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Comparison between intravenous sodium valproate and sodium phenytoin as second line treatment of status epilepticus in children

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Abstract

Background: Status epilepticus (SE) is one of the most significant neurological emergencies. It was previously defined as multiple seizures without recovery and regaining consciousness between intervals lasting for more than 30 min. **Subjects and Methods:** This study conducted in the Department of Pediatrics in the tertiary care centre. The duration of the study was over a period of six month. **Results:** Two groups were taken in this study, one is group P and another one group V .Group P was received sodium valproate and group V received phenytoin sodium intravenously as second line treatment. Sixty cases were involved in each group. Out of 60, 53.3% male & 46.7% female were found in Group P. Whereas, 60% male & 40% female were found in Group V .In the both group most prevalent age was 11-12 year followed by other age group. **Conclusion:** It was found to be safer also than phenytoin in terms of respiratory depression. But more studies are required to compare the efficacy of these two AEDs in the pediatric population.

Keywords: Sodium valproate, Sodium phenytoin, Status epilepticus.

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Introduction

Status epilepticus (SE) is a condition characterized by an epileptic seizure that is so frequent or so prolonged as to create a fixed and lasting condition.[1] In light of the seriousness of the condition and the urge to treat as early as possible to prevent refractory SE, the timeframe has been progressively shortened to a pragmatic definition of 5 min ongoing seizures.[2] SE can lead to irreversible brain damage, if left untreated. It has been estimated by population-based studies[3–8] that an incidence of up to 60 cases per 100,000 per year, with the highest incidence in young children and the elderly.[9] Thus, it represents one of the most common neurological emergencies.

Status epilepticus (SE) is one of the most significant neurological emergencies. It was previously defined as multiple seizures without recovery and regaining consciousness between intervals lasting for more than 30 min.[10-12] In various studies, this definition has been used for many years, but recently this definition has been changed. Now it has been defined as all epileptic seizures lasting more than 5 min require the same treatment as used for SE. In SE patients, mechanisms for self- termination of seizures fail. Thus, seizures can usually last for several minutes with the high possibility of recurrence.[11,13] Long-lasting SE can cause several complications such as multiple organ derangements, direct damage to the brain cells due to unclear mechanisms of excessive stimulatory neurotransmitters, and loss of inhibitory neurotransmitters gamma- aminobutyric acid (GABA).[10-11] It leads to high morbidity and mortality. To prevent organ failure and metabolic disorders and stabilize cardiopulmonary function, it is very important to diagnosis early and provide the treatment with effective anticonvulsants.[12] Intravenous benzodiazepines is the first line treatment that potentiates the inhibitory responses caused by GABA- A receptors. Though the early benzodiazepines may block the seizures, their efficacy decreases with refractory exclusivity of SE and they also may cause excessive sedation. It may affect patient's monitoring. Therefore, it cannot be administered for a long period.[14-15] Intravenous phenytoin (IV PHT) can be used in combination with the first- line medications to reduce recurrences. It is known as second- line therapy. But there are some disadvantages of this drug such as nervous system depression, cardiovascular collapse, or hypotension etc.[16,12,17,18]. In some cases, the seizures are so severe that they cannot be suppressed even by third- line therapy.[17] Unlike phenytoin[13,19,20] intravenous sodium valproate (IV VPA) can be used safely against various types of SE especially for patients with cardiorespiratory impairments[12]. This non-sedating drug has high acceptability and does not cause severe hemodynamic instability.[21] It has been observed in recent studies that IV VPA was more effective than phenytoin (79.0% vs. 25.0%). As the review of literature revealed that there are very few

studies that compares the efficacy and safety of IV VPA with IV PHT, in this study we aimed to compare the efficacy of IV VPA with IV PHT in treatment of SE.

Subjects and Methods

Study Population: Two groups were taken in this study, one is group P and another one group V. Group P was received sodium valproate and group V received phenytoin sodium intravenously as second line treatment. Sixty cases were involved in each group.

Study Area: This study conducted in the Department of Pediatrics in the tertiary care centre.

Study Duration: The duration of the study was over a period of six month.

Data Collection: Children of two to 12 years age group, who were admitted in Pediatric emergency ward and Pediatric Intensive Care Unit (PICU) with status epileptics, were included in the study. Those with a definite history of any allergic reaction to IV phenytoin or IV valproate, or any contraindications in giving these drugs were excluded from the study. All patients received IV diazepam or lorazepam as a first line medication before starting other AED.

Data Analysis: Data were analyzed by the using of Microsoft excel and Chi square test.

