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Levetiracetam and valproic acid in glioma: antiseizure and potential antineoplastic effects

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Abstract

Seizures are a frequent complication in glioma. Incidence of brain tumor-related epilepsy (BTRE) in high-grade glioma (HGG) is an estimated > 25% and in low-grade glioma (LGG) is approximately 72%. Two first-line antiseizure medications (ASMs) for BTRE include levetiracetam (LEV) and valproic acid (VPA). Use of VPA has decreased because of a broader side effect profile, potential interaction with chemotherapeutic drugs, and availability of newer generation agents. In refractory BTRE, LEV and VPA may be prescribed together to enhance seizure control. VPA and LEV have gained attention for their purported antineoplastic effects and synergistic role with temozolomide. VPA is suggested to modulate anticancer activity *in vitro* through multiple mechanisms. In addition, retrospective studies indicate increased overall survival in patients with epileptogenic HGGs who are managed with LEV or VPA rather than other ASMs. However, these studies have numerous limitations. It is also reported that patients with glioma and a seizure history have a longer survival. This extended survival, if one exists, may be only observed in certain gliomas with corresponding patient characteristics. We provide a brief overview of the management of BTRE, VPA and LEV as anticonvulsants and antineoplastics, and the factors that may be associated with survival in epileptogenic glioma.

Keywords: Brain tumor; brain-tumor related epilepsy; epilepsy; high-grade glioma; levetiracetam; valproic acid.