Original Research Article

Comparison of Levetiracetam and phenytoin for seizure control in children presenting with status epilepticus - A randomized, prospective single center study

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Abstract

Background: Convulsive status epilepticus (CSE) is the most common time-bound pediatric neurological emergency worldwide. The present study compared levetiracetam and phenytoin in children with status epilepticus.**Materials & Methods:**80 children diagnosed with status epilepticus of both genders were randomly divided into 2 groups of 40 each. Group 1 were given levetiracitam at a dose of 40 mg/kg diluted in 50 mL of normal saline. Group II (control group) were given IV phenytoin as 20 mg/kg diluted in normal saline over 20 minutes.**Results:** Type of seizure was generalized in 28 in group I and 24 in group II, focal seizure in 10 in group I and 12 in group II and complex partial seizure in 2 in group I and 4 in group II. The episode one was seen in 27 in group I and 13 in group II, two in 4 in group I and 17 in group II and more than three in 9 in group I and 10 in group II. Initial seizure control within 5 minutes was observed in 22 in group I and 10 in group II, 5-20 minutes in 12 and 10, 20-40 minutes in 6 and 4 in group I and II respectively. Seizure control within 24 hours was seen in 36 in group I and 24 in group II. The difference was significant (P< 0.05).**Conclusion:** Levetiracetam was more effective than phenytoin for seizure control in children.

Keywords: Levetiracetam, Phenytoin, Seizure

Introduction

Convulsive status epilepticus (CSE) is the most common time-bound pediatric neurological emergency worldwide, where delayed control is associated with neurological sequelae and risk of mortality. Half of the children in an Indian emergency department had convulsive status epilepticus at their first presentation without having any history of prior seizure. The available evidence supports that benzodiazepines should be the drugs of first choice for CSE[1].Status epilepticus is a common pediatric neurological emergency that requires immediate and vigorous management and at times poses a therapeutic challenge to the treating physician. If not managed promptly, it may result in significant neuromorbidity and mortality [2]. Early termination of the seizure activity and meticulous supportive care can circumvent most of the deleterious effects of SE and limit the morbidity and mortality. The correct management strategy involves initial stabilization of airways, breathing and circulation, prompt control of seizures, evaluation and treatment of the underlying etiology. The standard prototocol for treatment of pediatric status epilepticus involves use of a benzodiazepine first followed by a long- acting drug like phenytoin[3].Levetiracetam is a drug with a broad- spectrum antiepileptic activity and a unique preclinical and pharmacological profile.Levetiracetam binds to a unique binding site in the brain, the synaptic vesicle protein SV2A. Because levetiracetam does not appear to affect normal brain physiology, it is believed to modulate SV2A function only under pathophysiologic conditions[4].Among long- acting agents currently phenytoin is the most common agent used in the setting of acute seizure prevention in children. It acts by stabilizing the neuronal membrane. Phenytoin remains the drug of choice for second-line therapy in SE that does not respond to lorazepam or diazepam and is also used for maintaining antiseizure effect after the initial therapy with diazepam[5]. The present study compared levetiracetam and phenytoin in children with status epilepticus.

Materials & Methods

The present study comprised of 80 children diagnosed with status epilepticus of both genders. All were involved after obtaining their written consent.Demographic profile such as name, age, gender etc. was recorded. A thorough clinical examination was performed in all patients. Patients were randomly divided into 2 groups of 40 each. Group 1 were given levetiracitam at a dose of 40 mg/kg diluted in 50 mL of normal saline over 10 minutes followed by a maintenance dose of 20 mg/kg/day to be given in two divided doses 12 hours after initial dose. Group II (control group) were given IV phenytoin as 20 mg/kg diluted in normal saline over 20 minutes. Type, number and cause of seizures were recorded in both groups. Results thus obtained were assessed statistically. P value less than 0.05 was considered significant

.Results

Table 1: Distribution of cases

Group	Group I	Group II
Drug	Levetiracitam	Phenytoin
M:F	23:17	22:18

Table 1 shows that group I had 23 males and 17 females and group II had 22 males and 18 females.

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Table 2: Type of seizures

Type	Group I	Group II	P value
Generalized	28	24	0.01
Focal seizure	10	12	
Complex partial seizure	2	4	

Table 2,Fig 1shows that type of seizure was generalized in 28 in group I and 24 in group II, focal seizure in 10 in group I and 12 in group II and complex partial seizure in 2 in group I and 4 in group II. The difference was significant (P< 0.05).

