A Clinical Precision Medicine Approach Reduces Alzheimer’s, Dementia and Vascular Risk and Improves Cognition: A Prospective Cohort Study from the Alzheimer’s Prevention Clinic at Weill Cornell Medicine and NewYork-Presbyterian

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Objectives

Our primary outcome measure was change in six AD, dementia, and vascular risk scales in response to multi-modal interventions. Secondary outcome measures include overall and differential effectiveness of interventions on blood biomarkers and cognition (based on genotype and physician & patient-reported adherence).

Background

The Alzheimer’s Prevention Clinic provides direct clinical care to patients who receive evidence-based, individualized early interventions applying principles of pharmacogenomics, nutrigenomics and clinical precision medicine.

Study Design & Participants

This prospective cohort study includes patients with family history of AD and no or minimal cognitive complaints, and preclinical AD or MCI. 168 participants met inclusion criteria (mean age 63 ±14.6, 50.6% female). Using SPSS, paired sample t-tests were computed to compare changes in risk scales in subjects with blood biomarker data at baseline and six-months. Changes in blood biomarkers were compared using ANOVA within and across different genotype and adherence groups. Multiple repeated-measured general linear models were computed to compare changes in cognition per genotype and adherence. NIH Toolbox cognitive scores were corrected for age, gender, ethnicity, and education to account for multiple comparisons across groups.

Cognition: Tests of learning, memory, executive function and language improved in participants who completed cognitive assessments at baseline and 6 months (n=120).

Blood biomarkers: A host of blood biomarkers significantly improved in participants who completed labs at baseline and 6 months (n=142) see those with * in table on the right

Adherence: Higher patient-reported adherence resulted in significant changes in 9 additional blood biomarkers (20) than lower adherence (11), however there was no difference in physician-reported higher vs. lower adherence groups.

Conclusion

These data suggest a clinical precision medicine approach toward AD prevention reduces AD, dementia and vascular risk and improves cognition. Differential effects were observed based on genotype and adherence. These results are encouraging and warrant further evaluation via randomized trial utilizing AD-specific biomarkers pre vs. post-intervention.

Overall Results

Risk Scales: After 6 months, improvements were observed in all risk scales (CAIDE Midlife, p=.046; MLDR, p=.006; LDRI, p=.001; MAYO MCI, p<.001; Late-onset AD, p=.001; ANU-ADRI, p<.001).

Change in Risk Scales

Change in Cognitive Assessment

Change in Blood Biomarkers & Cognition Mediated by ApoE and MTHFR Status

Mediation by genotype: Stratification by APOE and MTHFR genotypes resulted in variations in response to a host of blood biomarkers and cognitive tests.

Results by Genotype

Conclusion

These data suggest a clinical precision medicine approach toward AD prevention reduces AD, dementia and vascular risk and improves cognition. Differential effects were observed based on genotype and adherence. These results are encouraging and warrant further evaluation via randomized trial utilizing AD-specific biomarkers pre vs. post-intervention.

Baseline vs 6 months changes in measures: Indicate improvements in tests and scores across cognitive, behavioral, and lifestyle measures at the six-month mark vs. baseline.

Clinical assessment

• Present with neurologist & neurological exam
• Anthropometrics: vital signs/biometric assessment
• Laboratory measures: blood biomarkers and genetics

Cognitive assessment

• Traditional tests: MMSE; FAS; ANT; Trails B; Boston Naming
• NIHTB-C8 tests: RAVLT Auditory Verbal Learning (Trials 1-3); RAVLT Delayed Recall & Recognition; Dimensional Change Card Sort (DOCS); Flanker Inhibitory Control and Attention; Pattern Comparison Process Speed; Odor Identification; Oral Symbol Digit (OSD); Picture Vocabulary; Oral Reading Recognition

Lifestyle & nutritional recommendations

• Preliminary evidence-based multi-modal lifestyle recommendations in accordance with clinical history; nutritional, exercise, cognitive training, social stimulation (Isaacson 2016, Ngandu 2015), stress reduction (Katz, 2016), sleep maintenance (Yaffe, 2014), hyperinsulinemia reduction (Luchinger, 2014)
• Recommendations refined based on clinical measures

Behavioral assessment

• Adapted MIND-DIET questionnaire (Patient-reported)
• Rapid Assessment of Physical Activity (RAPA) (Patient-reported)
• Adherence to recommendations (Physician-reported & Patient-reported)

Education via AlzU.org

• Evidence-based course on AD prevention
• Interactive lessons and activities throughout

Change in Cognitive Assessment

Baseline vs 6 months changes in measures: Indicate improvements in tests and scores across cognitive, behavioral, and lifestyle measures at the six-month mark vs. baseline.

Clinical assessment

• Clinical assessment
• Cognitive assessment
• Patient-reported behavioral assessment
• Lifestyle & nutritional recommendations

Recommendations refined by bloodwork & genetics

• Clinical assessment
• Cognitive assessment
• Behavioral assessment (Patient & Physician-reported)