

# Effectiveness of Levateracetam in Patients with Brain Tumors

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Brain TumorsNaeem ul Haq<sup>1</sup>, Rizwan<sup>2</sup>, Musawer Khan<sup>1</sup> and Brehna Rahim Khan<sup>1</sup>

## ABSTRACT

**Objective:** The present study aimed to assess the effectiveness of levateracetam in brain tumor's patients.

**Study Design:** A retrospective study

**Place and Duration of Study:** This study was conducted at the Neurosurgery, Mardan Medical Complex, Mardan from 16<sup>th</sup> April 2018 to 15<sup>th</sup> May 2023.

**Materials and Methods:** Patients diagnosed of brain tumors and placement on LEV were enrolled. All the patients with concomitant epileptic conditions were excluded. The frequency of seizure was calculated for each individual. The seizure frequency significant improvement was referred to seizure activity reduction (>50%) against pre-LEV baseline. Age, initial tumor location, gender, and treatment methods were also obtained for each patient.

**Results:** Of the total patients, there were 54 (55.1%) male and 44 (44.9%) females. The overall mean age was 48.62±12.86 years with an age range 20 to 80 years. Out of 98 BT patients, the incidence of partial seizure and generalized seizures was 84 (85.7%) and 14 (14.3%) respectively. Of the total, levetiracetam was administrated in 82 (83.7%) patients due to epilepsy diagnosis. Upon the final diagnosis, about 87.8% (n=72) patients taken levetiracetam were recovered and seizure free; due to intolerable adverse effects, 3 (3.7%) patients were withdrawn. There were no laboratory anomalies seen in subjects receiving concurrent treatment.

**Conclusion:** The present trial confirmed that levetiracetam is both effective and safe in brain tumor patients. As a result, brain tumor causing epileptic seizures can be treated with levetiracetam as a preferred or standard treatment.

**Key Words:** Levateracetam, Brain tumors, Effectiveness

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## INTRODUCTION

Brain tumors are serious medical disorders that cause significant morbidity and mortality.<sup>1</sup> Gliomas, metastases, meningiomas, and astrocytomas are different types of brain tumors.<sup>2</sup> Seizures are the most critical and severe consequences of brain tumors. The incidence of seizures reported in brain tumor's patients varied from 20% to 45% causing chronic morbidity and loss in life quality.<sup>3</sup> Craniotomy for tumor reduction or removal is the significant factor affecting the usage of antiepileptic medications (AEDs) in these individuals. In non-traumatic supratentorial craniotomy cases, the prevalence of seizures are expected to occur in 15-20%.<sup>4</sup> Tumor growth rate, seizure's prior history, location of tumor, and partial or full degree of tumor

resection in craniotomy are various factors that influence the onset of seizure.<sup>5</sup>

The first-line treatment for seizures is the new AEDs in the current clinical trends.<sup>6</sup> This is most likely due to the increased risk of side effects and medication interactions with other medicines.<sup>7</sup> Levetiracetam (LEV) is thought to alter synaptic neurotransmitter release in the brain by binding synaptic vesicle protein SV2A among these novel AEDs.<sup>8</sup> Seizures are prevalent in brain tumor patients, with rates ranging from 30% to 100% depending on the kind of tumor.<sup>9</sup> In fact, an epileptic seizure is the presenting sign of a tumor in 30-50% of patients, with 10-30% developing recurrent seizures during the course of the disease.<sup>10</sup> Seizures and convulsions have been demonstrated to cause significant morbidity in these individuals.<sup>11</sup> Due to these causes, levetiracetam might be beneficial medicine of brain tumor patients. As a result, the present study was carried out to assess the effectiveness of levateracetam in brain tumor's patients.

## MATERIALS AND METHODS

A retrospective study was carried out on 98 brain tumors in the Department of Neurosurgery, Mardan Medical Complex, Mardan from 16<sup>th</sup> April 2018 to 15<sup>th</sup> May 2023. Patients diagnosed of brain tumors and placement on LEV were enrolled. All the patients with concomitant epileptic conditions were excluded. The frequency of seizure was calculated for each individual.