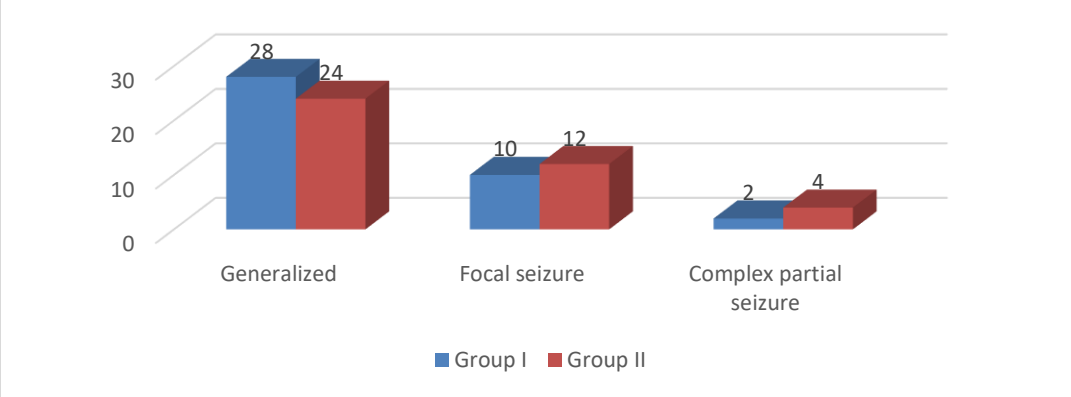

Fig 1:Type of seizures

Table 3: Comparison of parameters

Parameters	Variables	Group I	Group II	P value
Episode	One	27	13	0.02
	Two	4	17	
	More than three	9	10	
Initial seizure control	Within 5 minutes	22	26	0.05
	5-20 minutes	12	10	
	20-40 minutes	6	4	
Seizure control for 24 hours	Yes	36	24	0.03
	No	4	16	0.02

Table 3, Fig 2 shows that episode one was seen in 27 in group I and 13 in group II, two in 4 in group I and 17 in group II and more than three in 9 in group I and 10 in group II. Initial seizure control within 5 minutes was observed in 22 in group I and 10 in group II, 5-20 minutes in 12 and 10, 20-40 minutes in 6 and 4 in group I and II respectively. Seizure control within 24 hours was seen in 36 in group I and 24 in group II. The difference was significant (P< 0.05).

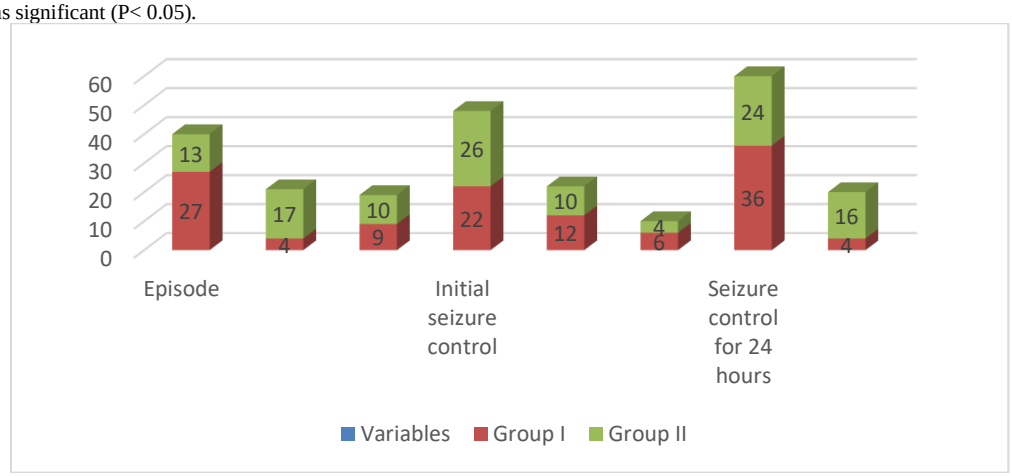

Fig 2:Comparison of parameters

Discussion

Convulsive status epilepticus (CSE) is the most common time-bound pediatric neurological emergency worldwide, where delayed control is associated with neurological sequelae and risk of mortality[6]. Half of the children in an Indian emergency department had convulsive status epilepticus at their first presentation without having any history of prior seizure.The available evidence supports that benzodiazepines should be the drugs of first choice for CSE[7]. Subsequently, intravenous phenytoin/ fosphenytoin remains the most used antiepileptic drug. The other reasonable options are valproate, levetiracetam and phenobarbital. There is insufficient evidence to support the use of one particular drug over the others[8].

