Antiepileptic drugs prevents seizures elicited by i.p. injection of thiosemicarbazide in the rat

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Alteration of GABAergique neurotransmission in the central nervous system is involved in the generation of neuronal hyperexitability and seizures. GABAergique transmission blocked by GABA antagonists injected i.p. intracerebrally induce seizures. In the present study, we characterize the effect of an inhibitory of glutamate decarbocylase, the enzyme responsible of the synthesis of GABA by injection of differentes doses of (TSC). Eight groups of six wistar rats were selected for behavioral assessement, seizure scoring, reactivity to sound and antiepileptic substances efficiency.

The dose of 2,5mg/kg did not induce noticeable behavioral reaction whereas 5mg/kg induce a significant reduction in rearing and grooming. However, this reduction was reversed at the dose of 7,5mg/kg and 10mg/kg. tonico-clonic seizure induction appeared at the dose of 7,5mg/kg with an incidence of 7,69% and a latency of 75 min. the incidence and the severity of seizures increased with the doses 10mg/kg and 20mg/kg wheras the latencies decreased. At 20mg/kg, status epilepticus and death were observed. Interestingly, audiogenic seizur (AG) susceptibility was elicited with the dose of 7,5mg/kg. AG included wild running fits followed by tonic seizure.

Phenobarbital (PB) (30mg/kg), Phenetoin (PH) (30mg/kg) and valproic acid (VA) (200mg/kg) inhibited tonico-clonic seizures elicited by 10mg/kg of TSC. PB resulted in 100% inhibition in minimal and maximal seizures. PH an VA reduced maximal seizures by 65,73% and 80,25% respectively. for minimal siezures, PH and VA induced similar reduction (46,16% and 44,42%) ($p<0.05$).

Gradual inhibition of GABAergique neurotransmission resulted in appearance of behavioral changes indicating anxiogenic effect then minimal tonico-clonic seizures followed by maximal tonico-clonic seizures and at the high inhibition status epilepticus and death. First generation of antiepileptic substances were effecient to reduce both minimal and maximal seizures. It is important to note that the dose of 7.5 mg / kg which does not induce convulsive seizures induced susceptibility to audiogenic epilepsy Statistically significant ($p<0,05$).