

Clobazam Efficacy as an Add-on Therapy for 121 Patients with Intractable Epilepsy

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Abstract

Background: Clobazam is a novel 1,5-benzodiazepine that was initially developed as an antianxiety treatment designed to decrease adverse Effects associated with 1,4-benzodiazepines while maintaining efficacy. It was later found to have antiepileptic properties.

Clobazam is well-tolerated and has shown efficacy as an adjunctive therapy for a variety of epilepsy types, including LGS. Studies have reported tolerance rates as high as 87%. Clobazam has an important antiepileptic effect and is less expensive than the new antiepileptic drugs, but still has not been considered as first-line drug in the treatment of epilepsy. Clobazam have been established as valuable add-on medication for refractory epilepsy. Clobazam have been used in our institution for more than 15 years; with benefit observe in many patients.

Methods and Results: Retrospective chart review of patient who were treated with Clobazam between 2008 and 2017 for treatment of intractable epilepsy. The following information were collected; age, sex, seizures type and frequency per month pre-and post Clobazam. Information was entered in Redcap database. 121 patients were reviewed to evaluate the response of seizures to the use of Clobazam. Age mean is 8 years old; male (73) and female (48). The median decrease in the average number of monthly seizures for all patients was 30. The seizures with highest response to Clobazam are myoclonic, atonic, infantile spasm more than generalized tonic clonic and partial seizures. The median decrease in the average monthly seizures following Clobazam was 30 among males and 40 among females no significant association between the sex and the decrease of average monthly seizures following Clobazam. Clobazam presented a stronger effect on younger children compared to the age above 15.

Conclusions: Our study confirmed the efficacy of Clobazam for treatment of intractable epilepsy. Clobazam efficacy more superior in generalized seizures type i.e. myoclonic, atonic, infantile spasm than GTC and partial seizures. Younger children response better than older children.

Keywords:

Cardiac arrest; Echocardiography; Hypovolemic; Sepsis

Introduction

Clobazam is a novel 1,5-benzodiazepine that was initially developed as an antianxiety treatment designed to decrease adverse Effects associated with 1,4-benzodiazepines while maintaining efficacy [1,2]. It was later found to have antiepileptic properties [2-5]. Clobazam appears to exert its effects by increasing c-amino butyric acid (GABA) mediated inhibitory effects through binding with the $\alpha 1$ subunit of the GABA receptor, increasing GABA transporters, and increasing glutamate reuptake [6,7]. Oral absorption of Clobazam is rapid and complete. The time to peak concentration ranges from 1 to 4 hour [8]. The drug is highly lipophilic and is rapidly distributed in fat and cerebral gray matter. Within 14 hours of administration it has accumulated in white matter and is then widely redistributed; the volume of distribution is large [9,10] Clobazam is well-tolerated and has shown efficacy as an adjunctive therapy for a variety of epilepsy types, including LGS [11]. Studies have reported tolerance rates as high as 87%. [12] Clobazam has an important antiepileptic effect and is less expensive than the new antiepileptic drugs, but still has not been considered as first-line drug in the treatment of epilepsy. Clobazam have been established as valuable add-on medication for refractory epilepsy. Clobazam have been used in our institution for more than 15 years; with benefit observe in many patients.

Objective

To Evaluate the Efficacy of Clobazam in Children as Add-on therapy with Refractory Epilepsy in Saudi Arabia.

Methods

Retrospective chart review of patients who were treated with Clobazam as add-on therapy between 2008 and 2017 for intractable epilepsy. In epilepsy clinics of King Faisal Specialist Hospitals and Research center. The following information were collected; age, sex, seizures type and frequency per month pre-

and post Clobazam. Clobazam mean dosage was 20 mg/day. 0.9 mg/kg/day (range 0.05-2 mg/kg/day). Mean use of Clobazam was 20 months. While keeping the previous AEDs regimens constant, the data were entered to Redcap database.

Results

There were a total of 121 epilepsy patients. Age mean is 8 years old; male (73) age ranged 1-17 year and female (48) age ranged 2-22 years old. (Graph 1) with different types of seizures; this figure illustrates the seizure types that were included. (Figure 1) the number of seizures pre-and post Clobazam. The median decrease in the average number of monthly seizures for all patients was 30 seizures per month. This shows a significant decrease with a p-value=0.0001. There were 10 Patients who presented with complex partial seizures. The median decrease in the average monthly number of seizures following Clobazam was 60. This is a statistically significant decrease with a p-value=0.0010.

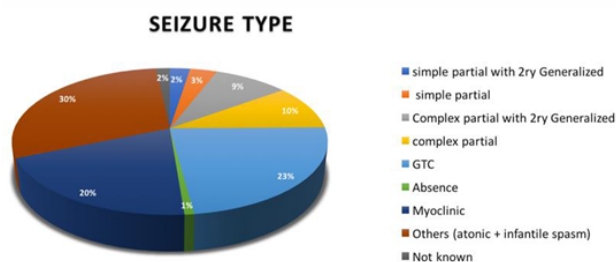
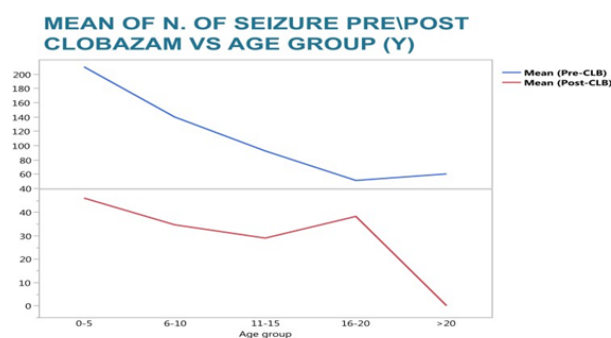


Figure 1: Illustrates the seizure types that were included.



Graph 1: Seizure frequency/month.

Discussion

Kaplan-Meier analysis showed the efficacy was reported in low doses. And the seizure freedom is most likely to be seen in patients on first and second add on therapy with Clobazam. [12] Our study provided the evidence for the same. The percentage of seizure reduction was reported only after the addition of Clobazam while keeping the other treatment regimens constant. Retrospective study on Clobazam efficacy [5] reported that patients with multiple seizure types, nearly 40% of patients had a 50% reduction in the frequency of all their seizure types, including 14% of patients who achieved seizure freedom across all seizure types. In our study revealed the median decrease in

the average number of monthly seizures for all patients in all seizure type (myoclonic, atonic, infantile spasm more than generalized tonic clonic and partial seizures) was 30 seizures per month with a p. value 0.0001. Randomized, double-blind study [11] reported imbalance in male-to-female enrollment which was not likely to influence the results of Clobazam efficacy. In comparison to our study there was no effect of gender on Clobazam efficacy in our group. In the literature, no reported relation between specific age group and efficacy to Clobazam. While in our study, CLB was found to be stronger effect on younger children compared to the age above 15 years.

Conclusion

Our study confirmed the efficacy of Clobazam for treatment of intractable epilepsy. Clobazam efficacy more superior in generalized seizures type i.e. myoclonic, atonic, infantile spasm than GTC and partial seizures. Younger children response better than older children.

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