# Combining Alzheimer’s Drugs May Offer Sustained Benefits

Physicians often prescribe an Alzheimer’s drug for patients newly diagnosed with the disease. A new study shows that combining two kinds of Alzheimer’s drugs may provide the greatest benefits in helping to delay the progression of symptoms.

Alzheimer’s drugs like Aricept, Exelon and Razadyne were approved by the Food and Drug Administration in the 1990s to treat early to mid-stage Alzheimer’s disease. These medications are known as cholinesterase inhibitors, because they slow the breakdown of a brain chemical called acetylcholine that aids memory.

More recently, in 2003, the drug memantine, sold under the brand name Namenda, was approved for the more advanced stages of Alzheimer’s. It is sometimes prescribed in combination with one of the older drugs. Namenda works in a different way than those drugs, shielding brain cells from the effects of overexposure to a chemical called glutamate. Excess levels of glutamate are thought contribute to the death of brain cells in people with Alzheimer's.

"There has been the impression that these drugs only work for some patients and for a limited amount of time," said Dr. Alireza Atri of the Massachusetts General Hospital Department of Neurology, lead author of the current study. "One of the problems in judging these drugs has been that patients naturally continue to decline, which can make them think the drugs have stopped working. But our study, which has some unique strengths, indicates that treatment does have long-term benefit."

In the study, researchers at the Massachusetts General Hospital Memory Disorders Unit in Boston analyzed the records of 382 patients who were treated at the clinic from 1990 to 2005. One group of 144 patients did not receive any medication. A second group got a cholinesterase inhibitor, while a third group took that drug plus Namenda. Patients were then given tests of memory and thinking and the ability to carry out everyday tasks every six months.

"Clinical trials that drug companies conduct for FDA approval may only last six months and enroll patients according to very specific criteria," Dr. Atri explained. "Only large-population studies can really tell us how these drugs work for the full range of patients in real-life situations." The current study lasted for two and a half years.

The results showed significant differences in the rate of symptom progression among all three groups – with the smallest level of decline in those receiving combination therapy.

The researchers also found that the longer patients took these drugs, the greater the differences observed between those not taking drugs and those taking the drugs — especially in those taking the combination of cholinesterase inhibitor and Namenda.

"Finding something that could actually modify the course of the disease is the Holy Grail of Alzheimer's treatment, but we really don't know if that is happening or what the mechanism behind these effects might be," Dr. Atri explained. "What we can say now is that providers should help patients understand that the benefits of these drugs are long term and may not be apparent in the first months of treatment. Even if a patient's symptoms get worse, that doesn't mean the drug isn't working, since the decline probably would have been much greater without therapy."

Dr. John Growdon, professor of Neurology at Harvard Medical School and senior author of the paper, added that the study results, if confirmed, could change the way that doctors prescribe Alzheimer's drugs. "Cholinesterase inhibitors are approved for use in mild to moderate dementia, while memantine has been approved for advanced dementia," he said "But it looks like there is an advantage in prescribing both drugs as initial treatment."

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By www.ALZinfo.org. Reviewed by William J. Netzer, Ph.D., Fisher Center for Alzheimer's Research Foundation at The Rockefeller University

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