Results

Two groups were taken in this study, one is group P and another one group V .Group P was received sodium valproate and group V received phenytoin sodium intravenously as second line treatment. Sixty cases were involved in each group. Out of 60, 53.3% male & 46.7% female were found in Group P. Whereas, 60% male & 40% female were found in Group V .In the both group most prevalent age was 11-12 year followed by other age group. In the V group 40 seizure was controlled in children presented within 2 hrs, whereas in the P group 34 of patients presenting within 2 hrs, had seizure controlled. Here the differences between these two groups of patients (V and P) were statistically significant (p value 0.008) and it concluded that V group of patients had better seizure control if presented within 2 hrs. But in case children presented with SE of more than 2 hours, there is no statistical difference between these two groups (p value 0.889). In V group of patients 46 patients had no recurrence of seizure in less than 12 hrs, whereas in P group of patients only 22 patients had no recurrence of seizure within 12 hrs. The P value was 0.002 which is statistically significant (<0.05).

Table 1: Distribution of cases according to gender.

Gender	Group P	%	Group V	%
Male	32	53.4%	36	60%
Female	28	46.7%	24	40%
Total	60	100%	60	100%

Table 2: Distribution of cases according to age.

Age	Group P	%	Group V	%
2-5	14	23.4%	12	20%
6-10	21	35%	22	36.7%
11-12	25	41.6%	26	43.3%
Total	60	100%	60	100%

Table 3: Distribution of cases according to seizure controlled within 2 hr.

Group	Sizure Controlled Presented Within <2 Hr	Sizure Not Controlled Presented Within <2 Hr	Total
V	40	0	40
P	34	14	48
Total	74	14	88
P Value = 0.008*			

Table 4: Distribution of cases according to seizure controlled more than 2 hr.

Group	Sizure Controlled Presented Within >2 hr	Sizure Not Controlled Presented Within >2 hr	Total
V	14	6	20
P	8	4	12
Total	22	10	32
P Value = 0.889			

Table 5: Distribution of cases according to recurrence of seizure.

Group	Sizure Controlled Presented Within <12 hr	Sizure Not Controlled Presented Within <12 hr	Total
V	14	46	60
P	38	22	60
Total	52	68	120
P Value = 0.002*			

Discussion

In the present study, most of the patients were male in both groups.[22] Agarwal P. et al conducted a study on patients of status epilepticus also observed male predominance in their study. This study administered IV Valproate in doses of 20 mg/kg as loading [23] dose which is similar to doses used by Limdi et al study. IV Valproate was used at rate of 40 mg/min. this dose was used in[24-26] other studies also. In this study the most common cause of status epilepticus was CNS infection i.e. 34 (56.67%) in both valproate and phenytoin group which was followed by inflammatory granuloma. Agarwal P. et al found the most common etiology of SE was antiepileptic drug noncompliance or withdrawal in 12 (24%) patients in valproate group and 14 (28%) in phenytoin group. The other etiologies involved inflammatory granuloma 12 (24%) in valproate group and 12 (24%) in phenytoin group, CNS infections. In the present study, status epilepticus in 90% of patients in Group V and 70% of patients in Group P ($p > 0.05$), was interrupted successfully.[27] Czapinski and Terezynski (1998) reported that in a series of 20 adult patients, 80% success rate was found in interrupting SE by using IV Valproic acid in a bolus dose of 15 mg/kg followed by an infusion of 1 mg/kg/h. Peters [28] and Pohlmann-Eden also conducted a study on 102 adult patients and found 85.6% success in controlling SE by using IV VA. Similar results were found by T iamkao et al. [29] In the present study, at the time of presentation, 33.33% of Group V and 20% of Group P were having duration of SE >2 h. This delay in presentation might be attributed to the lack of awareness amongst the general public, inadequacy of medical and health services etc. The response to treatment was significantly better in patients having SE <2 hrs than SE >2 hrs in both the groups. Similar results were found by Limdi et al. [30] The present study results showed that there was significant difference in recurrence of seizure within 12 hr between group V and group P. Though, in their study by Agarwal P. et al[8] reported that there were no significant differences between the treatments by valproate and phenytoin with respect to recurrence during the 12-hour study period. The differences between the present study and the study of Agarwal et al could be attributed to the differences in the study population and etiology of SE. In the present study, the mortality was 6.66% and 20%, respectively in V and P groups, without any statistical significance. The mortality of almost 89% of the patients during or after SE was ascribed to the etiology of the status, whereas only 2% of mortality could be directly 17 attributed to the SE itself. In the present study, one patient (3.33%) in group V and two patients (6.66%) in group P left against the medical advice.

Conclusion

To limit and prevent morbidity and mortality in children, quick and suitable treatment is required for SE. Early control of seizures has been reported to prevent neurological sequelae and improve outcome. Role of sodium valproate has been reported to be better in controlling SE with seizure duration less than 2 hours in comparison to phenytoin in reducing recurrence of seizure within 12 hours and between 12 to 24 hours. It was found to be safer also than phenytoin in terms of respiratory depression. But more studies are required to compare the efficacy of these two AEDs in the pediatric population.

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