

✓ ANTICONVULSANT ACTIVITY OF NIALAMIDE—A MONOAMINE OXIDASE INHIBITOR

By

S.K. BAPAT AND VIMAL CHANDRA

Department of Pharmacology M.L.N. Medical College, Allahabad.

INTRODUCTION

It has been reported that iproniazid, a monoamine oxidase (MAO) inhibitor reinforces the anticonvulsant actions of certain anticonvulsant drugs (8). Therefore, it was thought probable that other MAO inhibitors might possess anticonvulsant properties. Nialamide, a non-hydrazine MAO inhibitor has been studied for its anticonvulsant action. Moreover, a combination of nialamide and meclozine—an antihistamine which has anticonvulsant properties, (6) has also been tried.

MATERIALS AND METHODS

Healthy, albino rats of either sex weighing between 50-100 gm. were used in groups each of 10 animals. Supramaximal Electroshock Seizure pattern test was used to determine the anticonvulsant activity, using a current of 150 m.a. for 0.4 sec. delivered through corneal electrodes (5). Abolition of extensor component was taken as the criterion of protection.

Suspensions of meclozine and nialamide with 5% gum acacia in water were administered orally to the animals 1 hr. before challenging them to shock. Each animal of one group received the same dose. At least 3 doses of meclozine and nialamide each giving protection between 0% and 100% were employed. The ED₅₀ of the 2 drugs was determined by log dose—probit response method (3).

Next, groups of animals were administered with ED₅₀ dose of nialamide. Immediately after, different doses of meclozine were given in different groups. After 1 hr. the anticonvulsant activity was determined and ED₅₀ of the combination calculated by the same method (3).

RESULTS

The results are given in the Table 1

It has been found that nialamide possesses anticonvulsant properties. The ED₅₀ of meclozine is definitely reduced by the combination.

DISCUSSION

It has been reported that the drugs causing an increase in the concentration of catecholamines and 5-hydroxytryptamine (5-HT) in the central nervous system bring about an anti-

TABLE I

Ten animals were used for each dose

Drug	Dose mg/kg.	%Protection	ED50 mg/kg.
Nialamide	2.5	30	5.24
	5.0	50	
	10.0	80	
	20.0	60	
	40.0	60	
	100.0	40	
	200.0	20	
Meclozine	25	20	51.90
	50	40	
	100	60	
Meclozine given to rats which had received ED50 of nialamide.	25	50	34.61
	50	60	
	100	70	

convulsant effect (1). Nialamide, being a potent monoamine oxidase inhibitor, is expected to cause a significant rise in the concentration of catecholamines and 5-HT. Anticonvulsant activity as found out in the present communication supports this view. However, it is not possible to pinpoint the neurohumour. It could be due to the increase in concentrations of 5-HT or catecholamines or both. In lower doses of nialamide, the percentage protection increases with corresponding increase in the doses only upto a certain dose (1 mg/100 gm.—80%); above which, there was a gradual decline in the anticonvulsant activity (Table 1). Moreover, MAO inhibitors, in general, are known to be stimulants of central nervous system (2) as is also evidenced by the excitation we observed in the animals treated with nialamide. It has also been reported that the period of excitation fits in much more closely with the changes in brain nor-adrenaline than with those in brain 5-HT concentrations (7). An anticonvulsant synergism between the 5-HT precursor, 5-hydroxytryptophan (5HTP) and iproniazid—a MAO inhibitor has been observed (5). Moreover, the time course of anticonvulsant action of MAO inhibitors is similar to that of increase in the concentration of 5-HT (5). Further, it has been shown that 5-HT itself has some action against seizures induced by high oxygen pressure (4). These points suggest that 5-HT in brain may be playing a role in the anticonvulsant action of nialamide.

That nialamide enhances the anticonvulsant effect of meclozine suggests a possibility that both of them may be causing a rise in brain 5-HT.

SUMMARY

Nialamide, a MAO inhibitor has been tested for anticonvulsant activity by Supramaximal Electroshock Seizure pattern test and has been found to possess anticonvulsant action. Moreover, a combination of nialamide with meclozine, an antihistamine possessing anticonvul-

sant activity, has also been tried. It has been seen that nialamide reinforces the anticonvulsant action of meclozine.

A possible role of central neurohumours is discussed.

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