



Ebselen attenuates oxidative stress in ischemic astrocytes depleted of glutathione. Comparison with glutathione precursors

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Abstract:

In this study, we investigated the protective effect of ebselen, a seleno-organic compound with antioxidant activity, towards astrocyte degeneration caused by exposure to simulated *in vitro* ischemic conditions and simultaneous depletion of glutathione (GSH). Depletion of GSH was induced by 24 h pretreatment with L-buthionine-(S,R)-sulfoximine (BSO). In this experimental paradigm, we examined the effects of ebselen (1–40 μ M) on apoptosis, mitochondrial function, reactive oxygen species (ROS) production, intracellular GSH level and mitochondrial transmembrane potential (MTP). In addition, we also compared the antioxidant potential of ebselen with cystine and methionine as precursors of GSH synthesis as well as with GSH ethyl ester. Our study demonstrated that toxicity of simulated ischemia conditions was enhanced when intracellular GSH was depleted. Treatment with ebselen, especially at concentrations of 20 and 40 μ M prevented ischemia-induced cytotoxicity. Our study has shown that antiapoptotic effect of ebselen is associated with its strong antioxidant properties, preservation of MTP and possibly conservation of mitochondrial GSH during cytoplasmic GSH depletion caused by oxidative damage. Also, promoting GSH synthesis by the delivery of its substrates, like cystine or inhibition of the efflux by methionine may be a powerful strategy to minimize cell damage in the nervous tissue after ischemia.

Key words:

apoptosis, astrocytes, cystine, ebselen, glutathione, ischemia, methionine
