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ORIGINAL ARTICLE

Adjuvant therapy versus surgery in controlling seizure in patients with low-grade glioma tumor

Mehdi Nikoobakht[1] ✉, Maziar Azar[2], Amir Pakpour Hajiagha[3], Seyedeh Fahimeh Shojaei[4], Yasaman Khalili Baseri[5]

[1] *Assistant Professor of Neurosurgery, Department of Neurosurgery, Firoozgar Clinical Research and Development Center (FCRDC), Iran University of Medical Sciences (IUMS), Tehran, Iran*

[2] *Associate Professor, Neurosurgery ward of Rasool-e-Akram Hospital Complex, Department of Neurosurgery, Iran University of Medical Sciences, Tehran, Iran*

[3] *Associate Professor of health psychology, Department of Public Health, Faculty of Health, Qazvin University of Medical Sciences, Qazvin, Iran*

[4] *MSc, Clinical Psychologist, Firoozgar Clinical Research and Development Center (FCRDC), Iran University of Medical Sciences (IUMS), Tehran, Iran*

[5] *Medical Student, Young Researchers and Elites Club, Faculty of Medicine, Islamic Azad University, Yazd Branch, Yazd, Iran*

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Abstract

Introduction: Since surgical treatment for tumorous lesions does not always lead to complete patient recovery, it is possible for the attacks to continue. To help plan for the patients' health, this study aimed to compare the therapeutic effects of adjuvant therapy and surgery in controlling seizure of low-grade glioma (LGG) patients in Firoozgar Hospital in 2013-2014.

Methods: In this analytical cross-sectional study, 114 patients with LGG (grade 2) tumors admitted in Firoozgar Hospital during 2013-2014 were divided into two groups of adjuvant therapy and surgical treatment. All of these patients were followed by telephone and were asked about the incidence, frequency, and intensity of seizure attacks up to one year after surgery. The age and sex of the patients, along with the drug used after surgery, were also recorded on a checklist. Electroencephalography (EEG) was performed on all the patients under the supervision of a neurologist. Patient information was entered into the SPSS V.16 and analyzed. Chi-2 test was used to analyze and compare the qualitative variables, and T-test was employed to compare quantitative variables between the two groups. Alpha values below 0.05 were considered significant.

Results: In the present study, the incidence of seizure after surgery and adjuvant therapy were 16 (1.28%) and 20 (35.1%), respectively. The severity of seizure before and after treatment was not significantly different between the two groups. However, in both groups the severity and frequency of seizure decreased significantly after treatment, although there was no significant difference between the two groups before and after treatment. In the surgery group, 17 patients (29.82%) and in the adjuvant therapy group, 19 patients (33.33%) had an unusual EEG. There was a significant correlation between the post-treatment seizure and abnormal EEG ($p < 0.001$).

Conclusions: Based on the results of this study, it can be concluded that the incidence, severity, and frequency of seizure in patients with LGG were decreased after surgical treatment or adjunct therapy, but there is no significant difference between the two methods.

Key Words: Brain Neoplasm; Seizure; Adjuvant therapy; Glioma; Surgery

Introduction

Introduction

Low-grade glioma (LGG) is a progressive and invasive tumor that typically occurs in young adults. However, about half of LGG cases ultimately progress to malignant changes, and in such cases, the prognosis is mild. There is no standard strategy

Tel: +985632381203
Fax: +985632440488
Po Bax 97175-379
Email: jsurgery@bums.ac.ir

✉ **Correspondence to:**
Mehdi Nikoobakht, Assistant Professor of Neurosurgery, Department of Neurosurgery, Firoozgar Clinical Research and Development Center (FCRDC), Iran University of Medical Sciences (IUMS), Tehran, Iran;
Telephone Number: +989122029419
Email Address: mnikobakht@gmail.com

for LGG. Recently, the importance of extent of resection (EOR) for LGG has been reported, and maximum resection has recently been presented as a standard protocol (1).

