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Anticonvulsant Activity of Some Schiff bases

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These are the drugs which are capable of preventing convulsions. In clinical practice anticonvulsants are used eclampsia and poisoning with convulsant. The greatest use of these is in epileptic disorders.

Epilepsy: It is a collective term used for a group of chronic convulsive disorders characterized by loss of consciousness. Usually but not always with characteristic body movements and always correlated with excessive E.E.G. discharges.) Neurologically, it self-limiting. be defined paroxysmal cerebral dysrhythmia.

Types of Epilepsy:

According to characteristic seizure pattern and E.E.G. of the patient it can be divided in the following groups-

1. Grandmal Epilepsy:

Manifests as major convulsions, usually sequence of maximal tonic spasm of ail the body muscles followed by clonic jerking and prolonged depression of all the central functions.

2. Petitmal:

Characterized by brief attacks of loss of Consciousness usually with some clonic body movements varying from eyelid blinking to jerking of entire body. Sometimes no motor activity and sometimes complete relaxation of all the muscles (Akinetic petitmal).

3. Payco motor:

Manifests as attacks of confused behavior associated with increased generalized E.E.G. activity.

4. Focal Cortical:

A term with various manifestations Including convulsions confined to single 1imb or muscle group. (Jack Sonian motor epilepsy).

5. Myoclonic:

Characterized by isolated clonic jerks associated with brief bursts of multiple spikes in E.E.G.

Mechanism of Seizures:

Generalized convulsions occur when the normal brain tissues are invaded by the seizure, activity, initiated in the abnormal seizure focus - still there is no explanation of high frequency firing in the seizure focus.

Local biochemical and ischemic changes are among the possible mechanism, other pathological origin of such focci must Include congenital defects, hypoxia at birth, head Injury including compressed fractures of skull, Inflammatory vascular changes, brain abscess and neoplasm.

Classification of Anti Epileptics:

Chemical:

(i) Barbiturates - Phenobarbitone, methyl-phenobarbitones. prionidone.

(ii) Hydantoin Phenytoin, methoin, Ethotoin.

(iii) Oxazolidinediones - Trimethadiones, Paramethadione.

(iv) Succinamide-Phensuxamide,Ethosuxamide methsaxamide.

(v) Acetyl Urea - Phenyl acetyl urea (Phenacenidel).

(vi) Benzodiazepines - Clonazepam, Diazepam.

(vii) Miscellaneous Valproic acid (Sod. Valproate) Cartamaze zepine sulthanic, acetylamide.)

Mechanism of Action of Anticonvulsants:

1.On Neural Lesion:

Normalisation of the ischemic blood supply of typical cortical seizure foci. But typical automatic blocking or stimulating agents are of little value in the treatment of epilepsy.

2.Effect may Confined:

Effect may confined to the pathologically altered neurons of the seizure focus to prevent excessive electrical discharges.

3.These may Provide Theater Effect:

By acting on the normal neuronal tissue by raising their threshold against the seizure activity.

4. Post Tetanic Potentiation (P.T.P.):

It is an enhancement synaptic transmission. Thus, enhancement of synaptic transmission due to P.T.P. may produce transmission of tetanic impulses resulting in generalized grand mal Seizure.

In epileptic patients increased neural sodium concentration has been observed and this increased sodium concentration has been held responsible for the production of P.T.P. Certain drugs, like phenytoin lowers the neural sodium concentration thus diminished discharges, P.T.P. is not supposed to be involved in the petetmal epilepsy.

Drugs Like Diazepam and Nitrazepam:

It controls epileptic convulsions because these drugs increase the release and facilitate the activity of inhibitary transmitter G.A.B.A. Lin the brain tissue.

It is well known that cortisones and A.C.T.H. lowers the seizures threshold and may precipitate convulsions. In animal experiments it has been found out that DPH tends to counteract the seizure threshold lowering acting of cortisone and A.C.T. H. Thus, it has been thought that D.P.H. might produce its effect by producing a relative hypoadrenal cortical state. (Not yet confirmed).

Methodology:

In medical practice anticonvulsants are used to control convulsions occurring in epilepsy, tetanus, cerebral hemorrhage, eclampsia and in poisoning with convulsants. The greatest use is in epileptic disorders, characterized as petetmal triad, grand mal and

psychomotor seizure.

