

## Original Research Article

**An evaluation of anticonvulsant action of Vigabatrin on albino rats****Dr. Mohammad Imran<sup>1</sup>, Dr. Abhishek Singh<sup>2</sup>, Dr. Rakesh Tank<sup>3</sup>, Dr. Priyamvada Sharma<sup>4</sup>, Dr. Vinod Bhardwaj<sup>5</sup>**<sup>1</sup>Demonstrator, Department of Pharmacology, North Bengal Medical College and Hospital, Darjeeling, West Bengal<sup>2</sup>Assistant Professor, Department of Community Medicine, SHKM Govt. Medical College, Mewat, Haryana<sup>3</sup>Assistant Professor, Department of General Medicine, SHKM Govt. Medical College, Mewat, Haryana<sup>4</sup>Professor and Head, Department of Pharmacology, FH Medical College, Tundla, Uttar Pradesh<sup>5</sup>Professor, Department of Pharmacology, SHKM Govt. Medical College, Mewat, Haryana**\*Corresponding author**

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**Abstract:** Serious doubts have been cast on the original hypothesis that they may be used as a model of human absence seizures and they more probably represent a model of myoclonic seizures. The present study was planned to study the anticonvulsant action of Vigabatrin on albino rats. The current prospective study was conducted by the Department of Pharmacology of a tertiary care teaching institution. Study tools were convulsometer (electrically driven), Tuberculin syringe and Albino rats. Vigabatrin drug was used. Experimental animals were obtained from animal house of this tertiary care center. Effect of different doses of Vigabatrin against Metrazol induced convulsions was captured. Range of effective doses of Vigabatrin in 50% of animals was noted down. The peak period of Vigabatrin was determined. TD50 of Vigabatrin in the acute neurotoxicity test was ascertained. ED50 of Vigabatrin was observed to be 67 mg ± 10.20 mg/100gm of body weight. Effect of Vigabatrin starts within 60 minutes of the administration of the drug at dose of 500 mg per 100gm of body weight. The protective effect was seen maximum at 3 hours after the administration, after that the effect starts declining. TD50 of Vigabatrin was observed to be 425 mg ± 93.50 mg/100gm of body weight. Vigabatrin is relatively safe drug to use but not effective in absence seizure. Well-known side effect, visual field defect limits its use. Further elaborate screening of this drug by various experiments is needed.

**Keywords:** Anticonvulsant action, Vigabatrin, Albino rats, Patients

**INTRODUCTION**

The first anticonvulsant was bromide, suggested in 1857 by Charles Locock who used it to treat women with "hysterical epilepsy" (probably catamenial epilepsy) [1]. Anticonvulsants (also commonly known as antiepileptic drugs) are a diverse group of pharmaceuticals used in the treatment of epileptic seizures. Anticonvulsants are also increasingly being used in the treatment of bipolar disorder, since many seem to act as mood stabilizers, and for the treatment of neuropathic pain. The goal of an anticonvulsant is to suppress the rapid and excessive firing of neurons that start a seizure [2, 3].

Only two tests are obligatory in routine preclinical testing of potential antiepileptic drugs – minimal (clonic) Metrazol seizures and maximal electroshock seizures in rodents. Maximal electroshock seizures represent an adequate model of human generalized seizures of the "grand mal" type [4-6]. On

the contrary, there is no agreement about minimal Metrazol seizures. Serious doubts have been cast on the original hypothesis that they may be used as a model of human absence seizures and they more probably represent a model of myoclonic seizures [7]. Therefore it was decided to use this for testing the anticonvulsant action of vigabatrin, an antiepileptic drug, which was demonstrated to have only moderate action against minimal, clonic pentylenetetrazole-induced seizures.

**MATERIALS AND METHODS**

The current prospective study was conducted by the Department of Pharmacology of a tertiary care teaching institution. Study tools were convulsometer (electrically driven), Tuberculin syringe and Albino rats. Vigabatrin drug was used. Experimental animals were obtained from animal house of this tertiary care center.

Effect of different doses of Vigabatrin against Metrazol induced convulsions was captured. Metrazol (Pentylene tetrazole) was given in the dose of 80 mg/kg body weight S.C. after 150 minutes after the administration of Vigabatrin. A convulsion lasting more than 5 seconds was taken as the positive convulsion. The animals were observed for one hour and after 24 hours after the administration of Metrazol.

Range of effective doses of Vigabatrin in 50% of animals was noted down. Vigabatrin was administered through tuberculin syringe fitted with stomach canula. The dose administered ranges from 52 mg to 80 mg per 100gm of body weight. Two hours after the administration of the drug the electroshock of 210 mA for 0.4 second is applied through corneal electrode. Positive response was shown by absence of the tonic extensor component of the hind leg during the tonic phase of convulsion. Albino rats were observed for 1 hour after the application of electroshock.

The peak period of Vigabatrin was determined. The drug was administered orally with the help of stomach canula. The dose was kept of 500 mg per 100gm of body weight of albino rats. Shock was applied for 0.4 second of 210 mA intensity. Positive response was considered when the tonic extensor component of the hind leg during the tonic phase of convulsion was abolished. Albino rats were observed for 1 hour after the application of electroshock.