In general, the LGG treatment pattern includes surgical resection and then adjuvant therapy for patients at risk. These tumors are overwhelming and generally unconsolidated by surgical resection treatment (2).

The role of surgical removal is still unclear. The overall length of survival for this patient population is relatively long, and its precise determination is significant without a solid test by collecting long-term data (3). Moreover, cohort studies indicate that after complete tumor resection, seizures are controlled (4).

Studies have shown that patients treated with surgery are more likely to have problems with assessment, diagnosis, treatment, and rehabilitation and cognition than patients who have not undergone surgery. These disorders are difficult in patients with glioma tumors, and depression can be contributory to the survival and quality of life (5).

In particular, patients with incomplete resection and elderly people with LGG are more likely to be relapsed [6-10]. Adjuvant therapy includes chemotherapy, radiation therapy (RT), or both. Adjuvant therapy (RT) enhances seizure and progression-free survival (PFS) but has no effect on overall survival (11).

In this study, we compared the therapeutic effect of adjuvant therapy and surgery in controlling seizure of LGG patients in Firoozgar Hospital in 2013-2014.

Methods

This is an analytical cross-sectional study where all the patients with LGG (Grade 2) (114 patients) referred to Firoozgar Hospital in Tehran, Iran, were enrolled via the census method during 2013-2014. The data included the age and sex of the patients, the incidence of seizure, the severity and frequency of post-operative surgery, the severity of pre-surgical seizure, and post-surgical drug use as filled out on a checklist.

These patients were divided into two groups: adjuvant therapy or surgical treatment. The two groups were treated based on the indication of the disease and the standard treatment described in Youmans and Winn's *Neurological Surgery*.

Regarding the fact that chemotherapy does not obstruct blood-brain barrier, the treatment of adjuvant therapy in all patients with LGG, except those with oligodendroglioma, included about 30 radiotherapy sessions at a rate of 30 grams. In addition to radiotherapy, patients with oligodendroglioma were also treated with a standard oncology chemotherapy method.

All of these patients were followed by telephone and were asked about the incidence and frequency of seizure severity up to one year after surgery. The required information was recorded on the checklist and compared between the two groups. Seizure severity was scored by Engel criteria.

Electroencephalography (EEG) was performed on all the patients under the supervision of a neurologist.

According to the Helsinki Declaration, the information was recorded confidentially and explanations were given to patients before the study initiated. The ethics code was taken from the Ethics Committee affiliated with Iran University of Medical Sciences (Code: IR.IUMS.REC.1394.8521215641). All patient information remained confidential and no additional costs were imposed on patients.

The information was entered into and analyzed in the SPSS Software V.16. For descriptive analysis, frequency, mean, and standard deviation were used. Chi-2 test was used to analyze and compare the qualitative variables and T-test was used to compare quantitative variables between the two groups.

Categorical data are presented as numbers (%), and continuous data as mean ± SD. Correlations between seizures and other variables were calculated by logistic regression test. An α-value below 0.05 was considered significant.

Results

In this study, 57 patients with low grade glioma (Grade 2) in the treatment group and 57 patients in the adjuvant therapy group were evaluated.

The average age of the treatment group was 50.75 (SD = 11.17) years. The minimum age was 31 and the maximum age was 76 years. The mean age of the adjuvant therapy group was 52.56 (SD = 12.69) years. There was no significant difference between the mean age of the two groups (p = 0.42).

Among men undergoing surgical treatment, 32 (56.1%) were men and 25 (43.9%) were women, and among those treated with adjuvant therapy, 35 were men (61.4%) and 32 (38.6%) were women.

Seizure after surgery was 16 (28.1%) and seizure after adjuvant therapy was 20 (35.1%), which was not statistically significant (P = 0.42). The severity of seizure was not significant before treatment (P = 0.95). Also, after the treatment, the severity of the seizure was not significantly different between the two groups (P = 0.68). Moreover, the severity of seizure significantly decreased after treatment in both groups (p <0.001).

