The role of cellular antioxidant pathways in protecting neurons during photodynamic therapy

Conference or Workshop Item

THE ROLE OF CELLULAR ANTIOXIDANT PATHWAYS IN PROTECTING NEURONS DURING PHOTODYNAMIC THERAPY.

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The effect of photodynamic therapy (PDT) on neurons is an important consideration when treating cancers within or adjacent to the nervous system. The photosensitiser, meta-tetrahydroxyphenyl chlorin (mTHPC) is effective in destroying tumour cells but can spare neurons in culture. The aim of this study was to investigate the role of cellular antioxidant pathways in protecting neurons from damage during mTHPC-mediated PDT.

Exposing cells to 4 μg/ml mTHPC-mediated PDT in a 3D culture system resulted in substantial cell death among tumour cells and glia, but survival of neurons. To investigate this phenomenon, prior to PDT neurons were treated with drugs to block antioxidant pathways; L-buthionine sulfoximine (L-BSO) depleted glutathione, and diethyldithiocarbamate (DDC) and 2-methoxyoestradiol ($2MeOE_2$) were used to inhibit superoxide dismutase SOD 1 and SOD 2 respectively. Neuronal cell death was assessed 24 h later.

Neuronal death following mTHPC-mediated PDT was significantly increased in the presence of either DDC or L-BSO compared to PDT-only controls. There was a slight increase in neuronal death following PDT in neurons treated with $2\text{-}MeOE_2$, but this was not statistically significant. Overall, inhibition of glutathione resulted in 63 ± 7 % of neurons dying and inhibition of SOD 1 resulted in 42 ± 7 % neuron death.

These results suggest that the mechanism by which neurons show reduced sensitivity to mTHPC-mediated PDT involves endogenous antioxidant pathways, the blocking of which results in neuronal cell death. Of the antioxidant pathways investigated here it is apparent that glutathione and SOD 1 play an important role, whereas inhibition of SOD 2 had little effect. Further studies are required to understand fully the cellular mechanisms involved in protecting neurons during this treatment, and the culture system described here is a useful tool for such research. Ultimately, understanding the conditions under which neurons may be able to survive PDT or other oxidative damage is important in developing strategies for treating tumours within or adjacent to the nervous system, where avoidance of neuronal damage has the potential to reduce side effects.