

BRAIN CHOLESTEROL AND PHOSPHOLIPID LEVELS IN CYPROHEPTADINE TREATED ALBINO RATS

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Abstract : Effect of different doses (2.5 mg, 5 mg, 10 mg and 40 mg/kg), s.c., for 2 weeks, of cyproheptadine (CYP) on brain cholesterol and phospholipid of albino rats was investigated. Cyp. 2.5 mg/kg, showed increase in brain cholesterol and phospholipid contents whereas other doses caused a decrease in phospholipid level.

Key words : cyproheptadine brain cholesterol brain phospholipid

INTRODUCTION

Cyproheptadine (CYP) is an antiserotonergic drug commonly used as appetite stimulant in children, elderly patients and in cases of anorexia nervosa (1, 2, 3). Strosznajder and coworkers (4) observed moderate inhibition of brain choline and ethanolamine glycerophospholipid synthesis by 5-HT in rats. Because nervous tissue lipids play an important role in maintaining structural integrity which facilitates proper neuronal functions, the present study was carried out in albino rats to demonstrate the effect of Cyp on brain lipids.

METHODS

36 albino rats weighing 70-120 gms were divided to 5 groups, control and 4 experimental groups. Group I received Cyp, 2.5 mg/kg, group II, 5 mg, Group III, 10 mg and group IV, 40 mg/kg s.c. daily for 15 days. Commercially available diet in pellet form and water were given. Animals were sacrificed after two weeks. Weight of the fresh brain was recorded. Lipids from fresh brain were extracted with chloroform, methanol (2 : 1) mixture (5). Cholesterol (6) and lipid phosphorus were measured (7) and the phospholipid value was obtained by multiplying lipid phosphorus by factor 25. The levels were expressed as mg per gm wet weight of brain. Statistical analysis was done by

applying unpaired students 't' test.

RESULTS AND DISCUSSION

The wet brain weight was found to be unaltered in experimental groups as compared to the control. Cyp. 2.5 mg/kg caused an increase in phospholipid, however higher (5 mg-40 mg/kg) caused a decrease (Table 1). The brain cholesterol level also increased with 2.5 mg/kg of Cyp whereas its level remain normal with higher doses. Brain phospholipid level is usually maintained by denovo synthesis as blood brain barrier is impermeable to it (8). 5-HT is an important neuromodulator in brain. Strosznajder and coworkers by synaptosomal Studies observed that 5-HT is a receptor mediated moderate inhibitor of glycerophospholipid synthesis in brain (4). Cyp being a 5-HT receptor blocker, might be causing increase in phospholipid and cholesterol contents of brain at 2.5 mg Cyp/kg. Chlorpromazine, a phenothiazine on experimental animals showed at therapeutic doses chlorpromazine stimulates phospholipid synthesis measured by P³² labelling of brain phospholipid but at higher dose the drug had inhibitory effect (9). Further study is required to understand the Cyp receptor interaction, the nature and role of second messengers affecting lipid metabolism and their correlation with neuromal function.

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TABLE I: Brain weight, brain total cholesterol and phospholipid contents of adult Albino rats at different doses of Cyp.

	Control <i>n</i> = 8	Experimental (Cyp. mg/kg of body weight)			
		Group I (2.5 mg) <i>n</i> = 8	Group II (5 mg) <i>n</i> = 7	Group III (10 mg) <i>n</i> = 6	Group IV (40 mg) <i>n</i> = 7
Brain weight (gm)	1.44±0.14	1.4±0.16	1.4±0.08	1.3±0.008	1.3±0.08
Brain phospholipid (mg/gm of wet weight)	37.5±2.6	41.0±2.3*	32.8±2.1***	30.2±2.4***	28.1±3.2***
Brain total cholesterol (mg/gm of wet weight)	14.4±1.3	22.2±2.5***	15.1±1.3	13.7±1.9	12.8±2.5

*P < 0.05 ; ***P < 0.001

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