ABSTRACT

Alzheimer's disease (AD), a neurodegenerative disorder, is the most common form of dementia in the elderly individuals. Among the pathogenic mechanisms in AD, chronic systemic inflammation is described and characterized by massive production of proinflammatory cytokines by peripheral blood mononuclear cells (PBMCs), which may contribute to an altered immune response and exacerbation of neurodegeneration. Studies have also reported increased double-stranded RNA-dependent protein kinase (PKR) activation in the PBMCs of patients with AD. Interestingly, PKR could be involved in NF-κB activation, leading to production of a wide range of cytokines. We proposed to decrease proinflammatory cytokines production and release by treating the PBMCs in 25 patients with AD with a specific inhibitor of PKR. Our results showed that PKR inhibition greatly decreased tumor necrosis factor , interleukin (IL)-1α, IL-1β, and IL-6 production and release but did not affect the chemokine RANTES. Moreover, inhibition of the proinflammatory factors was correlated with prevention of caspase-3 activation. These results indicated that specific inhibition of PKR at the peripheral level might decrease the inflammatory response in AD.