Investigation Of Vitamin E In Alzheimer's Disease

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A. Statement of Study and Purpose Rationale

Alzheimer's disease is one of the most common forms of dementia, affecting approximately 11% of the population between 75 and 85. The pathology of AD may involve increased oxidative stress due to aging, resulting in an increased production of free radicals. Accumulation of free radicals has been postulated to cause the neuronal degeneration of the brain in AD patients. Vitamin E is a lipid-soluble vitamin that protects cell membranes from oxidative damage. Animal experiments have shown enhanced recovery of spinal cord injury in subjects taking supplemental vitamin E. The present study will attempt to show the potential efficacy of vitamin E on slowing the cognitive deterioration of Alzheimer's disease.

B. Study Design

This will be a multi-center, double-blind, placebo-controlled, parallel group design study. Patient selection will focus on male and female subjects between the ages of 55 and 85 years of age, from the current AD registry of each testing center. To be eligible for inclusion in the trial, patients were required to have a Mini-Mental Examination score between 10 and 26, and a Clinical Dementia Rating of 1. All patients must be fully ambulatory and have vision and hearing sufficient for compliance with testing procedures. Patients with evidence of other psychiatric or neurologic disorders, as well as those with significant gastrointestinal, renal, hepatic, endocrine, or cardiovascular diseases will be excluded from entering the trial. Patients with vitamin B 12 or folate deficiency, as well as those with current anticoagulant, alcohol or illicit drug use will also be excluded. At the time of enrollment, informed consent will be obtained from each patient or family member. All patients will be free of multivitamin and/or vitamin E supplements.

The patients will be randomly assigned to either treatment or placebo group and stratified by MMSE results. Racemic dl-alpha-tocopherol (vitamin E) will be given in a dose of 1000 IU BID. Patients will be assessed at a screening visit, at baseline, and 1, 4, 7, 10, and 13 months thereafter. At each visit, patients will be examined, vitals will be taken, routine bloodwork will be drawn (CBC, chem-7, liver panel, renal panel). Patients will then undergo a Mini-mental Examination and the Alzheimer's Disease Assessment Scale. Efficacy of the treatment will be based on the net change in score from baseline vs. end of study.

C. Statistical Analysis

Study size of 140 participants is intende d to achieve 80% power to detect a 2.5 point improvement in ADAS with $p < 0.05$ for vitamin E treatment compared to placebo. Analysis will be performed on an intention to treat population, which will include all patients who are randomly assigned to treatment, receiving at least one dose of study drug and at least one post baseline evaluation. Continuous variables will be examined by analysis of variance model and categorical variables will be analyzed by the Cochran Mantel-Haentzel test. Analysis of covariance will be used to examine the differences in efficacy measures across the two treatment groups. The primary efficacy parameters will be the change from baseline score for the ADAS and Mini-Mental examinations.

D. Study Procedures

Cognitive function testing will occur at baseline, months 1, 4, 7, 10, and 13. Testing will include the Alzheimer Disease Assessment Scale (cognitive section) and MiniMental Examination, to be performed by highly trained staff. Scores will be recorded at each visit. Special consideration will be given to data collection via telephone, due to the nature of the disease.

E. Study Drugs

Racemic dl-alpha tocopherol in dosage of 1000 IU will be given twice daily by mouth. Known side effects include hepatotoxicity, ascites, 'questionable increased risk of thrombophlebitis, and potentiation of anticoagulation medication.

F. Medical Devices

No medical devices will be used during, the study.

G. Study Questionnaires

Alzheimer's Disease Assessment Scale, Mini-Mental Status Examination, and Clinical Dementia Rating will be used during the study. (Refer to Appendix)

H. Description of Study Subjects and Method of Recruitment

Subjects diagnosed with Alzheimer's disease, who are currently seeking care at the participating centers will be recruited into the study. Subjects will be between the ages of 55 and 85, male or female, with an effort to recruit minority patients. In addition, a nationwide publicity campaign using public service forums will assist sites in attracting subjects.

a. Inclusion Criteria

1 Ages 55-85
2 Fully ambulatory with sufficient vision and hearing to participate in test procedures.
3 Mini-Mental status score of 10-26
4 Clinical Dementia Rating of 1

b. Exclusion Criteria

1 Other psycho-neurological disorders
2 Renal, hepatic, oncologic diseases.
3 Endocrine disorders, including thyroid and diabetes.
4 Vitamin B 12 or folate deficiency
5 Alcohol or drug abuse
6 Vitamin E or multi-vitamin supplementation with 3 weeks of the study.
7 Use of anti-coagulation medications. Confidentiality of Study Data:

All written data obtained during the study will be uniquely coded for each individual. This data will only be known to the investigators and will not be released to any other individual or institution. Results will be printed as aggregate data without individual identification.

I. Location of Study

The study will be conducted at the Neurology clinic in the Atchley Pavilion. Subjects will also be studied at participating medical centers.

J. Risks and Benefits

The anticipated benefits to the patient and the general public is an effective and safe treatment in slowing the cognitive deterioration associated with Alzheimer's disease. At present, alternative treatment options include cholinergic agonists, monoamine oxidase-B inhibitors, cholinesterase inhibitors, anti-inflammatory agents, and psychosocial interventions.

K. Compensation and Costs to Subjects

Patients who consent to participate in this study will not be offered any compensation for their involvement. No financial cost to the participant is expected except for transportation. Patients will receive the study drug free of charge.

L. Minors and Research Subjects

There will be no minors participating in this study.

M. Radiation or Radioactive Substances

There will be neither radiation nor radioactive substances used in this study.