

Original Research

Evaluation of Drug-Resistant Epilepsy Among Children

¹Dr. Syed Mohd Arshad, ²Dr. Gajendra Singh Dhakar, ³Dr. Chiya Chaudhary

¹Senior Resident, Department of Pediatrics, Shyam Shah Medical College Rewa, Madhya Pradesh, India

^{2,3}Junior Resident, Department of Pediatrics, Shyam Shah Medical College Rewa, Madhya Pradesh, India

Corresponding Author

Dr. Syed Mohd Arshad

Senior Resident, Department of Pediatrics, Shyam Shah Medical College Rewa, Madhya Pradesh, India

Received: 26 May, 2023

Accepted: 12 June, 2023

Abstract

Background: This study was a Retrospective Clinical Analysis of Epilepsy Treatment for Children with Drug-Resistant Epilepsy

Material and methods: Data from 100 DRE subjects were examined. The following were the inclusion criteria for patients: (1) belonged to the age range of 1 to 14 years; (2) had uncontrollably occurring seizures with the use of an AED and adrenocorticotrophic hormone therapy; (3) had undergone tests using MRI, CT, and VEEG; (4) follow-up data were available; and (5) guardians provided informed consent. Exclusion criteria included: (1) benign epilepsy syndromes in children, such as benign occipital epilepsy, benign childhood epilepsy with centro-temporal spikes, and other syndromes better managed with AEDs; (2) unclear recurrence of seizures or incomplete removal of epileptogenic foci (Figure 1); (3) patients with a history of surgical resection. Statistical analysis was conducted using SPS software.

Results: In this study of 100 subjects, there were 50 males and 50 females. Generalized tonic seizures were seen in 39 subjects, complex partial motor type was seen in 27 subjects, generalized tonic-clonic seizures were seen in 17 subjects and simple partial motor seizures were seen in 16 subjects. 40 subjects with epilepsy were treated by medication, 35 as well as 25 subjects had been managed with resection surgery as well as palliative surgery, respectively. Favourable seizure outcomes had been noticed among 10, 25, and 15 subjects on medication, resection surgery, as well as palliative groups, after 1-year follow-up; 8, 21, and 10 subjects after 3-year follow-up; 6, 17, and 9 subjects after 5-year follow-up.

Conclusion: Children's growth and cognitive ability were negatively impacted by recurrent seizures. Preventing mental retardation and controlling seizures could both benefit from early surgical intervention. Patients who were not good candidates for resection surgery might potentially consider palliative surgery.

Keywords: epilepsy, treatment, seizures.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Introduction

Seizures are common and are treated in all branches of medicine. Approximately 10% of the population will have one or more seizures during their lifetime. Seizures are symptoms that occur in acute illness, i.e., provoked seizures, or in epilepsy, i.e., unprovoked seizures. Epilepsy is any disorder in which spontaneous recurrence of unprovoked seizures is the main symptom. It is a common chronic neurologic disorder and affects 1% to 3% of the population. Classification of seizure type is important because it enables identification of the region of the brain where the seizure originated and guides initial diagnostic testing. Classification of epilepsy syndrome, rather than only type of seizure, is more important. Epilepsy syndromes are defined by many factors, including type of seizures, age at onset of seizures, family history of seizures, and findings at physical examination, electroencephalography (EEG), and neurologic imaging studies. Identifying the epilepsy

syndrome provides insight into natural history, prognosis, diagnostic testing, and therapy of the disorder and facilitates communication between health care professionals.¹ In most patients with epilepsy, seizures respond well to antiepileptic medication. Although antiepileptic drugs (AEDs) are used either alone or in combination, epileptic seizures cannot be controlled in 10%–20% of patients.^{2,3} Although drug-resistant epilepsy patients constitute a minor part of the patients with epilepsy, they suffer from the significant psychosocial and economic burden of the disease and require considerable time and effort from the physician. Drug-resistant epilepsy has generally been associated with intellectual disability, psychiatric comorbidity, physical damage, sudden unexpected death, and low quality of life.⁴ Children with refractory epileptic seizures use multiple antiepileptic drugs for long term, which may negatively affect their cognitive and physical development. Early prediction of drug-resistant epilepsy may enable patients to be

evaluated earlier in terms of alternative treatments such as ketogenic diet, epilepsy surgery, or vagal nerve stimulation. Providing patients with appropriate treatment in a timely manner may prevent the development of comorbidities associated with drug-resistant epilepsy.

