functional decline and delayed time to nursing home admission.

In summary, although the cognitive benefits of AD-approved medications might be modest, particularly in moderate to severe AD, the data suggests that there are significant other benefits to the patients, families and society for treating patients with moderate to severe AD.