The frequency of seizure was significantly reduced after treatment with both surgical and adjuvant therapy groups (P <0.001), although there was no significant difference between the two groups before and after treatment (P> 0.05).

In the surgery group, 17 patients (29.82%) and in the adjuvant therapy group, 19 patients (33.33%) had an unusual EEG. There was a significant correlation between post-treatment seizure and abnormal EEG (p <0.001)

Discussion

Previous studies indicate that some brain tumors are related to seizures. These studies have reported that about 95% of glioneuronal tumors and more than 75% of LGGs will develop tumor-related epilepsy. Moreover, the incidence of seizures in patients with high-grade glioma is about 30–50% and with meningioma 25 % (17).

Regarding the outcome in our practice, 48 (77.4%) of the patients became seizure-free within 24 months and experienced improvement after surgery, which is lower than the rate reported in Melo et al.'s study with an 85% seizure-free rate within 27 months (18). In the current practice, seizures occurred in 11.3% of the patients after six months and increased to 21% after 24 months of operation; in other words, 21% of the patients (13 out of 62) showed seizures within 24 months. The surgery outcome in our report was in contrast to the outcome reported in Kanchanatawan et al's study where the incidence of seizures decreased during follow-up (13). On the other hand, sex and age did not have an impact on the surgery outcome in the current practice, which is in contrast to Kanchanatawan et al.'s results where age, family history, preoperative symptoms, and location of the tumor correlated significantly with surgery outcomes.

However, in the current practice, the grade of the tumor predicted the presence of the seizure after surgery that is in line with Kanchanatawan et al.'s cohort study (13). In our cohort, the most important factor that impacted the outcome of the surgery was drug therapy. A study by Kahlenberg et al. evaluated the seizure prognosis of patients with low-grade tumors, showing new-onset seizures after tumor surgery in three of the 73 patients during a 3.8-year follow-up. They indicated that the most important factor associated with continued seizures after tumor surgery is the presence of seizure at presentation. Moreover, they indicated that pathology did not influence seizure outcome (14). However, as opposed to Kahlenberg et al., we revealed that the type of the tumor predicted the presence of seizures at 24 months after the operation.

Furthermore, in our experience, resection of the tumor predicted the presence of seizures 24 months after the operation. In line with our report, Chang et al. and Choi et al. indicate that gross-total resection of a LGG is correlated with better outcomes (12,15). Yet, as opposed to our study, Kahlenberg et al. and Al-Asmi et al. emphasize that the correlation between the extent of resection and seizure outcome is not significant (14,16). In the current cohort, the most frequent brain tumor was glioma followed by meningioma. This finding corresponds with the experience of previous studies by Fish et al. and Demierre et al., which report glioma as the most prevalent brain tumor associated with epilepsy (17,18).

In summary, the current study and previous reports indicate that to improve the success rate of epilepsy surgery, some criteria based on clinical and biological characteristics are highly important and strongly affect the incidence of postoperative seizures. In this case, it is clear that neurological predictors, type of resection, type and location of the tumor, grading, etc. (20-22) should be considered in patient selection to improve surgery outcomes.

There are a number of limitations in this study that warrant mention. The incomplete records of the patients were excluded from the study. Non-response to the calls was a limitation in which case the patients were contacted on the following days.

Further investigations are recommended with longer follow-up periods and larger series to validate the findings reported here. Additional follow-ups of current cohorts will answer the question regarding whether the surgery is a true disease modifier.

Conclusions

We revealed that incidence, severity, and frequency of seizure in patients with LGG were reduced after the surgical treatment and adjuvant therapy, but there was no significant difference between these two methods.

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Authors' Contribution

Dr.Mehdi Nikoobakht: the main idea of the study
Dr.Maziar Azar: Review of the literature
Dr.Amir Pakpour Hajiagha: Data analysis
Seyedeh Fahimeh Shojaei: Data collection
Dr .Yasaman Khalili Baseri: writing the manuscript

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Conflict of interest

There are no conflicts of interest to declare.

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