

PRIMIDONE IN EPILEPSY—ITS VALUE IN FRESH AND REFRACTORY CASES*

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There are several reports in the literature which claim superiority of primidone over phenobarbitone and phenytoin in the treatment of major epilepsy, (Nathan, 1954; Butter, 1953 and Oxley *et al.*, 1980). It has also been the impression of some workers that primidone is effective in controlling refractory cases either when given alone or in combination with phenytoin (Butter, 1953; Grant, 1971; and Goodman and Gillman, 1980). On the other hand Gruber *et al.* (1962) did not find primidone superior to phenobarbitone and other anticonvulsants. However, it is still believed that primidone is a more potent antiepileptic and may even be of help in refractory cases. Despite extensive clinical experience the drug at least in our country is still not used as a first line of treatment.

The present study therefore was designed to re-evaluate the efficacy of primidone as a first line treatment of epilepsy and reassess its value in refractory cases.

METHODOLOGY :

54 consecutive cases of major epilepsy comprising of grandmal, psychomotor and complex partial seizures were taken up for the study from the psychiatric Clinic of L. L. R. Hospital, Kanpur. Of the 54 cases who were started on primidone 4 patients dropped out without completing the trial and two had complaints of drowsiness and dizziness, severe enough to discontinue the medication. Of the 48 patients, 26 had either never received any

treatment or had discontinued treatment atleast 6 months prior to the commencement of primidone therapy. These were grouped as 'fresh cases'. The remaining 22 were termed as 'refractory cases' in whom the reduction in fit frequency by the adequate doses of previous anti-epileptic therapy was less than 50%.

Patients thus selected, were subjected to detailed clinical history, physical examination and a thorough neurological check up along with routine blood examination and urine analysis. Wherever necessary, X-rays of skull and E. E. G. were also done to arrive at a proper diagnosis. The patients received primidone in a range varying from 500 mg to 1500 mgs per day in divided doses. As one of the most common side effects of primidone is drowsiness the patients were started on a smaller dose. Fresh cases were given one-fourth of the 250 mg tablet at bed time initially while refractory cases were started on 125 mg at bed time. The doses were gradually increased every third day reaching the maximum level of 1000 to 1500 mg during a period 7 to 14 days. The patients were also properly warned of this side effect as to discourage them from discontinuing the medication on their own. The refractory cases were switched over to primidone after gradually discontinuing the previous medication and enhancing primidone. Only those are included in the study who have completed the trial period of one year.

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OBSERVATIONS

Out of 48 cases there were 34 men and 14 women, the age ranged from 7 to 60 years with a mean age of 32.5 years. 34 patients had typical grandmal epilepsy, 8 had psychomotor fits and 6 presented with complex partial seizures. Patients with complex partial seizures had been on some or the other anticonvulsants and belonged to the category of refractory cases. The mean duration of illness in fresh and refractory cases was 4.6 years and 7.2 years respectively.

The effectiveness of the drug was mainly evaluated on the basis of reduction in the fit frequencies. The response was categorised as 'good' when the reduction in the fit frequency was 75% or more, satisfactory when the decrease in the number of fits was between 50% and 75%, while response was considered poor if reduction in the fit frequencies was less than 50%.

There was a significant reduction in the fit frequencies of the fresh cases after primidone therapy (table 1). More than 60% fresh patients remained seizure free during the one year trial period.

TABLE 1. *Primidone in fresh cases (N=26)*

	Before primidone Therapy		After Primidone Therapy	
	N	%	N	%
<i>Fit frequencies</i>				
More than once in a month	6	23.1	2	7.7
Once in 1 to 3 months	12	46.1	3	11.5
Once in 3 to 6 months	4	15.4	2	7.7
Once in 6 month to 1 yrs.	4	15.4	3	11.5
Nil	16	61.3

Level of significance $p < .01$

The anticonvulsant drugs which the refractory cases have been taking are shown in table 2. The fits became significantly less frequent in refractory cases as well after primidone therapy (table 3). 50%

TABLE 2. *Previous antiepileptic therapy in refractory cases (N=22)*

Drugs	Number	Percentage
Phenytoin	5	22.7
Phenobarbitone	7	31.8
Carbamazepine	3	13.6
Phenytoin + Phenobarbitone	7	31.8

TABLE 3. *Primidone in refractory cases (N=22).*

	Before Primidone Therapy		After Primidone Therapy	
	N	%	N	%
<i>Fit frequencies</i>				
More than once in a month	4	18.2	1	4.5
Once in 1 to 3 months	8	36.4	4	18.2
Once in 3 in to 6 months	7	31.8	3	13.6
Once in 6 month to 1 year	3	13.6	2	9.1
Nil	—	—	12	54.6

Level of significance $p < .01$

TABLE 4. *Global response to primidone in fresh and refractory cases*

	Good		Satisfactory		Poor	
	N	%	N	%	N	%
Fresh cases (N=26)	19	73.1	3	11.5	4	15.4
Refractory cases (N=22)	14	63.6	2	9.1	6	27.3

Level of significance—N. S.

patients never had any fit during the trial period. It is further seen in table 4 that primidone is equally effective in fresh as well as refractory cases. 73% of the fresh and 67% refractory case have shown good response. The commonly

TABLE 5. Side effects of primidone

Side effects	Fresh cases (N=26)		Refractory cases (N=22)	
	N	%	N	%
	Drowsiness	14	53.8	8
Dizziness	9	34.6	6	27.3
Gastrointestinal upset	2	7.7	1	4.5

observed side effects were drowsiness and dizziness (table 5) which however, were less frequent in refractory cases.

DISCUSSION

Primidone, though an established anti-convulsant for over 30 years has mainly been used in our country as second line treatment of epilepsy. The present study was an attempt to reassess the value of primidone both in fresh as well as refractory cases. The results of our study as well as those of Livingstone and Peterson (1956), Timberlake *et al.* (1955) and Whitty (1953) who have also used primidone in fresh cases, found the drug to be a highly effective anticonvulsant in controlling major fits such as grandmal, psychomotor and complex partial seizures. Intolerable drowsiness is seen in only two cases.

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