Quantification of COX-2 Level in Alzheimer's Disease Patients to Develop Potential Blood-Based Biomarker for Early Diagnosis and Therapeutic Target

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Abstract: Background:Alzheimer's disease (AD) is a progressive neurodegenerative disease and symptoms develop gradually over many years. The current direction for medication development in AD is focused on neuro-inflammation and oxidative stress. Amyloid-β (Aβ) deposition activates microglia leading to neuro-inflammation and neurodegeneration induced by activation of COX-2 via NFκB p50 in glioblastoma cells. Objective:The study aimed to evaluate the concentration of COX-2 and NFκB p50 in serum of AD, mild cognitive impairment (MCI), and geriatric control (GC) and to establish a blood-based biomarker for early diagnosis and its therapeutic implications. Methods:Proteins and their mRNA level in blood of study groups were measured by surface plasmon resonance (SPR) and quantitative polymerase chain reaction (qPCR), respectively. The level of protein was further validated by western blot. The binding study of designed peptide against COX-2 by molecular docking was verified by SPR. The rescue of neurotoxicity by peptide was also checked by MTT assay on SH-SY5Y cells (neuroblastoma cell line). Results:Proteins and mRNA were highly expressed in AD and MCI compared to GC. However, COX-2 decreases with disease duration. The peptide showed binding affinity with COX-2 with low dissociation constant in SPR and rescued the neurotoxicity of SH-SY5Y cells by decreasing the level of Aβ, tau, and pTau proteins. Conclusions:It can be concluded that COX-2 protein can serve as a potential blood-based biomarker for early detection and can be a good platform for therapeutic intervention for AD.

Keywords: Alzheimer's disease, blood-based biomarker, COX-2, inhibitor, SPR

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