Tumor and antiepileptic drugs

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In the Journal of Neurosurgery, Saria and colleagues1^2 report on a retrospective analysis of their experience with 70 patients with primary brain tumors and refractory epilepsy treated with lacosamide (Vimpat, UCB Pharma). Ninety-six percent of patients had gliomas, with glioblastoma being the most frequent histology (40%). They found that 66% of patients reported a decrease in seizures, with another 30% reporting stable seizure activity. In their analysis, they found this medication to be highly tolerable, as 77% of patients reported no “toxicities.”

Seizures represent a difficult problem in patients with brain tumors. Thirty percent to 50% of patients with brain tumors will present with a seizure.17,19 A clinical seizure is the presenting sign in as many as 70% of patients with high-grade gliomas (HGGs).16 The risk of developing intractable epilepsy is a fear for practitioners, patients, and their families. In LGGs, increased seizures have been found to be associated with tumor progression, failure to achieve gross-total resection, and a poorer prognosis.4,10 Although a history of seizure prior to diagnosis of glioblastoma has been reported to be associated with increased survival,11 many have found seizures in patients with HGGs to be associated with postoperative complications, tumor progression, and end of life.1,14

The treatment of patients with brain tumors and epilepsy poses a difficult problem. Patients with brain tumors tend to express multidrug-resistant proteins, which inhibit the availability of antiepileptic drugs (AEDs) to brain parenchyma.3,17 Moreover, enzyme-inducing AEDs interact with other medications and often require alteration of dosing for chemotherapeutic regimens.8,18 Furthermore, the tolerability of AEDs is often a concern for patients and practitioners.

Lacosamide is a third-generation AED approved by the FDA in 2008 as an adjunctive therapy for partial-onset seizures in adults with uncontrolled epilepsy. Several randomized controlled trials have documented its efficacy in patients with epilepsy as well as diabetic neuropathy.1,5,6,13 These studies have consistently shown a statistically significant decrease in seizure frequency and rate of response as compared with placebo without altering plasma levels of concomitant AEDs. Lacosamide selectively enhances slow inactivation of voltage-gated sodium channels without induction or alteration of cytochrome p450 enzymes. Clinical trials have shown good tolerability with the most common side effects being dizziness, nausea, and vomiting.1,2,5,6,13

The strength of the authors’ study lies in its originality, as it is just the second to document the effects of lacosamide as an adjunctive AED in patients with brain tumor.9 As stated earlier, patients suffering from brain tumor–related epilepsy can be difficult to treat adequately, so any publication that informs health care professionals and patients of a new treatment with potential efficacy and tolerability will be welcomed. Maschio and associates8 reported similar results in their analysis of 14 patients with poor seizure control and brain tumors who were treated with adjunctive lacosamide. The heterogeneity of the patient population described by Saria and associates is beneficial to readers as it simulates the “real-life” patient population with brain tumors that most practitioners encounter.

They report several limitations to their study, which largely stem from its being a retrospective medical record analysis. Although we need retrospective reviews to build “consensus” on the important questions or end points that should be asked in a potential prospective study, the variability in dosage-prescribing patterns, concurrent AEDs, and severity or frequency of seizures makes it more difficult to find that consensus. In addition, with this retrospective approach, it is difficult to objectively measure “tolerability” or identify other variables, which may account for a decrease in seizure activity. That said, it is often difficult to obtain prospective randomized levels of evidence, and much medical practice comes from the accumulation of reports such as these.

Patients with brain tumors will always have some risk of suffering seizures. The exact pathophysiology is not entirely understood, and practitioners suffer from limited medical options as a result of several factors. Although not without its limitations, the authors’ study is both novel and informative. Reports like theirs that introduce physicians to another option in treating tumor-related epilepsy are welcomed.

Disclosure

The authors report no conflict of interest.
Editorial

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We concur with Drs. Ikeda and Chiocca’s statement that controlling multiple variables may be difficult in a retrospective study. Hence, a proposal for a prospective randomized trial evaluating the use of lacosamide as an adjunctive treatment in the management of patients with brain tumors is currently being developed to support the data reported in our paper. It is common knowledge that there is no gold-standard AED in the multidisciplinary treatment of seizures in patients with brain tumors. Having another option in this patient population is welcome, as we still need to define the optimal AEDs that are effective and tolerable and do not interact with the other drugs frequently administered to patients with brain tumors, for example, analgesics, antidepressants, antipsychotics, and antineoplastic drugs.

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