TD50 of Vigabatrin in the acute neurotoxicity test was ascertained. For this purpose 300 mg per

100gm of body weight in increasing order was administered. Acute neurotoxicity was tested with the help of position and sense test, Righting reflex test, Gait and stance test and Muscle tone test.

Permission of Institutional ethics committee (IEC) was sought before the commencement of the study. All the proforma were manually checked and edited for completeness and consistency and were then coded for computer entry. After compilation of collected data, analysis was done using Statistical Package for Social Sciences (SPSS), version 20 (IBM, Chicago, USA). The results were expressed using appropriate statistical methods.

**RESULTS AND DISCUSSION**

Vigabatrin ( $\gamma$ -vinyl GABA) is an irreversible inhibitor of GABA-transaminase [8]. It increases GABA levels at those sites, where GABA is physiologically present [9]. It is effective against various pharmacologically-induced seizures (strychnine, picrotoxin, isoniazid, 3-mercaptopropionic acid) as well as against maximal electroshock seizures in animals.<sup>10</sup> It is clinically effective against complex partial seizures [11] and also against one of the age-dependent epilepsies, the Lennox-Gas taut syndrome [12]. After the administration of Vigabatrin, mortality was recorded 40% at the dose levels varying from 52 to 65 mg/100gm of body weight and 30% at the dose levels varying from 70 to 80 mg/100gm. Vigabatrin was not so effective to protect chemo shock convulsion even in higher doses. (Table 1)

**Table 1: Effect of different doses of Vigabatrin against Metrazol induced convulsions**

Batch number of animals	Dose (mg/100gm of body weight)	Effect of drug on different batches of animals		Type of convulsion	% of protection	Death
		No. of protected animals	No. of unprotected animals			
1	52	0	10	CC, TE	0	4
2	60	0	10	CC, TE	0	4
3	65	0	10	CC, TE	0	4
4	70	0	10	CC, TE	0	3
5	75	0	10	CC, TE	0	3
6	80	0	10	CC, TE	0	3

CC: Clonic type of convulsion, TE: Tonic extensor type of convulsion

In adult rats, the 900mg/kg dose of vigabatrin suppressed generalized tonic-clonic seizures four and six hours after administration, whereas only the highest dose (1200 mg/kg) was active after 24 hours. Similar activity, i.e. specific suppression of GTCS exhibited only progabide and its metabolite SL75102 [13]. Valproate, phenobarbital and benzodiazepines were

found to block both GTCS and minimal seizures, GTCS being always more sensitive [14]. Fifty percent and/or higher range of protection were obtained only with vigabatrin dose of 70 mg/100gm of body weight or higher. ED50 of Vigabatrin was observed to be 67 mg  $\pm$  10.20 mg/100gm of body weight. (Table 2)

**Table 2: Range of effective doses of Vigabatrin in 50% of animals**

Batch number of animals	Dose (mg/100gm of body weight)	Effect of drug on different batches of animals		% of protection	Death
		No. of protected animals	No. of unprotected animals		
1	52	0	6	0	0
2	60	0	6	0	0
3	65	1	5	16.16	0
4	70	3	3	50	0
5	75	3	3	50	0
6	80	4	2	66.66	0

Results show that effect of Vigabatrin starts within 60 minutes of the administration of the drug at dose of 500 mg per 100gm of body weight. The

protective effect was seen maximum at 3 hours after the administration, after that the effect starts declining. (Table 3)

**Table 3: Determination of the peak period of Vigabatrin**

Batch number of animals	Time period (minutes)	Effect of drug on different batches of animals		% of protection	Death
		No. of protected animals	No. of unprotected animals		
1	30	0	6	0	0
2	60	1	5	16.16	0
3	90	3	3	50	0
4	120	3	3	50	0
5	180	4	2	66.66	0
6	240	3	3	50	0

Fifty percent and/or higher range of positive response were obtained only with vigabatrin dose of 450 mg/100gm of body weight or higher. TD50 of

Vigabatrin was observed to be 425 mg ± 93.50 mg/100gm of body weight. (Table 4)

**Table 4: Showing the range of TD50 of Vigabatrin in the acute neurotoxicity test**

Batch number of animals	Dose (mg/100gm of body weight)	Effect of drug on animals				+ve response	No. of animals showing -ve response	% of +ve response	Death
		NT-P	NT-R	NT-G	NT-M				
1	300	-	-	+	-	1	5	16.16	0
2	350	-	-	+	-	1	5	16.16	0
3	400	+	-	+	-	2	4	33.33	0
4	450	+	+	+	+	3	3	50.0	0
5	500	+	+	+	+	3	3	50.5	0
6	550	+	+	+	+	4	2	66.6	1

NT-P: Position sense test, NT-R: Righting reflex test, NT-G: Gait and stance test, NT-M: Muscle tone test

**CONCLUSIONS**

On the empirical evidences of this study it can be concluded that Vigabatrin is relatively safe drug to use but not effective in absence seizure. ED50 of Vigabatrin was observed to be 67 mg ± 10.20 mg/100gm of body weight. TD50 of Vigabatrin was observed to be 425 mg ± 93.50 mg/100gm of body weight. Well-known side effect, visual field defect limits its use. Further elaborate screening of this drug by various experiments is needed.

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