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The seizure frequency significant improvement was referred to seizure activity reduction (>50%) against pre-LEV baseline. Age, initial tumor location, gender, and treatment methods were also obtained for each patient. The seizure's cluster arisen within 24 hours was considered as a single event. Gender, onset to seizure type, lesion location, age at diagnosis, surgery types, chemotherapy, and seizure's emergency timing, post-operative radiation were recorded. SPSS version 27 was used for data analysis. Numerical variables were described as mean and standard deviation whereas categorical variables were expressed as frequency and percentages by taking 95% confidence interval and 5% level of significance.

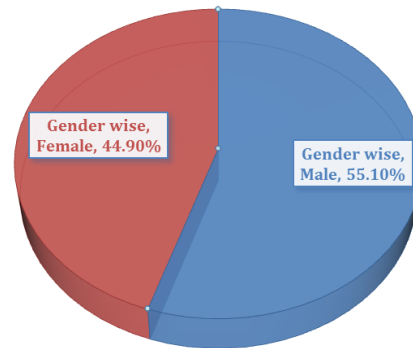
**RESULTS**

**Table No. 1: demographic details and onset of symptoms**

Parameters	N (%)
Age (years)	48.62±12.86
Gender N (%)	
Male	54 (55.1)
Female	44 (44.9)
Disease duration	12.6 [27 d to 2 y]
Onset of symptoms N (%)	
Epilepsy	38 (38.8)
Single seizure	6 (6.1)
Headache	26 (26.5)
Focal neurologic deficit	16 (16.3)
Memory deficit	8 (8.2)
Psychiatric symptoms	2 (2.04)
No symptoms	2 (2.04)

Of the total patients, there were 54 (55.1%) male and 44 (44.9%) females. The overall mean age was 48.62±12.86 years with an age range 20 to 80 years. Out of 98 BT patients, the incidence of partial seizure and generalized seizures was 84 (85.7%) and 14 (14.3%) respectively. Of the total, levetiracetam was administrated in 82 (83.7%) patients due to epilepsy diagnosis. Upon the final diagnosis, about 87.8% (n=72) patients taken levetiracetam were recovered and

seizure free; due to intolerable adverse effects, 3 (3.7%) patients were withdrawn. An administration of levetiracetam dosage (1500 to 3000 mg/d) led to long-lasting control of seizures in 46 (56.1%) cases and dosage of 4000 mg/d was needed in 12 (14.6%) patients in order to become seizure free. There were no laboratory anomalies seen in subjects receiving concurrent treatment. The demographic details and onset of symptoms are shown in Table-1. The tumor Histological Grades in Patients are shown in Table-2. Types of Seizures and Histological Grades in brain tumors Patients are shown in Table-3.



**Figure No. 1: Gender wise**

**Table No. 2: Tumor Histological Grades in BT Patients with epilepsy (N=82)**

Histological Grades	N (%)
Grade I-II (N=14) N (%)	
Pilocytic astrocytoma	2 (2.4)
Astrocytoma II	3 (3.7)
Oligodendroglioma II	7 (8.5)
Fibrillary astrocytoma	2 (2.4)
Grade III (N=16) N (%)	
Anaplastic oligodendroglioma	5 (6.1)
Anaplastic oligoastrocytoma	3 (3.7)
Anaplastic astrocytoma	8 (9.8)
Grade IV (N=52) N (%)	
Glioblastoma multiforme	48 (58.5)
Gliosarcoma	4 (4.8)

