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BRIEF COMMUNICATION

Phenoxybenzamine Reduces Mortality Associated With Intracerebral Injections of Excitatory Neurotoxins

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VANDERWOLF, C. H. AND R. K. COOLEY. *Phenoxybenzamine reduces mortality associated with intracerebral injections of excitatory neurotoxins*. PHARMACOL BIOCHEM BEHAV **38**(3) 689–690, 1991.—Intracerebral injections of kainic acid produce gross hematuria, renal cortical necrosis, and an associated high mortality. Hematuria is virtually eliminated and mortality significantly reduced by pretreatment with phenoxybenzamine.

Hematuria Kainic acid Mortality Neurotoxin Phenoxybenzamine

BOYKO (1) et al. have demonstrated that intrathalamic injections of kainic acid produced myocardial necrosis and gross hematuria in rats but did not report a satisfactory means of preventing these pathological conditions. During the course of a series of experiments on the effects of intracerebral injections of kainic acid and other neurotoxins (3–7), we too observed a pronounced hematuria and an associated high mortality among the experimental rats. Histological examination of the kidney suggested that an acute renal cortical necrosis formed a part of the overall pathology. An early report that strong brain excitation can lead to neurally mediated renal pathology (2) suggested to us that sympathetic blockade might reduce the mortality of our rats.

Consequently, we compared mortality rates in 300–500 g rats that had received unilateral injections of kainic acid in the basal forebrain (0.5–1.0 μl of a 1 μg/μl solution of kainic acid in Locke's solution, injected over a period of 6 min or longer at a site 1.8 mm posterior to bregma, 3.2 mm lateral to the midline, and 6.9 mm below the skull surface, with the dorsal surface of the skull in the horizontal plane), either with or without sympathetic blockade. Sympathetic blockade was produced by injection of phenoxybenzamine HCl (5–10 mg/kg, IP) or phenoxybenzamine plus propranolol HCl (5–10 mg/kg, IP) just before surgery.

Phenoxybenzamine, alone or in combination with propranolol, virtually abolished gross hematuria, and resulted in a significant improvement in the survival of the experimental rats (Table 1). Therefore, we recommend the use of sympathetic blockade as means of reducing mortality following intracerebral injection of excitatory neurotoxins.

TABLE 1

EFFECT OF SYMPATHETIC BLOCKADE ON THE MORTALITY RESULTING FROM UNILATERAL INJECTION OF KAINIC ACID INTO THE BASAL FOREBRAIN IN RATS

	Survival >10 Days	Survival <10 Days	Total
No treatment	12 (60)	8 (40)	20 (100)
Sympathetic blockade	43 (91.5)	4* (8.5)	47 (100)

*$p<0.001$, χ^2 test. Numbers in parentheses indicate percentages.

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