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ANTIEPILEPTIC DRUGS PREVENTS SEIZURES ELICITED BY I.P. INJECTION OF THIOSEMICARBAZIDE IN THE RAT

Anwar Satef[1], Abdallah Bagri[1] and Kawtar Tiamani[2]

[1]University of Hassan 1st, Morocco
[2]University of Khriwa, UG

Alteration of GABAergic neurotransmission in the central nervous system is involved in the generation of neuronal hyperexitability and seizures. GABAergic transmission blocked by GABA antagonists' injected i.p. intracerebrally induces seizures. In the present study, we characterize the effect of an inhibitory of glutamate decarboxylase, the enzyme responsible of the synthesis of GABA by injection of different doses of thiosemicarbazide (TSC). Eight groups of six Wistar rats were selected for behavioural assessment, seizure scoring, reactivity to sound and antiepileptic substances efficiency. The dose of 2.5 mg/kg did not induce noticeable behavioral reaction whereas 5 mg/kg induced a significant reduction in rearing and grooming. However, this reduction was reversed at the dose of 7.5 mg/kg and 10 mg/kg. Tonic-clonic seizure induction appeared at the dose of 7.5 mg/kg with an incidence of 7.69% and a latency of 75 min. The incidence and the severity of seizures increased with the doses 10 mg/kg and 20 mg/kg whereas the latencies decreased. At 20 mg/kg, status epilepticus and death were observed. Interestingly, audiogenic seizure (AG) susceptibility was elicited with the dose of 7.5 mg/kg. AG included wild running fits followed by tonic seizure. Phenobarbital (PB) (30 mg/kg), Phenetoin (PH) (30 mg/kg) and valproic acid (VA) (200 mg/kg) inhibited tonic-clonic seizures elicited by 10 mg/kg of TSC. PB resulted in 100% inhibition in minimal and maximal seizures. PH and 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 GABAergic neurotransmission resulted in appearance of behavioural changes indicating anxiogenic effect then minimal tonic-clonic seizures followed by maximal tonic-clonic seizures and at the high inhibition status epilepticus and death. First generation of antiepileptic substances were efficient 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 ($p<0.05$).

satefanwar02@gmail.com