



## Clobazam in childhood epilepsy

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### ABSTRACT

Different studies have shown that the outcome of treatment with clobazam in all types of seizures is good. The greatest success has been achieved in complex partial seizures. It is also found suitable for maintenance treatment. Although promising findings have been made with this drug, further studies are still required, especially in paediatric population.

*Keywords: Clobazam; Epilepsy; Complex partial seizures.*

### INTRODUCTION

Seizure is a common neurological disorder in paediatric age group and has the prevalence of 5.2 to 8.1 per one thousand population. Children with seizure disorders require prolonged antiepileptic drugs for at least two seizures per year. Recent trends in the therapy includes emphasis on monotherapy; this increases awareness of drug interactions between anticonvulsants themselves. There is also increasing awareness of the effects of anticonvulsants on cognition and behaviour. Unfortunately conventional anticonvulsant drugs are associated with some serious side effects like: hepatotoxicity, pancreatitis, mild hemolytic anemia to aplastic anemia, lymphadenopathy, abnormal behaviour, sensory neuropathy and connective tissue disorders. It is therefore important to identify a drug that control seizures effectively with minimal side effects.

Various studies showed that newer antiepileptic drug like clobazam has been found to possess good antiepileptic effects with less side effects as compared with conventional antiepileptic drugs.

Clobazam is a 1, 5 benzodiazepine; it was introduced as anxiolytic drug in 1975. Its anticonvulsant properties were first reported in 1978. Its effect in paediatric patients was first studied in 1981. In animal models with chemically-induced seizure, antiepileptic properties of clobazam have been shown to be more potent than the classic antiepileptic agent. Since then only few studies have been carried out in paediatric patients. However, the outcome of these studies was very good and promising.

### REVIEW OF LITERATURE

In the history, the fear of epileptic fits has been the main treat since time immemorial.

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No other illness has set the individual fear of ghost so far, so often and so long and these attitudes still persist in the present day. Until the mid 19th century, epilepsy continued to be regarded as an obsession by a devil or possibly consequence of sexual aberration or as contagious disease.

A major breakthrough in the drug treatment was achieved by Merritt S Putnam in 1938 when they discovered antiepileptic activity of Diphenyl hydantoin. Since then a number of other antiepileptics have been discovered and become well established in the treatment of epilepsy.

The antiepileptic effects of clobazam in patients were first described by Gastaut in 1978 and Gastaut and Low in 1979. Since these initial investigations, at least 50 open studies have been carried out. Few of these studies were concerned mainly with children.

Dulac (1983) *et al* treated 24 children aged between 6 months and 16 years for between 10 days and 36 months, depending on the outcome of treatment. Children were given 0.5 mg/kg and infants 1.0 mg/kg. 21 of the children were suffering from different forms of partial and complex partial seizures. Clobazam was effective (more than 75% showed reduction in seizure activity) in 17 of the 24 patients (71%).

Plouin and Jalin (1985) investigated the EEGs of 15 children included in the above study. The majority of normal EEG pattern was obtained in patients with benign partial epilepsy. Andre, Pechadre *et al* and Farrell reported on the treatment of the Lennox Gastaut Syndrome. Andre observed a

reduction in seizures of 75% or more i.e., in 22 out of 39 patients. Pechadre *et al* achieved 75% reduction in 15 out of 26 severely ill patients.

Fiqueroa *et al* treated 23 children; 16 patients showed a considerable reduction in seizures after 6 months of treatment. Shimizu *et al* studied the effect on generalised epilepsy. He observed a good reduction in frequency in 50% of patients after 12 months of treatment.

Munn *et al* studied 27 children of severe intractable seizure disorder; 56% of patients showed a good reduction in seizure frequency. CCCG (1991) studied on 440 children and found 50% reduction in 50% and 100% reduction seizure activity in 30% cases.

These above mentioned studies have been shown that clobazam may be suitable for use in children as antiepileptic in different types of seizures and has a rapid onset of effect.

### **Pharmacology**

- Has all pharmacological properties of benzodiazepine.
- Orally administered.
- Dosage - as Anxiolytic 5-10 mg/day in a single dose.
- As adjuvant in Epilepsy - loading dose - 5 mg/kg/day.
- Maintenance dose - 0.3-1 mg/kg/day.
- Usually given as a single dose at bed time or some time twice daily.
- After treatment dose gradually reduced.
- Prolonged spell of uninterrupted treatment should be avoided because of dependence and tolerance.

- Peak serum level achieved in 1-4 hrs. Serum level varies between 50-300 ng/ml.
- Bioavailability is 87%.
- Bounding to plasma protein is 85%.
- Elimination 1/2 life is 10-30 hrs.
- Active metabolite is N desmethyl clobazam, 8-10 times more potent than clobazam half life is 35-133 hrs. Serum concentration is 1000-4000 ng/ml.
- The anti epileptic effects developed fully after 14 days.
- Follows 1st order Kinetics,
- It acts after binding specific GABA receptors.

#### Indications

- Primary generalized epilepsies, partial seizures, Lennox Geastaut Syndrome and reflex epilepsy.
- It is indicated for all types of refractory seizures as adjunctive. The greatest success has been achieved in complex partial seizures.
- Also very useful adjunctive in secondary generalised tonic- closure seizures and atonic seizures.
- It is also suitable for maintenance treatment of Epilepsy and Febrile seizures..
- As anxiolytic.
- As weak hypnotic.

#### Contra Indications and Precautions

- Children below 3 years.
- Hypersensitivity of drug.
- First trimester of pregnancy and nursing mother.

- Myasthenia gravis, liver damage, spinal or cerebellar ataxia and severe respiratory diseases.

#### Adverse Reactions

The main adverse reactions are - drowsiness, vertigo, diplopia, ataxia, tremor, weight gain, headache, aggressiveness, impaired micturation and urticaria.

#### Drug Interactions

If clobanzam is administered simultaneously with anticonvulsants, analgesics, sedatives and hypnotics, the dosage must be adjusted under regular medical supervision.

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