Blood Test for Early Diagnosis of Alzheimer's Disease

SBU ALERT REPORT NO 2012-01 • 2012-12-12 • WWW.SBU.SE/ALERT

Summary and Conclusions

Alzheimer's disease (AD) is the most common cause of dementia [1]. The scientific literature offers a good description of the tissue changes in the brain resulting from Alzheimer's disease. The prevalence of certain substances, biomarkers, in the cerebrospinal fluid reflects these changes. Alzheimer's disease can be diagnosed by testing cerebrospinal fluid obtained by lumbar puncture (spinal tap). However, a blood test would be an easier way to diagnose the disease.

Four potential biomarkers that can be measured in plasma and serum have been studied for Alzheimer's disease: plasma or serum levels of amyloid β (Aβ), autoantibodies against Aβ, platelet amyloid precursor protein (platelet APP), and α1 antichymotrypsin (ACT).

Conclusions

- ❑ Currently, no biomarkers in blood can be used to diagnose Alzheimer's disease.
- ❑ Of the four biomarkers studied, only platelet APP has shown differences between sick and healthy individuals. For the other biomarkers, the difference between sick and healthy people is insignificant.
- ❑ Large, independent studies are needed to determine whether platelet APP in blood tests could serve as a diagnostic tool.
- ❑ Studies using refined, highly sensitive measurement methods are needed to identify more biomarkers that could serve as diagnostic tools.

Method and target group

Alzheimer's disease mainly affects the elderly, but the early-onset AD can debut before 65 years of age [1]. Most cases of AD are sporadic, while genetically inherited forms comprise less than 0.1% of cases. Inheritance is autosomal dominant. Today, patients with mild memory loss often seek care. At this early stage of the disease, diagnostic biomarkers that reveal the underlying disease process would be valuable. Such biomarkers are found in the cerebrospinal fluid (total tau, phosphorylated tau, and the 42-amino-acid-long isoform of amyloid β [Aβ42]). The biomarkers can be used to diagnose Alzheimer's disease with a sensitivity and specificity of 80% to 95%, 5 to 10 years before the patient meets the criteria for dementia [2]. Nevertheless, it would be desirable to have markers in blood that could be used diagnostically to avoid spinal tap, which is a more difficult and time consuming procedure than blood testing.

This report covers the literature on biomarkers in blood for diagnosis of Alzheimer's disease. We have included case-control studies and longitudinal studies of patients with mild cognitive disorders that later develop into Alzheimer's disease (prodromal Alzheimer's) [3].

Question

- What is the diagnostic accuracy of plasma or serum levels of Aβ, autoantibodies against Aβ, platelet APP ratio, and ACT in distinguishing people with Alzheimer's disease from cognitively healthy controls?

Patient benefits

- The scientific evidence is insufficient (two studies from the same research group and with deficiencies regarding study quality and directness) to determine whether the platelet APP ratio in blood tests can be used to estimate diagnostic accuracy in identifying Alzheimer's disease (⊕○○○).

This assessment included in total 45 studies: 21 on plasma or serum levels of Aβ, 8 on autoantibodies against Aβ, 6 on platelet APP ratio, and 10 on ACT. Study populations consisted mainly of patients with Alzheimer's disease who were compared with cognitively healthy controls. Some studies also investigated the association between the markers and future Alzheimer's disease in longitudinal cohorts of cognitively healthy elderly, or patients with mild cognitive symptoms that did not meet the criteria for Alzheimer's disease when tested. All studies

used the clinical NINCDS-ADRDA criteria from 1984 as a standard reference [4]. Some studies also used DSM or ICD criteria.

Most of the studies found no, or clinically insignificant, differences between Alzheimer's patients and controls for the biomarkers studied. The studies on Aβ, autoantibodies against Aβ, and ACT were excluded at this stage (39 studies) since they did not show any diagnostically relevant differences.

Six studies addressing platelet APP ratios show potentially useful diagnostic differences between clinically relevant comparison groups. Four of the six studies were excluded since they did not report on diagnostic accuracy. The two remaining studies were found to have medium quality, but were produced by the same research group. Hence, large and independent studies are needed.

Ethical aspects

If, in the future, a clinically useful blood test becomes available to diagnose the disease – in the absence of effective treatment – ethical considerations would be necessary. The possibility for early diagnosis, but not treatment, of Alzheimer's disease would cause distress for patients and families. In the worst case, a diagnosis could stigmatise people in a very early stage of Alzheimer's disease, even though they might never develop a serious case of the disease.

A clinically useful blood test could have several positive effects. For instance, early diagnosis could help explain altered and perhaps unusual behaviour. An early diagnosis could also increase opportunities to take steps in preparing for the later phase of disease.

Economic aspects

Costs and cost effectiveness were not analysed since accurate and diagnostically useful methods have yet to be identified.

Four levels are used in grading the strength of the scientific evidence on which conclusions are based:

Strong scientific evidence (⊕⊕⊕⊕). Based on high or medium quality studies with no factors that weaken the overall assessment.

Moderately strong scientific evidence (⊕⊕⊕○). Based on high or medium quality studies with isolated factors that weaken the overall assessment.

Limited scientific evidence (⊕⊕○○). Based on high or medium quality studies having factors that weaken the overall assessment.

Insufficient scientific evidence (⊕○○○). Scientific evidence is deemed insufficient when scientific findings are absent, the quality of available studies is low, or studies of similar quality present conflicting findings.

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SBU evaluates healthcare technology

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This assessment was published in 2012. Findings based on strong scientific evidence usually continue to apply well into the future. However, findings based on insufficient, limited, or contradictory evidence might have already been replaced by more recent findings.

The complete report is available in Swedish.

Publisher: Måns Rosén, Director, SBU
Program Manager: Sofia Tranæus, SBU
Graphic Production: Elin Rye-Danjelsen, SBU