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Plasma amyloid beta peptides and oligomers levels in Alzheimer's disease

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Introduction: Amyloid beta (Aβ) exists in different forms including Aβ peptides, oligomers, protofibrils, and fibrils. It has been believed that Aβ fibrils in Alzheimer's disease (AD) brain contribute to AD pathogenesis, but recent evidences suggest that Aβ oligomers have stronger relationship with AD pathogenesis.

Aims: To study the plasma $A\beta_{40}$, $A\beta_{42}$, and Aβ oligomers levels in AD patients and non-demented age-matched controls, and the correlations between plasma $A\beta_{40}$, $A\beta_{42}$, and Aβ oligomers levels and cognitive function.

Methods: We studied 44 AD patients and 22 controls. Cognitive functions were assessed by cognitive assessment tools: Chinese version of mini-mental state examination (MMSE), Abbreviated Metal Test (AMT), Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAS-cog), and Delayed 10-Word Recall Test (DWRT). Plasma $A\beta_{40}$ and $A\beta_{42}$ levels were measured by ELISA kits (Invitrogen). Plasma Aβ oligomers level was detected by ELISA, using Aβ oligomeric antibody as detecting antibody and Aβ N-terminal antibody (against residues 1-14) as capturing antibody.

Results: There was no difference in plasma $A\beta_{40}$ and $A\beta_{42}$ levels between AD patients (median $A\beta_{40}$ level 145.93 pg/mL, median $A\beta_{42}$ level 9.94 pg/mL) and controls (median $A\beta_{40}$ level 130.34 pg/mL, median $A\beta_{42}$ level 8.42 pg/mL; P=0.196 and P=0.187, respectively). In women with AD, increased plasma $A\beta_{42}$ level was associated with increased MMSE (P=0.043) and decreased ADAS-cog (P=0.034) suggestive of positive correlation between plasma $A\beta_{42}$ level with cognitive function. Plasma Aβ oligomers level was higher in AD patients (median 642.54 ng/mL, range 103.33-2676.93 ng/mL) than controls (median 444.18 ng/mL, range 150.19-1311.18 ng/mL; P=0.047), and was negatively correlated with cognitive function evidenced by increased plasma Aβ oligomers level associated with decreased MMSE, AMT, DWRT scores and increased ADAS-cog scores (P=0.037, P=0.043, P=0.025, P=0.036, respectively).

Conclusion: Plasma $A\beta_{42}$ and $A\beta_{40}$ levels are not suitable biomarkers for AD diagnosis; but plasma $A\beta_{42}$ level may reflect severity of cognitive impairment in women with AD. Plasma Aβ oligomers level may help diagnose AD patients, but the range is wide among AD patients, making it not an ideal biomarker for AD diagnosis.

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Introduction: Various forms of amyloid beta (Aβ) including Aβ peptides, oligomers, protofibrils and fibrils are thought to be pathogenic in Alzheimer's disease (AD). The exact pathophysiological role of endogenous Aβ autoantibodies (Ab) in healthy subjects and AD patients are uncertain. Potential protective role of Aβ Ab has been suggested.

Aims: To study the serum Aβ monomers and Aβ oligomers Ab levels in AD patients and non-demented age-matched controls, and the relationship between Aβ monomers and Aβ oligomers Ab levels and cognitive function.

Methods: A total of 44 AD patients and 22 controls were recruited. Cognitive functions were assessed by cognitive assessment tools: Chinese version of mini-mental state examination (MMSE), Abbreviated Metal Test (AMT), Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAS-cog). Aβ Ab levels were assayed by ELISA. $A\beta_{42}$ monomer and $A\beta_{42}$ oligomers were coated on 96-well plates for measuring Aβ monomer Ab and Aβ oligomers Ab levels respectively. The secondary antibody was rabbit-anti-human antibody (detecting antibody). Calibration curves were made by 2C8 (against Aβ residues1-16) and 7A1a (Aβ oligomers antibody) for Aβ monomer and Aβ oligomers Ab respectively. Negative control was incubating with secondary antibody only without incubation with patients/controls' serum.

Results: There was no difference in serum Aβ monomer Ab level between AD patients (median 177.43 μg/mL) and controls (median 190.88 μg/mL, P=0.55). In AD patients, Aβ monomer Ab level was negatively correlated with cognitive function evidenced by increased Aβ monomer Ab level associated with decreased MMSE, AMT and increased ADAS-cog scores (P=0.004, P=0.013, P=0.005, respectively). Serum Aβ oligomers Ab level was higher in AD patients (median 42.81 μg/mL, range 11.91-241.62 μg/mL) than controls (median 24.15 μg/mL, range 2.32-329.93 μg/mL; P=0.014).

Conclusion: Serum Aβ monomer Ab is not a suitable biomarker for AD diagnosis, but may reflect the severity of AD. Serum Aβ oligomers Ab level may help in AD diagnosis, but wide range of titers among AD patients makes it not an ideal biomarker for AD diagnosis.