Treatment of psychosis and agitation in Alzheimers disease

https://neurodegenerationresearch.eu/survey/treatment-of-psychosis-and-agitation-in-alzheimers-disease/

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Country

USA

Title of project or programme

Treatment of psychosis and agitation in Alzheimers disease

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NIH (NIA)

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Start date of award

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Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Mental Health... Mental Illness... Neurodegenerative... Neurosciences... Precision Medicine... Serious Mental Illness... Translational Research... Violence for Violence Against Women Subset... Violence for Youth Violence Subset

Research Abstract

DESCRIPTION (provided by applicant): Symptoms of agitation/aggression and psychosis commonly occur in patients with Alzheimer’s disease (AD), are distressing to patients and caregivers, often lead to institutionalization, are associated with increased mortality and financil burden to the healthcare system, and are very difficult to treat. Among the psychotropic medications, antipsychotics show superiority to placebo in randomized, double-blind, placebo-controlled trials in dementia, albeit with small to medium effect sizes. Antipsychotic side effects including the increased risk of mortality that led to an FDA black box warning, suggest that other treatments need to be evaluated. Our initial open treatment pilot data demonstrated that patients with AD who showed no response or partial response to antipsychotics improved on lithium, supporting the systematic study of lithium treatment for agitation/aggression with or without psychosis in AD. Low doses of lithium (150-600 mg daily) with low blood levels (0.2-0.6 mmol/l) are tolerated well in elderly patients with dementia. Our innovative project will examine, for the first time, the efficacy and side effects of low dose lithium treatment of agitation/aggression with or without psychosis in 80 patients with AD in a randomized, double-blind, placebo-controlled, 12-week trial. The results will determine the potential for a large-scal clinical trial to establish the utility of lithium in these patients. The primary hypothesis is tha the agitation/aggression domain score on the Neuropsychiatric Inventory (NPI) will decrease significantly more on lithium than placebo. The secondary hypothesis is that the proportion of responders on lithium will be significantly greater than the proportion of responders on placebo. The exploratory hypothesis is that the psychosis score, measured by the sum of the NPI domains for delusions and hallucinations, will decrease significantly more on lithium than placebo. We will also evaluate tolerability by assessing emergent somatic side effects over the course of the trial on lithium compared to placebo. We will evaluate plasma brain-derived neurotrophic factor (BDNF) at baseline and 12 weeks, a SNP on intron 1 of the ACCN1 gene, and the 7q11.2 gene locus, and examine whether these indices can predict lithium response with the goal of improving patient selection for clinical trials and eventually personalized treatment. Change over time in BDNF levels will be examined as a biomarker correlate of lithium treatment. Our study will provide initial data on three potential roles for low-dose lithiu treatment if it is found to be effective and safe (these roles are not mutually exclusive) in clinial practice: (1) first-line treatment; (2) adjunct treatment to antipsychotics in partial responders; 3) second-line agent after antipsychotic non-response or intolerability. If positive effects in the piot trial are confirmed in a large-scale trial there is considerable potential to markedly alter clinicl practice to benefit these patients in the United States and around the world.

Lay Summary

PUBLIC HEALTH RELEVANCE: Patients with Alzheimer’s Disease (AD) frequently develop psychosis and/or agitation/aggression; these symptoms are very difficult to treat and often lead to institutionalization. The efficacy and side effects of low dose lithium treatment of agitation/aggression with or without psychosis in 80 patients with AD will be examined in a

randomized, double-blind, placebo-controlled, 12-week trial. The results will determine the potential for a large-scale clinical trial to establish the utility of lithium in these patients. I low-dose lithium proves to be superior in efficacy to placebo without a significant increase in side effects, this will be very important in addressing this widespread clinical problem that broadly impacts health care.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A