**ORIGINAL RESEARCH**

# Evaluation of 50 Epileptic Patients Treated with Sustained Release Valproate at a Tertiary Care Centre

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Received: 21 April, 2021 Accepted: 24 May, 2021

## ABSTRACT

**Background:** The present study was conducted for assessing 50 epileptic patients treated with sustained release valproate. **Materials & methods:** The present study was conducted for assessing 50 epileptic patients treated with sustained release valproate (SRVPA).In this study, patients between the ages of 10 and 75 having a confirmed diagnosis of epilepsy and using SRVPA as monotherapy were included. Following the initial medication, the patients were requested to return for follow-up reviews at the second week, the first month, the third month, the sixth month, and at successive half-year intervals. Time to treatment failure was the main outcome of this study, along with other AED discontinuation due to ineffectiveness, discontinuation of SRVPA due to ineffectiveness [LE], intolerable adverse events [IAEs], ineffectiveness combined with intolerable adverse events [LE & IAEs], poor adherence, patients' financial hardship, or a pregnancy plan. A patient who had low compliance was one who had voluntarily stopped receiving SRVPA treatment. Following a statistical analysis using SPSS software, all the results were entered into a Microsoft Excel spreadsheet. **Results:** Mean age of the patients was 30.8 years. 56 percent of the patients were males while the remaining were females. Most common type of epilepsy found in the present study was cryptogenic type. Majority of patients had two or three seizures. Treatment failure was encountered in 30 percent of the patients. Common reasons for treatment failure were lack of efficacy, adverse events, poor compliance and financial hardship. **Conclusion:** Lack of efficacy, intolerable adverse events were the most frequent reason for treatment failure.

**Key words:** Sustained release, Valproate, Epilepsy



## INTRODUCTION

In epilepsy, the brain or some parts of the brain are overactive and send too many signals. This results in seizures, also referred to as epileptic fits. Seizures sometimes only cause a few muscles to twitch – but they may also cause your whole body to convulse (shake uncontrollably) and result in loss of consciousness. Epilepsy can arise at any age. Some people already have their first seizure in childhood, and others have their first seizure in older age. There are usually no physical symptoms in between seizures.[1, 2] Many people worry about having another seizure, though. Medication can help to prevent seizures and maintain a good quality of life. Unfortunately, it doesn't always help: About 3 out of 10 people still have regular seizures. This makes it particularly difficult for them to live with epilepsy. Epileptic seizures can vary greatly from person to person. Some only last a few seconds and even go unnoticed, some only affect one arm or one leg, whereas others affect the whole body. Sometimes people become unconscious, sometimes they are just mentally absent for a short while, and sometimes they remain fully conscious.[3, 4] It has been suggested that sustained-release valproate (VPA) formulations may be more effective and better tolerated than conventional VPA due to better compliance and lower fluctuations in VPA serum concentrations.[5, 6] Hence; the present study was conducted for assessing 50

epileptic patients treated with sustained release valproate (SRVPA).

## MATERIALS & METHODS

The present study was conducted for assessing 50 epileptic patients treated with sustained release valproate (SRVPA).In this study, patients between the ages of 10 and 75 having a confirmed diagnosis of epilepsy and using SRVPA as monotherapy were included. The patient's demographics, past antiepileptic medication use, history of febrile seizures, birth traumas, epilepsy in first-degree relatives, and neurological conditions were all noted during the initial visit. Both a general physical check and a neurological evaluation were carried out. Examinations in the lab were done. If necessary, electrocardiogram (ECG) tests were also carried out. Following are the recommendations for the initial medication dose and titration. The initial dose of SRVPA for children and adolescents was 10-15 mg/kg/day, with weekly increases of 5–10 mg/kg/day; the goal dose was 20–30 mg/kg/day. The recommended dose of SRVPA for adults was between 1000 and 2000 mg/day, with a weekly increase of 250 mg/day. Typically, small beginning dosages of the drug were administered, and the doses were gradually raised until the seizures were under control. The dosage adjustments for antiepileptic medicines (AED) struck a balance between effectiveness and undesirable side effects. Following the initial medication, the patients were requested to return for follow-up reviews at the second week, the first month, the third month, the sixth month, and at successive half-year intervals. Time to treatment failure was the main outcome of this study, along with other AED discontinuation due to ineffectiveness, discontinuation of SRVPA due to ineffectiveness [LE], intolerable adverse events [IAEs], ineffectiveness combined with intolerable adverse events [LE & IAEs], poor adherence, patients' financial hardship, or a pregnancy plan. A patient who had low compliance was one who had voluntarily stopped receiving SRVPA treatment. Following a statistical analysis using SPSS software, all the results were entered into a Microsoft Excel spreadsheet.

## RESULTS

Mean age of the patients was 30.8 years. 56 percent of the patients were males while the remaining were females. Most common type of epilepsy found in the present study was cryptogenic type. Majority of patients had two or three seizures. Treatment failure was encountered in 30 percent of the patients. Common reasons for treatment failure were lack of efficacy, adverse events, poor compliance and financial hardship.

