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Intrathecal chemotherapy for leptomeningeal disease in high-grade gliomas: a systematic review

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Abstract

Background: Leptomeningeal disease (LMD) secondary to high grade glioma (HGG), such as glioblastoma (GBM), are characterized by the spread of tumor cells to the leptomeninges which further complicates treatment approaches. Intrathecal (IT) chemotherapy has surfaced as a potential strategy to bypass the blood-brain barrier and address the challenges posed by disseminated disease. Here, we present a review of the safety and efficacy of IT chemotherapy in the treatment of LMD secondary to HGG.

Methods: A systematic review following PRISMA guidelines was conducted searching PubMed and Embase from January 1995 to September 2022 using specified terms related to IT chemotherapy for LMD. Included articles involved patients diagnosed with LMD from HGG, treated with intrathecal chemotherapy, and provided survival data. Data, including demographics, tumor characteristics, treatment, and survival information, were collected and independently extracted.

Results: A total of 68 patients across 10 clinical studies were diagnosed with LMD from HGG and included in the review. Among these patients, the average age at diagnosis was 44.2 years. GBM was the most common tumor type (n = 58, 85.3%). A majority of the patients presented with recurrent disease (n = 29, 60.4%). The review encompassed various IT chemotherapy regimens, including mafosfamide, thio-TEPA, 5-fluoro-2'-deoxyuridine (FdUrd), methotrexate (MTX), and cytarabine; however, dosages and frequencies were inconsistently reported. The mean progression-free survival (PFS) and overall survival (OS) for this cohort were 7.5 months and 11.7 months, respectively. Common side effects of IT chemotherapy included headaches, nausea, and vomiting, with more severe complications such as myelotoxicity, disseminated intravascular coagulopathy, meningitis, and gastrointestinal toxicity reported in some cases.

Conclusion: LMD continues to be an uncommon complication associated with HGG with a poor prognosis. This article provides an overview of the presently available literature on IT chemotherapy for LMD secondary to HGG, and their respective treatment protocols with overall survival attributes. Additional research is warranted to ascertain how to maximize the potential efficacy of IT chemotherapy as a treatment option.

Keywords: Adjuvant therapies; Glioblastoma; Intrathecal chemotherapy; Leptomeningeal disease; Systematic review.

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