Blood Biomarkers May Help Diagnose Alzheimer's

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September 14, 2010

MedPage Today Action Points

- Point out that the study compared patients with Alzheimer's disease and controls but did not study patients with other forms of dementia.

- Also point out that current therapeutic approaches based upon clinical diagnoses are unlikely to change with the development of sensitive assays.

Review

A blood test that looks at hundreds of protein biomarkers may accurately diagnose Alzheimer's disease, especially when combined with clinical characteristics, researchers say.

Screening for these biomarkers and factoring in age, sex, education, and *APOE* status led to a sensitivity of 0.94 and a specificity of 0.84, Sid O'Bryant, PhD, of Texas Tech University, in Lubbock, Texas, and colleagues reported in the *Archives of Neurology*.

O'Bryant told *MedPage Today* that the study is a "first step," but that eventually a blood test can "open access to care to anyone," particularly because it is not as invasive as detecting biomarkers in spinal fluid and won't preclude patients who can't have radiological imaging.

Alzheimer's researchers approached the findings with caution.

"When you measure anything in blood, we have to be very careful that the changes we see really are Alzheimer-related," Peter Davies, PhD, Albert Einstein College of Medicine, in Bronx, N.Y., said in an e-mail. "Many of the proteins in this study ... will change if the patient gets -- or is even exposed to -- another disease or illness. This is especially true when the proteins being measured are immune-system related."

Richard Caselli, MD, of the Mayo Clinic in Scottsdale, Ariz., said even with a simpler test, treatment options wouldn't change.

"There is no disease-modifying therapy, so we can try the usual meds with or without this test," he said in an e-mail. "We do not need this to decide who should get a marginally effective but generally well-tolerated medication like a cholinesterase inhibitor."

Attempts to find a lone biomarker for Alzheimer's disease -- whether it's in blood, spinal fluid, or the brain -- have largely failed.

"In all likelihood, just one biomarker isn't going to work," O'Bryant said. Rather, he and his team have instead focused on a large array of blood-based proteins, especially since assay technology has now made it possible to evaluate tremendous amounts of data.

So to develop an algorithm that separates patients with Alzheimer's disease from controls, the researchers conducted a longitudinal case-control study, using stored blood samples from the Texas Alzheimer's Research Consortium project.

They assessed biomarker data from these 197 Alzheimer's patients and compared it with 203 controls.

The biomarker assays looked at hundreds of proteins, including thrombopoietin, TNF-alpha, creatine kinase, and various interleukins. A previous team of researchers had suggested that just 18 such biomarkers are sufficient for diagnosis, but O'Bryant said his team did not want to restrict its analyses.

All Alzheimer's patients had been diagnosed via an extensive workup that included blood work, neuroimaging, and evaluations by a neurologist (and in some cases a psychiatrist and a geriatrician) -- a process that can take up to three days total and is "quite expensive," O'Bryant said.

Alzheimer's patients were significantly older, less educated, and more likely to carry at least one copy of the *APOE-e4* allele than controls ($P<0.001$).

The researchers found their biomarker assay alone had a sensitivity of 0.80 and a specificity of 0.91, as well as an area under the curve of 0.91 in detecting the disease.

When age, sex, education, and *APOE* status were added to the algorithm, the sensitivity, specificity, and area under the curve were 0.94, 0.84, and 0.95, respectively.

They also saw that many of the proteins with the highest importance were inflammatory in nature, which suggests that the existence of an inflammatory-related endophenotype of Alzheimer's disease "may provide targeted therapeutic opportunities for this subset of patients," they wrote.

Still, O'Bryant cautioned that more work needs to be done: "We have to see if it can distinguish between Alzheimer's and other forms of dementia."

Davies said the authors certainly need to look at a "'real-world' population of non-Alzheimer's disease cases, not just their healthy controls. I have heard that the earlier test was very good at identifying sick people, almost regardless of the nature of their illness."

The Texas Alzheimer's Research Consortium was funded by the state of Texas through the Texas Council on Alzheimer's Disease and Related Disorders. The study was partially supported by a grant from the National Institutes of Health.

A patent is being filed covering the biomarker algorithm used in the study, and O'Bryant and several co-authors are named on the patent.

Primary source: Archives of Neurology
Source reference:
O'Bryant SE, et al "A serum-based algorithm for the detection of Alzheimer disease" *Arch Neurol* 2010; 67(9): 1077-1081.
