NIH NEWS RELEASE

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12:01 a.m. EDT Friday, October 12, 2001

Antioxidant Vitamins and Zinc Reduce Risk of Vision Loss from Age-Related Macular Degeneration

Same Nutrients Have No Effect on the Development of Cataract

High levels of antioxidants and zinc significantly reduce the risk of advanced age-related macular degeneration (AMD) and its associated vision loss. These same nutrients had no significant effect on the development or progression of cataract. These findings from a nationwide clinical trial are reported in the October 2001 issue of Archives of Ophthalmology.

Scientists found that people at high risk of developing advanced stages of AMD, a leading cause of vision loss, lowered their risk by about 25 percent when treated with a high-dose combination of vitamin C, vitamin E, beta-carotene, and zinc. In the same high risk group -- which includes people with intermediate AMD, or advanced AMD in one eye but not the other eye -- the nutrients reduced the risk of vision loss caused by advanced AMD by about 19 percent. For those study participants who had either no AMD or early AMD, the nutrients did not provide an apparent benefit. The clinical trial -- called the Age-Related Eye Disease Study (AREDS) -- was sponsored by the National Eye Institute (NEI), one of the Federal government's National Institutes of Health.

"This is an exciting discovery because, for people at high risk for developing advanced AMD, these nutrients are the first effective treatment to slow the progression of the disease," said Paul A. Sieving, M.D., Ph.D., director of the NEI. "AMD is a leading cause of visual impairment and blindness in Americans 65 years of age and older. Currently, treatment for advanced AMD is quite limited. These nutrients will delay the progression to advanced AMD in people who are at high risk -- those with intermediate AMD in one or both eyes, or those with advanced AMD in one eye already.

"The nutrients are not a cure for AMD, nor will they restore vision already lost from the disease," Dr. Sieving said. "But they will play a key role in helping people at high risk for developing advanced AMD keep their vision."

A common feature of AMD is the presence of drusen, which are yellow deposits under the retina. Often found in people over age 60, drusen can be seen by an eye care professional during an eye exam in which the pupils are dilated. Drusen by themselves do not usually cause vision loss, but an increase in their size and/or number increases a person's risk of developing advanced AMD, which can cause serious vision loss.

The three stages of AMD analyzed in this study are:

1. *Early AMD.* People with early AMD have, in one or both eyes, either several small drusen or a few medium-sized drusen; these people do not have vision loss from AMD.
2. *Intermediate AMD.* People with intermediate AMD have, in one or both eyes, either many medium-sized drusen or one or more large drusen; in these people, there is usually little or no vision loss.
3. *Advanced AMD.* In addition to drusen, people with advanced AMD have, in one or both eyes, either:
    - A breakdown of light-sensitive cells and supporting tissue in the central retinal area (advanced dry form); or
    - Abnormal and fragile blood vessels under the retina that can leak fluid or bleed (wet form).

These two forms of advanced AMD can cause serious vision loss. Scientists are unsure about how or why an increase in the size and/or number of drusen can sometimes lead to advanced AMD, which affects the sharp, central vision required for the 'straight ahead' activities in our daily routine, such as reading, driving, and recognizing faces of friends. One observation is that the larger and more numerous the drusen, the higher the risk of developing either form of advanced AMD. People who have advanced AMD in one eye are at especially high risk of developing advanced AMD in the other eye. The formulation used in the study contained several antioxidant vitamins, which are nutrients that can help maintain healthy cells and tissues. They also contained zinc, which is an important mineral incorporated into many body tissues.

The nutrients evaluated by the AREDS researchers contained 500 milligrams of vitamin C; 400 international units of vitamin E; 15 milligrams of beta-carotene; 80 milligrams of zinc as zinc oxide; and two milligrams of copper as cupric oxide (Copper was added to the AREDS formulations containing zinc to prevent copper deficiency, which may be associated with high levels of zinc supplementation). In this trial, the NEI collaborated with Bausch & Lomb, an eye care company that provided the formulation evaluated by the AREDS researchers and financially supported the laboratory testing and distribution of study medications.

