Vitamin E Beneficial in Some Diabetes Patients

BY MITCHEL L. ZOLER
Philadelphia Bureau

ORLANDO — Vitamin E has fulfilled its promise as an antioxidant that can slow the progression of cardiovascular disease.

Patients with diabetes who also had the haptoglobin 2-2 genotype and who were treated with 400 IU of vitamin E daily for 18 months had about half the incidence of cardiovascular death, myocardial infarction, and stroke, compared with patients who received placebo in a study with 1,434 patients that was done in Israel, Dr. Shany Blum reported at the annual scientific sessions of the American Heart Association.

Further analysis showed that the benefit was concentrated in patients with poorly controlled diabetes—those with a hemoglobin A_{1c} (HbA_{1c}) level of at least 7.0%, said Dr. Blum, a cardiologist at the Technion-Israel Institute of Technology, Haifa.

Haptoglobin is an antioxidant protein that blocks hemoglobin-induced tissue oxidation. Humans have two different haptoglobin alleles, 1 and 2. The protein that's made in people who carry the Hp 1-1 or 2-1 genotype has normal antioxidant activity. The protein that's made in people who have an Hp 2-2 genotype is a much less effective antioxidant. The poor activity of the Hp 2-2 protein seems to be exacerbated when it tries to block glycosylated hemoglobin, Dr. Blum said in an interview. Vitamin E seems to supply the antioxidant activity that's missing in people with the Hp 2-2 genotype.

The genotype determines which diabetics are at greatest risk of developing vascular complications affecting the heart, kidney, and eyes.

Genotyping for the haptoglobin alleles is easily done. In the United States, the prevalence of the Hp 2-2 genotype is about 36% in both whites and African Americans. The prevalence is much higher in certain other populations, reaching about 85% in people of Southeast Asian ancestry, said Dr. Andrew P. Levy, also a cardiologist at the Technion-Israel Institute of Technology and the senior author of the study.

A simplified, inexpensive haptoglobin genotyping kit is being developed by a U.S. company, Synvista Therapeutics Inc. The current study was supported by the Kennedy Leigh Charitable Trust, London, and had no commercial funding. Dr. Levy is a consultant to Synvista Therapeutics.

The study enrolled 3,054 people with type 2 diabetes aged 55 or older who were patients in the primary health care clinics of the Clalit Health Services in Israel. All patients underwent haptoglobin genotyping, which identified 1,434 of the patients (47%) as carriers of the Hp 2-2 genotype. This subgroup was then randomized to receive 400 IU vitamin E daily or placebo, and the patients were followed for 18 months.

The patients who received vitamin E had a significantly lower incidence of cardiovascular death, myocardial infarction, and stroke. The event rate in the vitamin-E–treated patients was very similar to the event rate in the remaining 1,620 patients who had Hp 1-1 and Hp 2-1 genotypes and who received no investigational treatment.

A second analysis divided the Hp 2-2 patients based on their HbA_{1c} levels. Patients with an HbA_{1c} level of less than 7.0% who received vitamin E had about a 1.5% event rate. Patients with an HbA_{1c} level of less than 7.0% treated with placebo had an event rate of 3.4%. Among the patients with an HbA_{1c} level of 7.0% or greater, those treated with vitamin E had a 2.9% event rate, and those treated with placebo had a 6.2% event rate.

No interaction between HbA_{1c} levels and the rate of cardiovascular events was seen in the patients with the Hp 1-1 and Hp 2-1 genotypes, Dr. Blum said. Results from other studies also have shown no relationship between haptoglobin genotypes and cardiovascular risk in people without diabetes. However, patients with type 1 diabetes seem to behave the same way as the type 2 patients in the current study, Dr. Levy said.

A similar, larger study that is being planned will enroll patients entirely in the United States, Dr. Levy said in an interview. He also noted that the haptoglobin genotype has no relationship to the risk of developing diabetes. The genotype determines only which individuals with diabetes are at greatest risk of developing vascular complications affecting the heart, kidney, and eyes. ■

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