This study was a Retrospective Clinical Analysis of Epilepsy Treatment for Children with Drug-Resistant Epilepsy

In this study of 100 subjects, there were 50 males and 50 females. Generalized tonic seizures were seen in 39 subjects, complex partial motor type was seen in 27 subjects, generalized tonic-clonic seizures were seen in 17 subjects and simple partial motor seizures were seen in 16 subjects. 40 subjects with epilepsy were treated by medication, 35 as well as 25 subjects had been managed with resection surgery as well as palliative surgery, respectively. Favourable seizure outcomes had been noticed among 10, 25, and 15 subjects on medication, resection surgery, as well as palliative groups, after 1-year follow-up; 8, 21, and 10

subjects after 3-year follow-up; 6, 17, and 9 subjects after 5-year follow-up.

Material and methods

Data from 100 DRE (Drug Resistant Epilepsy) subjects were examined. The following were the inclusion criteria for patients: (1) belonged to the age range of 1 to 14 years; (2) had uncontrollably occurring seizures with the use of an AED and adrenocorticotrophic hormone therapy; (3) had undergone tests using MRI, CT, and VEEG; (4) follow-up data were available; and (5) guardians provided informed consent. Exclusion criteria included: (1) benign epilepsy syndromes in children, such as benign occipital epilepsy, benign childhood epilepsy with centro-temporal spikes, and other syndromes better managed with AEDs; (2) unclear recurrence of seizures or incomplete removal of epileptogenic foci (Figure 1); (3) patients with a history of surgical resection. Statistical analysis was conducted using SPS software.

Results

Table 1: Gender-wise distribution of subjects

Gender	Number of subjects	Percentage
Males	50	50%
Females	50	50%
Total	100	100%

In this study of 100 subjects, 50 were males and 50 were females.

Table 2: Seizure types

Types of seizures	Number of subjects	Percentage
Generalized tonic seizure	39	39%
Complex partial motor	28	28%
Generalized tonic-clonic seizures	17	17%
Simple partial motor	16	16%

Generalized tonic seizures were seen in 39 subjects, complex partial motor type was seen in 27 subjects, generalized tonic-clonic seizures were seen in 17 subjects and simple partial motor seizures were seen in 16 subjects.

Table 3: Treatment groups for epilepsy.

Treatment	Number of subjects	Percentage
Medication	40	40%
Resection surgery	35	35%
Palliative surgery	25	25%
Total	100	100

40 subjects with epilepsy were treated by medication, 35 as well as 25 subjects had been managed with resection surgery as well as palliative surgery, respectively. Favourable seizure outcomes had been noticed among 10, 25, and 15 subjects on medication, resection surgery, as well as palliative groups, after 1-year follow-up; 8, 21, and 10 subjects after 3-year follow-up; 6, 17, and 9 subjects after 5-year follow-up.

Discussion

Epilepsy is among the most common chronic neurological disorders affecting the quality of life in patients. Children constitute the majority of epilepsy patients with an annual incidence rate of 41–187/100,000, which is much higher than that of adults.⁵ In China, this ratio reaches 151/100,000.⁶ The causes of seizures are diverse and are generally classified as genetic, structural and metabolic, and unknown.⁷

Antiepileptic drugs (AEDs) are the main form of treatment. About 70% of patients respond well to

AEDs and achieve seizure-free outcome. In 20%–30% of cases, however, seizures remain uncontrollable.⁸⁻¹⁰ The International League Against Epilepsy (ILAE) defined drug-resistant epilepsy (DRE) as a failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.¹¹ In such cases, surgical intervention is widely used as the primary treatment for pediatric epilepsy.¹²

This study was a Retrospective Clinical Analysis of Epilepsy Treatment for Children with Drug-Resistant Epilepsy

Karaoğlu P et al (2021)¹³ determined the clinical, electroencephalographic, and radiological factors associated with medically intractable childhood seizures. Data regarding 177 patients diagnosed with drug-resistant epilepsy were compared with 281 patients with drug-responsive epilepsy. Univariate analysis showed that age at seizure onset, having mixed seizure types, history of status epilepticus, history of neonatal seizures, history of both having febrile and afebrile seizures, daily seizures at the onset, abnormality on the first electroencephalogram, generalized epileptic abnormality on electroencephalogram, abnormal neurodevelopmental status, abnormal neuroimaging, and having symptomatic etiology were significant risk factors for the development of drug-resistant epilepsy ($p < 0.05$). In multivariable analysis, having mixed seizure types, history of status epilepticus, having multiple seizures in a day, intellectual disability, symptomatic etiology, and neuroimaging abnormality remained significant predictors for developing drug-resistant epilepsy. In the course of childhood epilepsy, some clinical features may predict the outcome. Early identification of patients with high risk for drug-resistant epilepsy will help plan the appropriate treatment option. Further prospective studies should confirm these findings.

