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CARTAS AL EDITOR

Dantrolene Prevents Hyperthermia Induced Seizures in Rat Pups

Different studies have been reported that hyperthermia induced seizures in rat pups are similar to febrile seizures in children (2, 4). On the other hand experimental evidence suggests to us that calcium plays an important role in temperature regulation in mammals (1). Thus, we studied the effects of sodium dantrolene, a drug which affects intracellular calcium mobilization. Wistar albino rat pups aged 15 days were used (n = 34). Acute hyperthermia was induced by placing rats in a ventilated incubator (Unitemp) at a constant temperature of 40° C with 55 % humidity. Rats were unrestrained during the experiments and rectal temperatures were measured with a thermometer (ELLAB TF 3) connected to RM 6 thermocouple probes. The temperatures were recorded immediatelty after placing the rats in the chamber (time 0) and thereafter at 10 min intervals for a total of 90 min. The rats were injected i.p. with 0.2 ml of 0.9 % NaCl (saline, n = 15) and sodium dantrolene (5 mg/kg, n = 9 or 10 mg/kg, n = 10). Animals were observed for onset of generalized seizures and for death. Data were analyzed by Student's *t* test and analysis of variance.

Table I shows the results obtained with the different experimental groups. Saline injected rats had a progressive increase in temperature reaching a maximal value at 50 min exposure. Both groups injected with sodium dantrolene also showed a marked increase in body temperature, nevertheless, temperatures were significantly lower than in saline injected animals ($p < 0.001$).

At 30 min, saline injected animals had a temperature of 40.8 ± 0.2° C and 13 % showed generalized tonic-clonic seizures. All these animals (100 %) had seizures at 50 min exposition. After 50 min exposure

Table I. *Effects of sodium dantrolene (DAN) on temperature induced seizures.*

Time	Saline (n = 15)			DAN (5 mg/kg, n = 9)			DAN (10 mg/kg, n = 10)		
min	T °C	% S	% D	T °C	% S	% D	T °C	% S	% D
0	35.8 ± 0.1	0	0	35.9 ± 0.2	0	0	35.0 ± 0.3	0	0
30	40.8 ± 0.2	13	0	40.1 ± 0.2	0	0	39.2 ± 0.4	0	0
50	42.0 ± 0.1	100	100	40.9 ± 0.2	0	0	40.3 ± 0.4	0	0
70	—	—	100	41.6 ± 0.1	0	0	41.2 ± 0.2	0	0

T °C = Rectal temperature. % S = Percent seizures. % D = Percent death.

to the 40° C environment, animals receiving sodium dantrolene (5 or 10 mg/kg) reached a rectal temperature of 40.9 ± 0.2° C and 40.3 ± 0.4° C respectively. None of the sodium dantrolene treated animals had seizures within the observation period.

Animals treated with sodium dantrolene had lower body temperatures than the controls, indicating that calcium-dependent mechanisms may be involved in temperature regulation and adaptation. Similarly, these results indicate that sodium dantrolene at clinically relevant dosages prevents hyperhermia induced seizures in the rat pup model, providing us comprehensive *in vivo* data on the importance of calcium in the mechanism of seizures. In this way we have demonstrated that a calcium antagonist diltiazem prevented hyperthermia induced seizures in the rat pups (3). These data also confim the role of calcium in the pathophysiology of seizures.

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Key words: Hyperthermia, seizures, Dantrolene.

Palabras clave: Hipertermina, Convulsiones, Dantrolene.

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