According to neurological theory epilepsy is a paroxysmal, self-limited cerebral dysrthythmia.[3] It is accompanied by abnormal pattern on the electrocephalograph and severe seizures may cause a loss of consciousness. Most of the experimental methods for detecting anticonvulsant activity convulsions and their involve the artificial induction of inhibition with organic compounds.

Screening Methods:

Convulsions can be induced by two methods: -

(1) Chemical Methods (2) Physical Methods

Chemical Methods:

In these methods an appropriate dose of chemical drug known to induce convulsions is given to experimental animal.

Generally used drugs are:

(a) Metrazol (80mg/Kg S.C.) induced convulsions.

(b) Picrotoxin test (2.0mg/Kg S.C.)

(c) Strychnine test (0.3 mg/Kg. S.C.)

1. Metrozol Induced Convulsions:

Rats are divided into two groups. One group is not given the test drug and serves as control and the animals of another group are given the test drug. After 30 minutes of administration of drug, animals of the groups are given metrozol (80mg/ Kg. S.C.) Animals of test group will show convulsions.

If the Animals of the group treated with test drug are protected from the meterozol convulsions then this will be suggestive of anticonvulsant activity of test drug.

At place of metrazol strychnine (0.3 mg/Kg S.C.) and picrotoxine (2.0 mg/Kg. S.C.) can also be used to give chemoshok.

Physical Methods:

Electroshok Method (Holland's Method) :

It is a simple method most commonly used and yields authentic results. In our experiment we have used this method to study the effect. In this method experimental animals are rats. They are divided into two groups. First group serves as control and is not given any drug and the other group is treated with the test drug. Maximal electroshock seizures are induced with a stimulus of 0.2 sec. duration and a current of 120 milli ampere.

Firstly, electroshock is given to the animals of control group. Animals exhibit a seizure pattern. The tonic flexar component of the hind limb is seen first of all, following this is the tonic extensor component[4-8], the phase of intermittent whole-body clonus is seen in the last. Now the electroshock of same intensity is given to the animal of drug treated group. Absence or diminisation in the intensity of convulsions indicate that the drug has protected[9-17] the animal from the convulsions and has got anticonvulsant activity.

Sound Induced Seizures in Rats:

The sound used to induce seizures was a 60 sec. exposure to a door bell ringing with a intensity of 90 decibels in a sound proof box. The seizures evoked were a rapid and wild running about and then tonic and clonic convulsions. Animals treated with anti-convulsant drugs do not respond to this stimulus.

Significance of the Experiment:

By these Methods anticonvulsants activity of a new drug can be found out and these drugs may prove of value in the treatment of various convulsive, disorders. Drugs protecting animals from electroshock convulsions may prove effective in Grand mal and drugs protecting animals from Chemoshok may prove of value in patient mal epilepsy.

We have used two drugs Schiff Base (SB1) derived from (2-pyridine carboxal-dehyde and 2-Amino pyridine), (SB2) from (3,4,5 triomethoxy benzaldehyde and 2-amino-6-methy1 pyridine). Two concentrations of both the drugs namely 300 mg/Kg and 375mg/Kg body weight were given to rats of test group and observations were made.

Control rats show convulsions and effect was observed even after one hour. But rats of test group show no anticonvulsant effect. Therefore we may confer that drug are not potent against convulsions. Results are summarised in the table below.

Table 5.4: Anticonvulsant Activity of Some Schiff Bases.

Group Treated with	Dose Mg/kg	No. of Animals	Effect 20 mts.	Observed 40mts.	After 60 mts.
Control	-	6	Convulsant	Convulsant	Convulsant
Test (SB_1)	300	6	Convulsant	Convulsant	Convulsant
(SB_1)	375	6	Convulsant	Convulsant	Convulsant
Test (SB_2)	300	6	Convulsant	Convulsant	Convulsant
(SB_2)	375	6	Convulsant	Convulsant	Convulsant

Result and Discussion:

Schiff bases have received renewed attention in recent years because of their proven antitumor, antibacterial, anticonvulsant and cariostatic activities[18-21] A number of papers dealing with the studies of metal complexes of the Schiff bases derived from hetero cyclic aldehydes with various aromatic amines have appeared in literature[22-23].

Table 5.4 shows anticonvulsant activity of synthesized Schiff bases when doses of 300 mg/Kg and 375 mg/Kg body weight are given no anticonvulsant activity is observed. It shows our compound is not having effect which prevent convulsions given by electroshock method of Hollands et. Al.

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