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Radiation Effects on Rat Brain

Metalloporphyrin antioxidants ameliorate normal tissue radiation damage in rat brain

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Abstract

Purpose: We examined the effects of manganese (III) meso-tetrakis (diethyl-2-5-imidazole) porphyrin, a metalloporphyrin antioxidant (MPA), on neural tissue radiation toxicity in vivo and on tumour cell radiosensitivity in vitro.

Materials and methods: MPA was administered directly into the right lateral ventricle of young adult, male Sprague-Dawley rats (0 or 3.4 µg) 3 h before treatment with a single fraction, 100 Gy radiation dose delivered to the left brain hemisphere. The effects of treatment on radiation responses were assessed at different time points following irradiation.

Results: MPA treatment prior to brain irradiation protected against acute radiation-induced apoptosis and ameliorated delayed damage to the blood-brain barrier and radiation necrosis, but without producing a discernible increase in tissue superoxide dismutase (SOD) activity. In vitro, MPA pretreatment protected against radiation-induced apoptosis in primary neuronal cultures and increased clonogenic survival of irradiated rat glioma C6 cells, but had no discernible effect on radiation-induced DNA double-strand breaks. MPA, a low molecular weight SOD mimic, significantly increased mitochondrial SOD activity in C6 cells, but not total cellular SOD activity. MPA up-regulated C6 expression of heme-oxygenase 1 (HO-1), an endogenous radioprotectant, but had no effect on HO-1 levels in human astrocytoma U-251 cells, human prostatic carcinoma LNCaP cells, or primary rat brain microvascular endothelial cells in vitro, nor on brain tissue HO-1 expression levels in vivo.

Conclusions: Metalloporphyrin antioxidants merit further exploration as adjunctive radioprotectants for cranial radiotherapy/radiosurgery applications, although the potential for tumour protection must be carefully considered.

Keywords:

- antioxidant
- radioprotection
- normal tissue complication probability
- pre-conditioning

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Declaration of interest: One of the authors JDC is a patent holder for the compound manganese (III) meso-tetrakis (diethyl-2-5-imidazole) porphyrin used in this study. None of the other authors report any conflicts of interest.

Related Research Data

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Source: Free Radical Biology and Medicine

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Source: Journal of Neuroscience

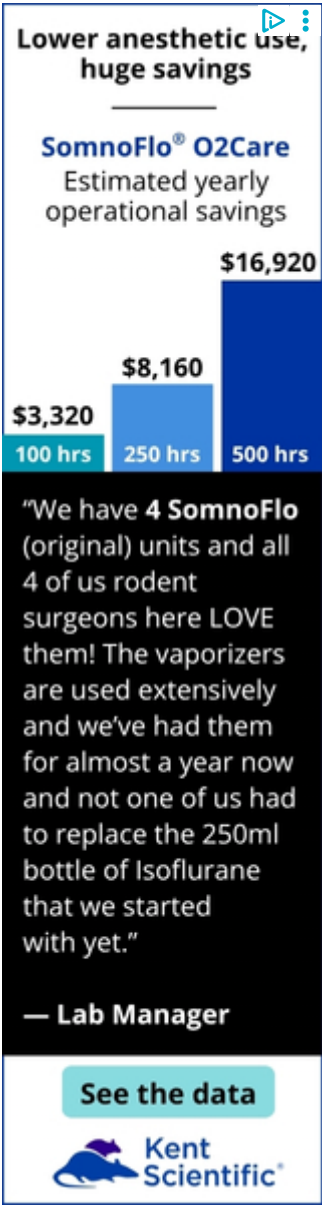
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