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Toxicol Open Access 2019, Volume 5
DOI: 10.4172/2476-2067-C1-009

Therapeutics effect of Idebenone in murine colitis

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Idebenone short chain quinone has been described as a potent antioxidant and mitochondrial electron donor. Its therapeutical potential has been described extensively in numerous pathological conditions ranging from neurodegenerative, neuromuscular to diverse metabolic conditions. There is also some emerging evidence that Idebenone has some anti-inflammatory activity. Oxidative stress is one of the key players of the inflammatory cascade responsible for the initiation of Ulcerative Colitis (UC). Therefore, we investigated the anti-oxidative and anti-inflammatory properties of Idebenone in Dextran Sodium Sulfate (DSS) induced mouse model of acute colitis. Acute colitis was introduced in female C57BL/6J mice by administering 2.5% of DSS in autoclaved water continuously for seven days. Changes in body weight, Disease Activity Index (DAI), colon length and histopathological parameters were evaluated and scored. Colonic contents of Malondialdehyde (MDA), a marker of lipid peroxidation were also examined as a parameter of disease-associated redox state. Protein expression of the oxidative stress induced redox factor NAD(P)H dehydrogenase Quinone-1 (NQO-1) was determined by western blot, while the levels of various pro-inflammatory cytokines were quantified using Bio-Plex assay. On Oral administration of Idebenone at a dose of 200 mg/kg body weight significantly against body weight loss and improved DAI, colon length and histopathology. Idebenone also significantly reduced MDA content as well as pro-inflammatory cytokine levels such as IL-1α, TNF-α, G-CSF, GM-CSF, MIP-1α, MIP-1β, RANTES and EOTAXIN and furthermore, Idebenone upregulated NQO1 protein levels. These results suggest that Idebenone could represent a promising therapeutic strategy to interfere with disease pathology in UC by inducing anti-oxidative and anti-inflammatory pathways.

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