PATIENT PAGE

Can naproxen slow the progression of Alzheimer disease?

Steven Karceski, MD

Neurology® 2019;92:e2181-e2184. doi:10.1212/WNL.0000000000007418

In their study "INTREPAD: A randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease," Dr. Meyer and colleagues[1] studied how naproxen—a common over-the-counter medicine—could help to prevent the progression of Alzheimer disease (AD). The reason for this is that there have been several observational studies that suggest that nonsteroidal anti-inflammatory drugs (NSAIDs) can prevent people from developing AD. Other studies have not shown this effect. In fact, other studies have shown that long-term use of NSAIDs not only is not helpful for AD, but causes side effects.

It was because of this that Dr. Meyer developed the Investigation of Naproxen Treatment Effects in Pre-symptomatic Alzheimer's Disease (INTREPAD) study. The primary difference between prior studies and INTREPAD is that INTREPAD is a randomized study. In INTREPAD, participants were assigned to 1 of 2 groups. They either took naproxen or they took placebo. People were followed for 2 years, and the effect of naproxen was carefully measured. In addition, Dr. Meyer evaluated how safe it was to take naproxen daily. In short, he looked at both the risks and the benefits of taking this medication.

RELATED ARTICLE

Article
INTREPAD: A randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease
Page 835

How was the study done?

The study involved 462 healthy adults over age 55. All had a family history of AD (either in 1 parent or 2 siblings). When they entered the trial, none of them had problems with thinking. The investigators determined this through interviews as well as using scales that assess cognitive function. The 2 scales they used were the Montreal Cognitive Assessment and the Clinical Dementia Rating scale. Of the healthy 462 people, a total of 195 were randomized to either naproxen or placebo. A total of 102 took naproxen and 93 took placebo.

During the 2-year study, the patients underwent extensive medical testing. The tests were performed at the beginning of the study, and were repeated at 3 months, 12 months, and 24 months of participation. Patients had 2 kinds of MRI: one that looked at the structure of the brain and another that measured certain brain functions (functional MRI). Each person had neuropsychological testing called RBANS. This test measures immediate memory, delayed memory, attention, language, and visuospatial abilities. A total of 93 of the participants agreed to also have lumbar punctures at each of these time points. The CSF was analyzed for specific proteins that have been found in high concentrations in people with AD.

What were the results?

First, Dr. Meyer evaluated the safety of taking naproxen over a 2-year period. More people reported side effects in the naproxen group than in the placebo group. The most common side effects were stomach upset, constipation, and shortness of breath. Ten people

reported serious side effects. Of these, 8 were taking naproxen. In these people, the drug was stopped.

Although it may have caused side effects, did naproxen help? The results of the various tests were combined. The composite score, called the AD Progression Score (APS), was used to measure the difference between the 2 groups. The study showed that there was no difference in the APS between the 2 groups. In other words, naproxen was no different from placebo in slowing the progression of AD.

What does this mean?

Studies like this are considered Class I. What this means is that participants are randomized to 1 of 2 groups. People in the study do not know if they are taking a study drug or if they are taking a placebo (sugar pill). Further, the doctors who follow the participants do not know to which group they have been assigned. In this way, errors are eliminated. These kinds of studies are considered the most rigorous. Results of these studies are highly regarded.

PATIENT PAGE

About Alzheimer disease

Steven Karceski, MD

Neurology® 2019;92:e2181-e2184. doi:10.1212/WNL.0000000000007418

Adapted from: Doria J, Karceski S. About Alzheimer disease. Neurology 2019;92:e1003–e1006. doi: 10.1212/WNL.0000000000006997

What is Alzheimer disease (AD)?

AD is a neurologic disease that affects the brain very gradually. One of the more common symptoms is a slow worsening of memory, especially short-term memory. For instance, a person with AD may recall childhood memories well (long-term memory), but have trouble recalling what he or she had for breakfast (short-term memory). Other problems include problems with language, like trying to find the right word to say. In some people with AD, there are gradual changes in mood or behavior. For instance, a person who is usually calm may become more easily angered. The loss of neurologic function often occurs very slowly over 5–20 years. At some point, if the disease becomes severe, a person with AD will need help with daily tasks such as eating, grooming, and proper hygiene. In its more severe stages, AD affects both the patient and the people around the patient.