**Table No. 3: Types of Seizures and Histological Grades in Patients with Primary Brain Tumor and Epilepsy (N=82)**

Parameters	Seizure Free (N=72)	Drug resistance (N=10)	Total (N=82)
Types of Seizures			
Complex partial	26/26 (100)	0 (0)	26/82 (31.7)
Simple partial motor	13/18 (72.2)	5/18 (27.8)	18/82 (22)
Simple partial sensory	9/11 (81.8)	2/11 (18.2)	11/82 (13.4)
Secondary generalization	17/17 (100)	0 (0)	17/82 (20.7)
Histological Grades			
I-II	14/14 (100)	0 (0)	14/82 (17.1)
III	14/16 (87.5)	2/16 (12.5)	16/82 (19.5)
IV	48/52 (92.3)	4/52 (7.7)	52/82 (63.4)

## DISCUSSION

The present study mainly focused on the effectiveness of levetiracetam in brain tumor patients and found that in brain tumor patients with epilepsy, levetiracetam is both effective and safe. As a result, levetiracetam can be used as a preferred or standard therapy for brain tumors that cause epileptic seizures. About 4% to 5% epilepsy cases are caused by brain tumors in patients suffering from seizure disorders.<sup>11,12</sup> The initial symptom of seizures confirmed their diagnosis that arises in later stages. As a result, even in the absence of seizures, the brain tumors patients taking AEDs is the prevalent practice, despite mounting evidence that AEDs do not prevent epileptogenesis and that most of them may lower anti-tumoral medication levels and chemotherapy effectiveness.<sup>13</sup> Regarding the levetiracetam efficacy in brain tumor's patients, it was shown earlier that older practice of AEDs in limited patients were less effective.<sup>14</sup> The present study findings are comparable to a previous study according to which the brain tumor with symptomatic epilepsy could be effectively treated with levetiracetam. Seizures are common in individuals with BT, ranging from 27 to 50%.<sup>15</sup>

The present study revealed that effective way of treating the AEDs in brain tumor patients are LEV. Additionally, the frequency of seizure significantly improved with starting LEV is a treatment modality. The LEV uses as monotherapy appears to be more beneficial. About 87.8% patients were seizure free upon the usage of LEV for epilepsy in brain tumor patients. An earlier study conducted on adult patients revealed that LEV as monotherapy is an active, effective, and well-tolerated treatment.<sup>16</sup>

Another study reported that carbamazepine is a similar efficacy in newly diagnosed epilepsy treatment.<sup>17</sup> According to AAN (American Academy of Neurology), there is limited evidence of LEV used as monotherapy for newly diagnosed epilepsy or partial seizures.<sup>18,19</sup> When choosing suitable AED medication, tumor-induced seizures must be examined independently from typical epilepsy. The side effect of severe AEDs are significantly higher (approximately 20% to 40%) than AEDs required in general population. Thrombocytopenia, ataxia, Myelosuppression, and increased liver enzymes are the most often reported AED adverse effects in individuals with brain tumors.<sup>21</sup> AEDs associated insufficient blood levels, chemotherapeutic drugs, and corticosteroids interaction in brain tumor's patient's results suboptimal malignancy therapy and seizure control. Valproate is a recognized inhibitor, which can result in elevated and potentially hazardous blood levels of chemotherapy drugs.<sup>22,24</sup> LEV has less chance of unfavorable drug-drug interactions is a better AED option brain tumors patients.<sup>25,26</sup>

Other studies found that adding levetiracetam to the mix resulted in seizure reduction or complete control of seizure. Similar to other study findings, it's enticing to believe that levetiracetam's greater antiepileptic effect in tumors such as a disease involving astrocytes, is due, at least in part, to its unusual antiepileptic properties.

## CONCLUSION

The present trial confirmed that levetiracetam is both effective and safe in brain tumor patients. As a result, brain tumor causing epileptic seizures can be treated with levetiracetam as a preferred or standard treatment.

### Author's Contribution:

Concept & Design of Study:	Naeem ul Haq
Drafting:	Rizwan, Musawer Khan
Data Analysis:	Brehna Rahim Khan
Revisiting Critically:	Naeem ul Haq, Rizwan
Final Approval of version:	Naeem ul Haq

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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