Liu C et al (2022)¹⁴ investigated the clinical characteristics and seizure outcomes of patients aged 1–14 years with drug-resistant epilepsy (DRE) who were treated by different typologies of therapy. Four hundred and eighteen children with DRE were recruited from Sanbo Brain Hospital of Capital Medical University from April 2008 to February 2015. The patients were divided into three groups: medication ($n = 134$, 32.06%), resection surgery ($n = 185$, 44.26%), and palliative surgery ($n = 99$, 23.68%) groups. Demographic characteristics were attained from medical records. All patients were followed up for at least 5 years, with seizure outcomes classified according to International League Against Epilepsy criteria. The psychological outcome was evaluated with the development quotient and Wechsler Intelligence Quotient Scale for children (Chinese version). The most frequent seizure type was generalized tonic seizure in 53.83% of patients. Age at seizure onset in 54.55% of patients was < 3 years. The

most frequent etiologies were focal cortical dysplasia (FCD). West syndrome was the most common epilepsy syndrome. Favorable seizure outcomes at the 5-year follow-up in the medication, resection surgery, and palliative surgery groups were 5.22%, 77.30%, and 14.14%, respectively. The patients showed varying degrees of improvement in terms of developmental and intellectual outcomes post-treatment. Pediatric patients with DRE were characterized by frequent seizures, a variety of seizure types, and complex etiology. Recurrent seizures severely affected the cognitive function and development of children. Early surgical intervention would be beneficial for seizure control and prevention of mental retardation. Palliative surgery was also a reasonable option for patients who were not suitable candidates for resection surgery.

Conclusion

Children's growth and cognitive ability were negatively impacted by recurrent seizures. Preventing mental retardation and controlling seizures could both benefit from early surgical intervention. Patients who were not good candidates for resection surgery might potentially consider palliative surgery.

References

1. Shneker BF, Fountain NB. Epilepsy. *Dis Mon.* 2003 Jul;49(7):426-78.
2. Berg AT, Shinnar S, Levy SR, Testa FM, Smith-Rapaport S. Early development of intractable epilepsy in children: a prospective study. *Neurology* . 2001;56:1445–1452.
3. Berg AT, Rychlik K. The course of childhood-onset epilepsy over the first two decades: a prospective longitudinal study. *Epilepsia* . 2015;56:40–48.
4. Trinka E, Hirsch LJ, Cendes F, Langfitt J. The consequences of refractory epilepsy and its treatment. *Epilepsy and Behaviour* . 2014;37:59–70.
5. Camfield P., Camfield C. Incidence, prevalence and aetiology of seizures and epilepsy in children. *Epileptic Disord. Int. Epilepsy J. Videotape.* 2015;17:117–123.
6. Hong Z. New progress of epidemiological research in epilepsy. *Chin. J. Contemp. Neurol. Neurosurg.* 2014;14:919–923.
7. Berg A., Berkovic S., Brodie M., Buchhalter J., Cross J., van Emde Boas W., Engel J., French J., Glauser T., Mathern G., et al. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia.* 2010;51:676–685.
8. Lee K., Lee Y., Seo J., Baumgartner J., Westerveld M. Epilepsy surgery in children versus adults. *J. Korean Neurosurg. Soc.* 2019;62:328–335.
9. Wirrell E., Wong-Kissel L., Mandrekar J., Nickels K. “Predictors and course of medically intractable epilepsy in young children presenting before 36 months of age: A retrospective, population-based study. *Epilepsia.* 2012;53:1563–1569.
10. Liu C., Wen X., Ge Y., Chen N., Hu W., Zhang T., Zhang J., Meng F. Responsive neurostimulation for the treatment of medically intractable epilepsy. *Brain Res. Bull.* 2013;97:39–47.

11. Kwan P., Arzimanoglou A., Berg A.T., Brodie M.J., Allen Hauser W., Mathern G., Moshe S.L., Perucca E., Wiebe S., French J. Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia*. 2010;51:1069–1077.
12. De Knecht V.E., Hoei-Hansen C.E., Knudsen M., Jakobsen A.V., Muller E., Thomsen K.M., Jespersen B., Uldall P.V., Borresen M.L. Increase in cognitive function is seen in many single-operated pediatric patients after epilepsy surgery. *Seizure*. 2020;81:254–262.
13. Karaoğlu P, Yaş U, Polat Aİ, Ayanoglu M, Hız S. Clinical predictors of drug-resistant epilepsy in children. *Turk J Med Sci*. 2021 Jun 28;51(3):1249-1252.
14. Liu C, Hu Y, Zhou J, Guan Y, Wang M, Qi X, Wang X, Zhang H, Adilijiang A, Li T, Luan G. Retrospective Clinical Analysis of Epilepsy Treatment for Children with Drug-Resistant Epilepsy (A Single-Center Experience). *Brain Sci*. 2022 Dec 21;13(1):14.