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Blood Circulatory Level of Seven Sirtuins in Alzheimer's Disease: Potent Biomarker Based on Translational Research

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Abstract

Alzheimer's disease (AD) is an accelerating neurodegenerative disorder. Dysfunction of mitochondria and oxidative stress contributes to the pathogenesis of AD. Sirtuins play a role in this pathway and can be a potential marker to study neurodegenerative changes. This study evaluated serum levels of all seven sirtuin (SIRT1-SIRT7) proteins in three study groups: AD, mild cognitive impairment (MCI) and geriatric control (GC) by surface plasmon resonance (SPR) technique. Further, it was validated by the Western blot experiment. ROC analysis was performed to differentiate the study group based on the concentration of serum SIRT proteins. Out of seven sirtuins, serum SIRT1, SIRT3 and SIRT6 levels (mean ± SD) were significantly decreased in AD (1.65 ± 0.56, 3.15 ± 0.28, 3.36 ± 0.32 ng/µl), compared to MCI (2.17 ± 0.39, 3.60 ± 0.51, 3.73 ± 0.48 ng/µl) and GC (2.84 ± 0.47, 4.55 ± 0.48, 4.65 ± 0.55 ng/µl). ROC analysis showed the cut-off value with high sensitivity and specificity for cognitive impairment (AD and MCI). The concentration declined significantly with the disease progression. No specific difference was observed in the case of other SIRTs between the study groups. This study reveals an inverse relation of serum SIRT1, SIRT3 and SIRT6 concentration with AD. ROC analysis showed that these serum proteins have greater accuracy in diagnosing of AD. This is the first report of estimation of all seven serum sirtuins and the clinical relevance of SIRT3 and SIRT6 as serum protein markers for AD.

Keywords: Alzheimer's disease; Mild cognitive impairment; Protein marker; SPR; Sirtuins.