Enhanced cytotoxic effects of 5-aminolevulinic acid-mediated photodynamic therapy by concurrent hyperthermia in glioma spheroids.

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Abstract
During photodynamic therapy (PDT) both normal and pathological brain tissue, in close proximity to the light source, can experience significant temperature increases. The purpose of this study was to investigate the anti-tumor effects of concurrent 5-aminolevulinic acid (ALA)-mediated PDT and hyperthermia (HT) in human and rat glioma spheroids. Human or rat glioma spheroids were subjected to PDT, HT, or a combination of the two treatments. Therapies were given concurrently to simulate the conditions that will occur during patient PDT. Predictions of diffusion theory suggest that brain tissue immediately adjacent to a spherical light applicator may experience temperature increases approaching 8 degrees C for laser input powers of 2 W. In the in vitro model employed here, HT had no effect on spheroid survival at temperatures below 49 degrees C, while sub-threshold fluence PDT results in only modest decrease in survival. HT (40-46 degrees C) and PDT interact in a synergistic manner if the two treatments are given concurrently. The degree of synergism increases with increasing temperature and light fluence. Apoptosis is the primary mode of cell death following both low-fluence rate PDT and combined HT + PDT.

PMID: 15662970 [PubMed - indexed for MEDLINE]

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