DRUG REVIEW

Paediatric Epilepsy:Treatment Updates

S.K Gupta, Shruti Gupta, Ajay Gupta*, HK Sharma

Introduction

Seizure disorders are one of the common neurologic problems observed in childhood. Paediatric epilepsies constitute a heterogeneous group of conditions with different diagnostic criteria and management. Despite recent developments in the treatment of epilepsy, it is observed that many clinical questions remain unanswered. However, a number of new treatments promise a better quality-of-Life for individuals with epilepsy (1).

Common Type of Seizures in Paediatric Age Group

A) Symptomatic myoclonic and generalized tonic - clonic seizures; B) Complex partial seizures; C) Infantile Spasms; D) Juvenile Myoclonic Epilepsy; E) Benign Childhood Epilepsy with Centro Temporal spikes; F) Absence Epilepsy; G) Febrile Seizures; H) Neonatal Seizures.

Symptomatic Myoclonic & GTC Seizures: For Symptomatic myoclonic and generalized tonic-clonic seizures among Children, valproate has been the treatment of choice (1). For children of any age, it is recommended that the therapy should begin with at least two and possibly three trials of monotherapy, before trying at least two or possibly three combinations of 2 antiepileptic drugs. If combination therapy with (2) agents is ineffective, then a combination of (3) antiepileptic drugs is recommended. Of the available agents, valproate is recommended as treatment of choice for symptomatic generalized tonic-clonic seizures. Other drugs which can be used are Lamotrigine, levetiracetam & topiramate.

Complex Partial Seizures: Non-lesional cryptogenic complex partial seizures in an otherwise healthy child is treated with two or even three trials of monotherapy before trying one or two trials of a combination of 2 antiepileptic drugs. However, if these strategies are not successful then an evaluation for epilepsy surgery or additional trials of combinations of 2 or 3 antiepileptic drugs is recommended. For a healthy child with mesial temporal sclerosis and complex partial seizures, two to three trials of monotherapy and would then consider a trial of a combination of 2 antiepileptic drugs or an evaluation for epilepsy surgery.In temporal lobe epilepsy, surgical intervention may result in improved quality-of-life for the child. For initial monotherapy carbamazepine and oxcarbazepine are considered as treatments of choice, and valproate is also considered as an appropriate firstline agent.

Neonatal Seizures: Neonatal seizures are a common problem that affects about 1 to 4 infants out of every 1,000 live births (2). There are no standard treatment protocols for treating neonatal status epilepticus. However, a panel of experts suggested initiating therapy with an intravenous, intramuscular, or rectal benzodiazepine or an intravenous or intramuscular anti epileptic drug.If this therapy fails then second dose of the same anti epileptic drug or benzodiazepine is recommended. If this strategy fails then, benzodiazepine and anti epileptic drug back-to-back or monotherapy with a different IV, IM or rectal benzodiazepine or with a different IV or IM antiepileptic drug should be considered. Once the seizure stops, preventive treatment should be continued for 3 to 4 months. Among the available agents, intravenous phenobarbital is the treatment of choice. If initial therapy fails then intravenous phenobarbital and intravenous phenytoin are considered treatments of choice for the next option. In routine oral phenobarbitone to be given for preventive therapy of Neonatal seizures.

Infantile Spasma: For a healthy 6-month-old with infantile spasms three trials of monotherapy before trying one or more combinations of 2 antiepileptic drugs are recommended. Multiple trials of medication are to be considered before evaluation for epilepsy surgery for the treatment of infantile spasms. Vigabatrin is the treatment of choice for spasms caused by tuberous sclerosis. For spasms that are symptomatic in etiology, the treatment of choice was also vigabatrin, with ACTH and prednisone also usually appropriate.

Febrile Seizures: As an acute treatment for prolonged febrile seizure or cluster of febrile seizure, rectal diazepam therapy or intranasal midazolam is considered as a treatment of choice. Rectal diazepam in prolonged febrile seizures is supported based on its efficacy as a T/t for acute seizures (3). Valproate is regarded as the treatment of choice as preventive therapy for febrile seizures. Phenobarbital & valproic acid are the only two drugs, which are efficacious in preventing febrile seizures (4).

From the Department of Neurology & *G. Medicine Govt Medical College, Jammu (J&K) - India
Correspondence to : Dr. S.K Gupta Prof & Head Neurology Govt Medical College, Jammu (J&K)-India

Juvenile Myoclonic Epilepsy: For juvenile myoclonic epilepsy in adolescent males, valproate is treatment of choice, with lamotrigine another first-line option; for juvenile myoclonic -epilepsy in adolescent females, lamotrigine is treatment of choice, with valproate another first-line option. Valproate continues to be rated as the most effective agent in the treatment of JME and idiopathic generalised seizures, a view supported by two recent review articles and supported by the recent SANAD randomised controlled trial (1). Sometimes Levetiracetam can also be used as an additional drug where seizures are not controlled.

Benign Childhood Epilepsy With CentroTemporal Spikes: Valproate is the treatment of choice and also carbamazepine is sometimes appropriate. Sulthiame is considered a first-line drug depending on its availability (5). Gabapentin is considered third-line drug despite documented efficacy and safety profile in benign childhood epilepsy with centro-temporal spikes (6). Gabapentin and sulthiame are the only drugs that are evaluated in the treatment of benign childhood epilepsy with centro-temporal spikes (7,8). Carbamazepine and oxcarbazepine which are often used in the treatment of benign childhood epilepsy with centro-temporal spikes are associated - with rare cases of seizure aggravation in benign childhood epilepsy with centro-temporal spikes (8-10) In such cases valproate is to be used.

Absence Epilepsy: Valproate is the drug of choice for childhood absence epilepsy._ Ethosuximide and lamotrigine are the other first-line drugs. However if the initial therapy with ethosuximide fails, then valproate is the drug of choice and next option is lamotrigine. According to researchers ethosuximide, lamotrigine, and valproate are commonly used drugs in the treatment of absence seizures in children, but more trials of better quality are needed (11). Open-label trials of zonisamide and topiramate have suggested that these broad-spectrum antiepileptic drugs may have efficacy in childhood absence 'epilepsy (12, 13). Valproate is the treatment of choice with lamotrigine another firstline option for juvenile absence epilepsy, reflecting their efficacy for both absence and generalized tonic-clonic seizures. Ethosuximide is not the first-line drug for juvenile absence epilepsy due to its lack of efficacy in generalized tonic-clonic seizures. If there is no response to valproate, lamotrigine is the treatment of choice as the next option, with ethosuximide considered as high second-line option. Lamotrigine is the only new anti epileptic drug recommended by the American Academy of Neurology and the American Epilepsy Society for the treatment of newly diagnosed absence seizures (14, 15,16,17,18)

Conclusion

Antiepileptic drugs represent the primary treatment option and mainstay of treatment for most children with epilepsy. The choice of treatment for the various pediatric epilepsies depend on the type of seizure or epilepsy syndrome. However, valproate stands out as a broad spectrum antiepileptic - drug. Also, it is the treatment of choice as preventive therapy for febrile, seizures, and childhood epilepsy with centro-temporal spikes. Further, while, making decisions, it is appropriate to select an option that is optimal for the specific patient.

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