Therapeutic Effects of Benzoylacetonitrile on Microglia Activation in Multiple Sclerosis

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Abstract

Background: Multiple Sclerosis (MS) is an autoimmune disease of the central nervous system (CNS). Pathogenic T cells, such as Th1 and Th17, infiltrate the CNS, resulting in neuroinflammation, demyelination and axonal damage. Th1 activates microglia (MG) in the CNS and Th17 acts as a chemokine to recruit immune cells into the CNS. MG is a resident immune cell in the CNS and its activation is associated with destruction of myelin and secretion of inflammatory cytokines such as IL-12, IL-23 and IL-1β. IL-12 and IL-23 are important for Th1 and Th17 differentiation and reactivation, respectively. IL-1β is a key mediator of the inflammatory response. Benzoylacetonitrile (BTN) has been shown to reduce disease severity in mouse model of MS and reduce Th1 and Th17 differentiation in vitro. However, the effects of BTN on MG are unknown, and this study was aimed to investigate the effects of BTN on MG activation in vitro. We hypothesize that BTN can suppress MG activation and decrease the production of inflammatory cytokines.

Methods: Primary MG were pretreated with BTN at concentration of 200μM or 300μM for 2 hours or with DMSO (vehicle), followed by lipopolysaccharide (LPS) 100ng/ml stimulation for 1.5 or 3 hours. RNA was isolated from MG and mRNA expression levels of IL-12, IL-23, IL-1β were measured using Q-PCR.

Results: Our results showed that BTN suppressed MG activation and reduced inflammatory cytokine production. The mRNA expression levels of IL-12, IL-23, and IL-1β in LPS and BTN-treated MG were significantly lower than LPS-treated MG.

Conclusion: This study demonstrated that BTN was able to suppress MG expression of inflammatory cytokines in vitro, suggesting that BTN exhibits immunomodulatory effects on MG activation in vitro. BTN has a potential to attenuate neuroinflammation in MS through the reduction of inflammatory cytokines.