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Enhancing radiation sensitivity in malignant brain tumors with chloroquine: a systematic review

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Abstract

Purpose: Chloroquine (CQ) has been studied for over 50 years as a potential adjuvant to cancer therapy. However, clinical studies investigating CQ combined with radiotherapy for brain tumors have yielded conflicting results. We aimed to synthesize existing evidence on the safety and efficacy of adjuvant CQ with radiotherapy for treatment of high-grade gliomas (HGG) and brain metastases.

Methods: We conducted a systematic review using the PubMed, Embase, Scopus, and Web of Science databases with no date restrictions. We included English-language clinical studies (n ≥ 5 patients) that evaluated the combination of CQ or its analogues with radiotherapy for HGG or brain metastases and reported overall survival (OS) outcomes. Pre-clinical studies and reviews were excluded.

Results: We identified 13 eligible studies with 789 patients. Across both HGG and brain metastases, the median CQ dose was 250 mg daily, with whole-brain radiotherapy as the most common radiotherapy modality. For HGG, 3 out of 8 controlled trials reported significant benefit from treatment, with median survival ranging from 7.9 to 36.6 months. By comparison, only a single study of brain metastases found significantly improved progression-free survival relative to control. The safety profile of adjuvant CQ was generally favorable, with mild adverse effects reported in both patient populations.

Conclusions: For HGG, CQ combined with radiotherapy shows promise but modest, inconsistent survival benefits. For brain metastases, evidence is limited and less favorable, with no consistent benefit across tumor types or study designs. Adverse events are generally mild, though most studies used low CQ doses and long-term safety remains uncertain.

Keywords: Autophagy; Brain metastases; Chloroquine; High-grade glioma; Radiosensitivity; Radiotherapy.