About 5.5 million Americans have AD. It is estimated that more than 360,000 new cases occur each year. This number will probably increase as the population ages because aging itself is a major risk factor for the development of AD. AD is the sixth leading cause of death for adults. It kills more than 100,000 Americans each year.[2]

What are the symptoms?

Loss of recent memories (also called short-term memory) is usually the earliest warning. For instance, the person will repeat stories in the same conversation. People with AD may forget the details of the previous day. For instance, they may not recall what they had for lunch, or they cannot recall the details of a movie they recently watched. Other features include misplacing belongings or difficulty doing familiar tasks. They might have trouble finding the right words to say and may not follow the details of long conversations. For some people, there can be changes in mood, behavior, or personality.

Because AD is so gradual, in its early stages, many people fail to recognize that something is wrong. They may assume that such behavior is a normal part of getting older: "just a senior moment." Although forgetting things is common, if it is something that is getting worse, it may be a sign of a more serious problem. The key to treatment of AD is early diagnosis. It is critical to see a doctor when one recognizes or suspects AD symptoms.

How is AD diagnosed?

When AD is suspected, it is important to have a complete medical and neurologic workup. In the first doctor's visit, a detailed history and examination is needed. Often, blood tests are ordered, and brain imaging studies are requested (like MRI).

What causes AD?

The cause of AD is not fully known. It is not contagious. Although genetic forms have been identified, the most common form of AD does not run in families.

What are the treatments?

Although there is currently no cure for AD, there are treatments that may help the symptoms of AD.

Memory symptoms

The cognitive symptoms of AD should be treated as early as possible to slow the progression of the disease. Drugs called cholinesterase inhibitors may be considered in people with mild to moderate disease. Vitamin E may also slow progression, but should only be used if prescribed by the doctor.

Behavioral problems

Suspiciousness, aggression, or resistance to care may be treated first by understanding what triggers these behaviors. Caregivers may learn how to change things in the environment to avoid or minimize these triggers. Some examples include providing low lighting and music to improve eating, taking regular walks, scheduling toileting, and following consistent routines. Sometimes medications are needed to help with problems with mood, like depression.

Ongoing research suggests many ways to keep your brain healthy:

Avoid harmful substances: alcohol and drugs should be avoided. In certain situations, these substances can cause damage to brain cells.

Challenge yourself: read frequently, do crossword puzzles, play games that constantly challenge the mind. In short, keep mentally active. Learn new skills. This strengthens brain connections and promotes new ones. One way of thinking about this is that a person needs to exercise the mind as well as the body.

Exercise regularly: even low to moderate level activity such as walking or gardening 3 to 5 times per week can be effective. A combination of both physical and mental exercise goes a long way to preventing the problems due to AD.

Stay socially active: stay in contact with family, friends, church, and the community. Social interactions challenge our brains and contribute to better brain health.

Caregiver health: Caregivers need caring too

Families and friends need to recognize that AD affects not only the patient, but also the caregiver. To take the best care of the patient with AD, the primary caregiver must take care of himself or herself. The caregiver should be encouraged to learn more about the disease, and seek support from family, friends, and professionals.

For more information

Brain & Life
brainandlife.org

Alzheimer's Association
alz.org

Family Caregiver Alliance
caregiver.org

References

1. Meyer PF, Tremblay-Mercier J, Leoutsakos JM, et al. INTREPAD: a randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease. Neurology 2019; 92:e2070–e2080.
2. Alzheimer's Association. Available at: alz.org. Accessed December 10, 2018.

Can naproxen slow the progression of Alzheimer disease?

Steven Karceski and Steven Karceski

Neurology 2019;92;e2181-e2184
DOI 10.1212/WNL.0000000000007418