Levetiracetam binds to a unique binding site in the brain, the synaptic vesicle protein SV2A. Because levetiracetam does not appear to affect normal brain physiology, it is believed to modulate SV2A function only under pathophysiologic conditions. Levetiracetam is also known to selectively inhibit N-type calcium channels and to block the inhibition of GABAand glycine-gated currents by negative allosteric modulators[9]. The present study compared levetiracetam and phenytoin in children with status epilepticus.In present study, group I had 23 males and 17 females and group II had 22 males and 18 females. Dar et al[10] conducted a prospective, randomized, study done on pediatric patients in the age group of 2 months to 16 years who present actively convulsing to the emergency department of pediatrics. At 24 hours seizures were controlled in 44 (88%) patients out of 50 patients in phenytoin group, 39 (78%) out of 50 patients in levetiracetam group and 46 (92%) out of 50 patients in valproate group (p-value 0.115). The relative risk of seizure recurrence for levetiracetam and phenytoin groups when compared to valproate was 2.75 and 1.5, respectively.We found that type of seizure was generalized in 28 in group I and 24 in group II, focal seizure in 10 in group I and 12 in group II and complex partial seizure in 2 in group I and 4 in group II. Vignesh et al[11] included 110 children aged three months to 12 year with convulsive status epilepticus. Patients not responding to 0.1 mg/kg intravenous lorazepam were randomly assigned (1:1:1) to receive 20 mg/kg of phenytoin (n=35) or valproate (n=35) or levetiracetam (n=32) over 20 minutes. The study was stopped after the planned mid-interim analysis for futility. Intention to treat analysis was done. There was no difference in primary outcome in phenytoin (31/35, 89%), valproate (29/35, 83%), and levetiracetam (30/32, 94%) (P=0.38) groups. There were no differences between the groups for secondary outcomes. One patient in the phenytoin group had a fluid-responsive shock, and one patient in the valproate group died due to encephalopathy and refractory shock.We found that episode one was seen in 27 in group I and 13 in group II, two in 4 in group I and 17 in group II and more than three in 9 in group I and 10 in group II. Initial seizure control within 5 minutes was observed in 22 in group I and 10 in group II, 5-20 minutes in 12 and 10, 20-40 minutes in 6 and 4 in group I and II respectively. Seizure control within 24 hours was seen in 36 in group I and 24 in group II. Wani et al[12] found that a total of 104 children were randomly allocated to either group 1 (levetiracetam) or group 2 (phenytoin) on the basis of computer-generated random number table. The mean age was 4.09 years with a male preponderance with the most common type of seizure being generalized type (74%). The seizures were controlled in all 104 patients initially within 40 min. Seizure control for 24 h was significantly better in group 1 (96%) when compared with group 2 (59.6%) (P = 0.0001). Minibolus of drug was given in 28.8% in group 1 and 46.2% in group 2 (P = 0.068). The seizure recurrence in groups 1 and 2 in the first hour was 1.9% and 5.8%, respectively (P = 0.61), whereas the recurrence between 1 and 24 hours was significantly more in group 1 (34.6%) when compared with group 2 (3.8%) (P=0.0001).The mean time to control seizure was comparable between both the groups (P = 0.71). There was no significant adverse effect in both the groups.

Conclusion

Authors found that levetiracetam was more effective than phenytoin for seizure control in children.

References

1. Singhi S, Singhi P, Dass R. Status epilepticus: Emergency management. Indian J Paediatr. 2003;70:S1-22. 4
2. Hanhan UA, Fiallos MK, Orlowski JP. Status epilepticus. Pedia Clin North Am. 2001;48:683- 94.
3. Raj D, Gulati S, Lodha R. Status epilepticus. Indian J Pediatr. 2011;78(2):219-26.
4. Shearer P,Riviello J. Generalized convulsive status epilepticus in adults and children: treatment guidelines and protocols. Emerg Med Clin North Am. 2011;29(1):51-64.
5. Mikati MA. Status epilepticus. In: Kliegman RM, Stanton BF, Schor NF, St. Geme JW, Behrman RE, eds. Nelson Textbook of Pediatrics. 19th ed. Philadelphia: Saunders; 2011: 2013-2017.
6. Kälviäinen R,Eriksson K, Parviainen I. Refractory generalised convulsive status epilepticus: a guide to treatment. CNS Drugs. 2005; 19(9): 759-68.
7. Arif H, Hirsch LJ. Treatment of status epilepticus. Semin Neurol. 2008;28(3):342-54.
8. Misra UK, Kalita J, Patel R. Sodium valproate vs phenytoin in status epilepticus: a pilot study. Neurol. 2006;67(2):340-2.
9. Kwan SY. The role of intravenous valproate in convulsive status epilepticus in the future. Acta Neurol Taiwan. 2010;19(2):78-81.
10. Dar SA, Wani WA, Nazir M, Hussan ZE. Comparative efficacy of IV phenytoin, IV valproate and IV levetiracetam in childhood seizures. Int J Contemp Pediatr 2019;6:1592-7.
11. Vignesh V, Rameshkumar R, Mahadevan S. Comparison of phenytoin, valproate and levetiracetam in pediatric convulsive status epilepticus:a randomized double-blind controlled clinical trial. Indian pediatrics. 2020;57(3):222-7.
12. Wani G, Imran A, Dhawan N, Gupta A, Giri JI. Levetiracetam versus phenytoin in children with status epilepticus. Journal of family medicine and primary care. 2019;8(10):3367.

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