"Previous studies have suggested that people who have diets rich in green, leafy vegetables have a lower risk of developing AMD," said Frederick Ferris, MD, director of clinical research at the NEI and chairman of the AREDS. "However, the high levels of nutrients that were evaluated in the AREDS are very difficult to achieve from diet alone.

"Almost two-thirds of AREDS participants chose to take a daily multivitamin in addition to their assigned study treatment," Dr. Ferris said. "The AREDS also showed that, even with a daily multivitamin, people at high risk for developing advanced AMD can lower the risk of vision loss by adding a formulation with the same high levels of antioxidants and zinc used in the study."

The Age-Related Eye Disease Study involved 4,757 participants, 55-80 years of age, in 11 clinical centers nationwide. Participants in the study were given one of four treatments: 1) zinc alone; 2) antioxidants alone; 3) a combination of antioxidants and zinc; or 4) a placebo, a harmless substance that has no medical effect. The benefits of the nutrients were seen only in people who began the study at high risk for developing advanced AMD -- those with intermediate AMD, and those with advanced AMD in one eye only. In this group, those taking "antioxidants plus zinc" had the lowest risk of developing advanced stages of AMD and its accompanying visual loss. Those in

the "zinc alone" or "antioxidant alone" groups also reduced their risk of developing advanced AMD, but at more moderate rates compared to the "antioxidants plus zinc" group. Those in the placebo group had the highest risk of developing advanced AMD.

Dr. Ferris said some people with intermediate AMD may not wish to take large doses of antioxidant vitamins or zinc because of medical reasons. "For example, beta-carotene has been shown to increase the risk of lung cancer among smokers," he said. "These people may want to discuss with their primary care doctor the best combination of nutrients for them. With the use of the high levels of zinc, it is important to add appropriate amounts of copper to the diet to prevent copper deficiency."

In the cataract portion of the study, researchers discovered that the same nutrients had no significant effect on the development or progression of age-related cataract. A cataract is a clouding of the eye's lens that blocks some light from reaching the retina and interferes with vision. "Participants taking the 'zinc alone' treatment, the 'antioxidants alone' treatment, or the combination of zinc and antioxidants were all about as likely to develop a cataract as those taking a placebo," Dr. Ferris said.

"At the time the study was planned, laboratory and animal research had suggested that antioxidants might be of benefit in treating or preventing cataract," he said. "Also at that time, limited epidemiologic and clinical trial data suggested that antioxidants might affect the development of cataract. However, our analyses did not find any connection between the antioxidant vitamins used in the AREDS and cataract development."

Despite the evidence that these nutrients did not lower the risk of cataract development over the seven-year period of the study, Dr. Ferris noted that an effect over a longer period of time, or with different doses of these or other antioxidants, cannot be ruled out.

The AREDS participants reported few side effects from the treatments. About 7.5 percent of participants assigned to the zinc treatments -- compared with five percent who did not have zinc in their assigned treatment -- had urinary tract problems that required hospitalization. Participants in the two groups that took zinc also reported anemia at a slightly higher rate; however, testing of all patients for this disorder showed no difference among treatment groups. Yellowing of the skin, a well-known side effect of large doses of beta-carotene, was reported slightly more often by participants taking antioxidants.

"The AREDS formula is the first demonstrated treatment for people at high risk for developing advanced AMD," he said. "Slowing the progression of AMD to its advanced stage will save the vision of many who would otherwise have had serious vision impairment."

A list of studies centers is available.

The National Eye Institute (NEI) is part of the National Institutes of Health (NIH) and is the Federal government's lead agency for vision research. NEI-supported research leads to sight-saving treatments and plays a key role in reducing visual impairment and blindness. The NIH is an agency of the US Department of Health and Human Services.

We welcome your questions and comments. Please send general questions and comments to the NEI Office of Communication, Health Education,

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