ABSTRACT

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# Can tumor treating fields induce DNA damage and reduce cell motility in medulloblastoma cell lines?

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OBJECTIVE: Medulloblastoma (MB) is the most common malignant pediatric brain tumor and accounts for approximately 20% of all pediatric CNS tumors. Current multimodal treatment is associated with a 70%-90% 5-year survival rate; however, the prognosis for patients with tumor dissemination and recurrent MB remains poor. The majority of survivors exhibit long-term neurocognitive complications; thus, more effective and less toxic treatments are critically needed. Tumor treating fields (TTFields) are low-intensity, alternating electric fields that disrupt cell division through physical interactions with key molecules during mitosis. Side effects from TTField therapy are minimal, making it an ideal candidate for MB treatment.

METHODS: To determine if TTFields can be an effective treatment for MB, the authors conducted an in vitro study treating multiple MB cell lines. Three MB molecular subgroups (SHH [sonic hedgehog], group 3, and group 4) were treated for 24, 48, and 72 hours at 100, 200, 300, and 400 kHz. Combinatorial studies were conducted with the small-molecule casein kinase 2 inhibitor CX-4945.

RESULTS: TTFields reduced MB cell growth with an optimal frequency of 300 kHz, and the most efficacious treatment time was 72 hours. Treatment with TTFields dysregulated actin polymerization and corresponded with a reduction in cell motility and invasion. TTFields also induced DNA damage (γH2AX, 53BP1) that correlated with an increase in apoptotic cells. The authors discovered that CX-4945 works synergistically with TTFields to reduce MB growth. In addition, combining CX-4945 and TTFields increased the cellular actin dysregulation, which correlated with a decrease in MB migration.

CONCLUSIONS: The findings of this study demonstrate that TTFields may be a novel and less toxic method to treat patients with MB.

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