An evaluation of the safety and feasibility of convection-enhanced delivery of carboplatin into the white matter as a potential treatment for high-grade glioma.


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Abstract

Glioblastoma multiforme (GBM) is the most common and most aggressive form of intrinsic brain tumour. Despite standard treatment involving surgical resection, chemotherapy and radiotherapy this disease remains incurable with the majority of tumours recurring adjacent to the resection cavity. Consequently there is a clear need to improve local tumour control. Convection-enhanced delivery (CED) is a practical technique for administering chemotherapeutics directly into peritumoural brain. In this study, we have tested the hypothesis that carboplatin would be an appropriate chemotherapeutic agent to administer by CED into peritumoural brain to treat GBM. Within this study we have evaluated the relationships between carboplatin concentration, duration of exposure and tumour cell kill in vitro using GBM cell lines and the relationship between carboplatin concentration and clinical and histological evidence of toxicity in vivo. In addition, we have used laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) to evaluate the distribution properties of carboplatin following CED into rat brain and to determine the rate at which carboplatin is cleared from the brain. Finally, we have compared the distribution properties of carboplatin and the MRI contrast agent gadolinium-DTPA in pig brain. The results of these experiments confirm that carboplatin can be widely distributed by CED and that it remains in the brain for at least 24 h after infusion completion. Furthermore, carboplatin provokes a significant GBM cell kill at concentrations that are not toxic to normal brain. Finally, we provide evidence that gadolinium-DTPA coinfusion is a viable technique for visualising carboplatin distribution using T1-weighted MR imaging.

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