Artesunate inhibits prostaglandin E₂ (PGE₂) production in LPS + IFN-γ activated BV-2 microglia cells.

UP Okorji, OA Olajide University of Huddersfield, Huddersfield, UK

Neurodegenerative disorders, including Alzheimer’s disease (AD), associated with the aging process have been shown to be linked with microglia activation and inflammatory processes [1]. Microglial activation releases various mediators including prostaglandin E₂ (PGE₂). The transcription factor, nuclear factor kappa B (NF-κB) has been shown to control inflammatory responses in microglia cells. Artesunate has been reported to have anti-inflammatory properties in experimental colitis [2]. In this study the effects of artesunate were investigated in BV-2 stimulated microglia cells. BV-2 cells were pre-treated with artesunate (0.5-4µM) for 30min and stimulated with LPS (1µg/ml) + IFN-γ (5ng/ml) for 24h. Thereafter, supernatants were analysed for PGE₂ production. COX-2 and m-PGES1 protein expressions were also measured in cell lysates by western blot. The effect of artesunate on the transactivation of NF-κB was assessed in transfected HEK293 cells using luciferase reporter gene assay. Values of all experiments were represented as a mean ± SEM of at least 3 experiments. Values were compared using one-way ANOVA followed by a post-hoc Student Newman-Keuls test. Pre-treatment with artesunate significantly (p<0.05) inhibited LPS + IFN-γ-induced PGE₂ production in a dose-dependent manner with an IC₅₀ value of 3.2µM. Artesunate (0.5-4µM) suppressed COX-2 protein expression significantly (p<0.05) in LPS + IFN-γ stimulated BV-2 cells. At 4µM, artesunate significantly suppressed COX-2 protein expression by 52% compared to the LPS+IFN-γ control (IC₅₀= 3.8µM) (Fig.1). In addition, artesunate decreased m-PGES1 protein expression significantly (p<0.05) with 25% decrease at 4µM compared to LPS+IFN-γ control (IC₅₀= 0.62µM) (Fig.1). However, artesunate significantly (p<0.05) inhibited NF-κB transactivation in transfected HEK293 cells with an inhibition of 40% compared to the positive control at all concentrations (0.5-4µM).

These data have demonstrated that artesunate inhibits PGE₂ through interference with COX-2 and m-PGES1 protein expressions in BV-2 activated microglia. Artesunate also inhibited NF-κB transactivation in transfected HEK293. These results suggest that artesunate blocks the NF-κB signalling by inhibiting transactivation of NF-κB and its downstream signals PGE₂, COX-2 and m-PGES1.

Figure 1: Artesunate inhibits COX-2 and m-PGES1 protein expression in LPS-activated BV-2 microglia cells

References
