Plasma β-Amyloid 1-42/1-40 Ratio Provides Insight into the Presence of Alzheimer’s Disease

Background

- Alzheimer’s disease (AD) is a chronic neurodegenerative disease characterized by extracellular brain aggregates of β-amyloid peptides. These peptides originate from the amyloid precursor protein (APP). Cleavage of APP primarily yields 2 peptides: β-amyloid 1-42 and β-amyloid 1-40. Measurement of β-amyloid peptide 1-42 in cerebral spinal fluid (CSF), as well as tau and hyperphosphorylated tau, has become a standard diagnostic tool for AD. A blood-based method would avoid the invasiveness of collecting a CSF specimen.

- In addition, some studies suggest that the ratio of 1-42/1-40 in plasma can help identify patients with AD.**

Objective: The investigators of this study developed a method to simultaneously measure β-amyloid 1-42 and 1-40 in plasma specimens. They also evaluated the correlation of the 1-42/1-40 ratio with mild cognitive impairment and AD.

Methods

- A highly sensitive multiplex assay for the simultaneous measurement of β-amyloid 1-42 and 1-40 was developed and validated at Quest Diagnostics.

- Clinical specimens were selected from 100 patients who were categorized based on the Clinical Dementia Rating test and the Montreal Cognitive Assessment. The categories were as follows:
  - Normal (n=35)
  - Early mild cognitive impairment (MCI; n=25)
  - Late MCI (n=15)
  - AD (n=25)

- β-amyloid 1-42 and 1-40 were measured using the assay, and 1-42/1-40 ratios were calculated.

- Categories were compared using the Kruskal-Wallis H test.

Results

- β-amyloid 1-42/1-40 ratios were generally higher in specimens from normal patients than those from AD-affected patients. Pairing AD with late MCI data and normal with early MCI data slightly improved the distribution. For identifying patient with AD vs normal patients, the clinical specificity was 71% and sensitivity was 76%.

Conclusions

- The investigators developed an assay that simultaneously measures β-amyloid peptides 1-42 and 1-40 in plasma specimens.

- The assay allows assessment of the 1-42/1-40 ratio, which may help identify patients with AD.