**Table 1: Demographic and clinical details**

| Variable | | Number | Percentage |
|---|---|---|---|
| **Mean age (years)** | | 30.8 | |
| **Gender** | **Males** | 28 | 56 |
| | **Females** | 22 | 44 |
| **Type of epilepsy** | **Idiopathic** | 5 | 10 |
| | **Symptomatic** | 12 | 24 |
| | **Cryptogenic** | 33 | 66 |
| **Seizures at baseline** | **One seizure** | 18 | 36 |
| | **Two to three seizures** | 20 | 40 |
| | **More than three** | 12 | 24 |

**Table 2: Intention-to-treat analysis of clinical outcome**

| Outcome | Number | Percentage |
|---|---|---|
| **Treatment failure** | 15 | 30 |
| **12- month remission** | 28 | 56 |
| **24-month remission** | 7 | 14 |

**Table 3: Reasons for treatment failure**

| Reasons | Number | Percentage |
|---|---|---|
| **Lack of efficacy** | 5 | 33.33 |
| **Adverse events intolerable** | 3 | 20 |
| **Poor compliance** | 4 | 26.67 |
| **Financial hardship** | 3 | 20 |
| **Total** | 15 | 100 |

## DISCUSSION

The World Health Organization (WHO) and its partners have recognized epilepsy as a major public health concern. Epilepsy occurs due to hyperexcitability and an imbalance between excitation and inhibition, leading to seizures. According to the WHO, around fifty million people worldwide are affected by epilepsy, making it one of the most

common neurological diseases globally. Epilepsy is a neurological disorder characterized by recurrent seizures caused by sudden surge in electrical activity of the brain. This is due to abnormal neuronal discharges or hyperexcitability of neurons with synchronicity. However, the frequency of these seizures varies for different people.Epilepsy is a multifactorial neuronal disorder. Epileptic seizures are abnormal jerky or trembling movements in the body due to abnormal neuronal activity and can result in damage to the brain or other parts of the body. Even a single seizure can cause changes in neural development and can lead to behavioural and cognitive changes. Epileptic seizures have adverse clinical characteristics. These seizures have a negative impact on the lives of patients especially those who have frequent reoccurrence.The epileptic seizures cause emotional, behavioural and neurological disturbances in patients. Seizures can occur in various regions of the brain and the degree of effectiveness depends upon the characteristic area, types of seizures and the area where abnormal neuronal activity is occurring. Epileptic patients suffer from social stigma and discrimination; misconception and negative attitudes of society towards this disorder may prevent epileptic patients from seeking treatment and leading a confident life.[1, 7- 10]Valproic acid is an anticonvulsive and mood stabilizer medication. It is extensively used in the adult population to treat convulsions, migraines, and bipolar disorders. Valproic acid's primary use is as an anti-seizure medication, as well as in migraine, bipolar, mood, and anxiety disorders. Recent work has also demonstrated its efficacy as adjuvant therapy in HIV, cancer, and neurodegenerative diseases as its histone deacetylase (HDAC) inhibition property. Valproic acid is a widely used therapy for pediatric epilepsy for its multiple targets and acceptable safety profile. The highly variable dose requirements and interactions with a wide range of drugs warrant regular patient follow-up and therapeutic drug monitoring.[11]Hence; the present study was conducted for assessing 50 epileptic patients treated with sustained release valproate.

Mean age of the patients was 30.8 years. 56 percent of the patients were males while the remaining were females. Most common type of epilepsy found in the present study was cryptogenic type. Majority of patients had two or three seizures. In an observational study conducted by Stefan H et al, after administration of once daily evening dosing of valproate sustained release minitablets were recorded in 359 patients with epilepsy aged between 12 and 86 years. Patients were either newly treated with valproate sustained release minitablets (N = 58) or switched from conventional valproate (N = 124) or from sustained release valproate (N = 138) to the once daily evening dosing. In 39 patients other antiepileptic drugs were replaced. At the final examination 137 patients (62.3 %) were seizure free, and further 60 patients (27.3 %) experienced a seizure reduction of more than 50 % (responder) of those 220 patients who experienced seizures in the last 7 weeks before the study. The efficacy and tolerability was rated in more than 95 % of the cases by the patient and the investigator as good or very good. The compliance/acceptance of the valproate sustained release minitablets was rated as good or very good in almost all patients.[4]

In the present study, treatment failure was encountered in 30 percent of the patients. Common reasons for treatment failure were lack of efficacy, adverse events, poor compliance and financial hardship. Hu, Yida et al, in another previous study compared two broad spectrum AEDs, the traditional drug of sustained-release formulation of valproate (SRVPA) and the new-generation drug of topiramate, in patients with epilepsy as monotherapy in this multi-centre, observational cohort study from 2000 to 2011. The primary outcome was time to treatment failure.Of the 1008 recruited patients, 519 received SRVPA and 489 received topiramate. SRVPA was better than topiramate in primary outcome, and in time to first seizure. No significant difference was observed between two groups in time to 12-month remission and time to 24-month remission. 36 patients (6.9%) in SRVPA group and 37 patients (7.6%) in topiramate group presented treatment failure associated with intolerable adverse events, there was no significant difference between the two groups.[12]

## CONCLUSION

Lack of efficacy, intolerable adverse events were the most frequent reason for treatment failure.

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