The dual reno- and neuro-protective effects of dimethyl fumarate against uremic encephalopathy in a renal ischemia/reperfusion model

Hanan Salah ,Diaa Ragab, Dalaal M Abdallah

Abstract

Background: Dimethyl fumarate (DMF), a Nrf2 activator approved for multiple sclerosis (MS) in 2013, showed promising antioxidant and anti-inflammatory effects against cerebral injury. However, its mechanistic maneuver in renal ischemia/reperfusion (I/R) injury and its associated uremic encephalopathy has not been previously highlighted.
Methods: To fulfill this aim, rats were divided into 4 groups; sham-operated, renal I/R, and 14 days pretreated DMF (15 and 25 mg/kg/day, orally).
Results: The small molecule drug reduced renal I/R-induced elevation in serum creatinine and blood urea nitrogen, the renal content of interleukin (IL)-18 and its pro-activator caspase-1. The DMF antioxidant potential was confirmed by the increased renal Nrf2 mRNA expression/content associated wit an enhanced total antioxidant capacity and an inhibition of lipid peroxidation. This character entailed the suppression of the assessed inflammatory markers, such as nuclear factor (NF)-əB, p38 mitogen-activated protein kinase, and tumor necrosis factor-Ŭ. Remotely, DMF protected against uremic encephalopathy signified by the suppressed cortical/hippocampal contents of glial fibrillary acidic protein through suppressing 2 trajectories, the NF-əB/inducible nitric oxide synthase/nitric oxide/guanylyl cyclase/cyclic guanosine monophosphate and IL-6/signal transducer and activator of transcription 3. Moreover, the open field test revealed an enhanced locomotor activity in DMF pretreated rats, reflecting counter ability against functional and behavioral effects of acute uremic encephalopathy.
Conclusion: The current study advocates the novel DMF dual protection potential against renal I/R insult and its remote brain injury to compensate uremic encephalopathy and acute kidney injury as well.

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