Indian J Physiol Pharmacol 1996; 40(1): 105-106

LETTER TO THE EDITOR

RENAL LIPIDS IN CYPROHEPTADINE TREATED ALBINO RATS

Sir,

(Received on January 23, 1995)

It has been reported that brain membrane phospholipids and cholesterol levels are altered in the rat when treated with cyproheptadine (Cyp) (1). Kidney is a metabolically active organ like the liver and the brain. Renal cells have the ability to metabolize glycerol rapidly. It synthesises phospholipids, cholesterol and even triacylglycerol *de novo* and adds to the plasma lipid pool (2). Hence we examine the Cyp effects on renal lipids in the present study. In addition we measured the enzyme glucose-6-phosphate dehydrogenase (G6PD) activity in renal tissues as it generates NADPH in hexose menophosphate shunt pathway of glucose metabolism. NADPH is required for *de novo* lipid synthesis.

Thirty eight albino rats weighing 90-125 gms were divided into control and four experimental groups. Experimental animals received Cyp 2.5-20 mg/kg, s.c. daily for 15 days. The dose and number of animals in each experimental group are mentioned in Table I. Water and commercially available diet in pellet form were given in adequate amounts to all the animals. The animals were sacrificed after 2 weeks of drug therapy. One kidney was homogenised in ice-chilled 0.32 M sucrose to prepare a 10% kidney homogenate. The homogenate was centrifuged at 3,500xg in Remi-refrigerated centrifuge for 30 minutes at 4°C and the supernatant was stored at —20°C for G6PD assay (3). The enzyme activity was expressed in U/mg protein. One unit of enzyme is taken as the amount of the enzyme which produces one nanomole of NADPH per min at 25°C. The protein content of supernatant was measured by modified Lowry method (4). The other kidney was subjected to lipid extraction with chloroform : methanol (2:1) mixture (5). Cholesterol (6), triacylglycerol (7) and lipid phosphorous (8) were estimated. Phospholipid value was calculated by multiplying lipid phosphorous by factor 25. The levels were expressed in mg/gm wet weight of kidney. Statistical analysis was done by applying the unpaired student 't' test.

TABLE I : Total phospholipids, cholesterol and triacylglycerol content and glucose-6-phosphate dehydrogenase (G6PD) activity in kidney of albino rats at different doses of cyproheptadine (Cyp).

	Renal lipids (mg/gm wet wt)			*Renal G6PD activity*
	Cholesterol	*Phospholipids*	*Triacylglycerol*	*μ/mg protein*
Control (9)	6.9 ± 1.0	9.7 ± 1.1	6 ± 0.9	12.2 ± 1.2
Experimental				
Group I (8) (2.5 mg Cyp/kg body weight)	9.0 ± 1.3***	9.1 ± 1.1	4.8 ± 0.7***	13.5 ± 1.1*
Group II (7) (5 mg Cyp/kg body weight)	6 ± 1.3	8.5 ± 1.0**	5.5 ± 0.7	12 ± 2.4
Group III (7) (10 mg Cyp/kg body weight)	6.2 ± 1.1	7.8 ± 1.5**	5.4 ± 0.7	12.4 ± 2.1
Group IV (7) (20 mg Cyp/kg body weight)	6.1 ± 1.4	7.9 ± 1.1***	6.3 ± 1	11.5 ± 2.3

*P<0.05; **P<0.02; ***P<0.01

The levels of different renal lipids and G6PD activity are presented in Table I. At 2.5 mg/Cyp/kg body weight dose, renal cholesterol level was significantly raised ($P<0.01$); G6PD activity was increased ($P<0.05$); total phospholipids level was normal as compared to control. In contrast triacylglycerol content was markedly lowered indicating depressed lipogenesis. Rats who received Cyp in the range of 5-20 mg/kg showed significant decrease in renal total phospholipids ($P<0.02$). The levels of total cholesterol, triacylglycerol and G6PD activity remained normal.

Reports show that high doses of Cyp (40-45 mg/kg) cause degranulation and vacuolation of β-cell with concurrent reduction of pancreatic and plasma insulin, the action appears to be unrelated to the known antiserotonergic and antihistaminic properties of the drug, however at lower doses (5-11 mg/kg), the drug has no effect on insulin level (9, 10). The doses of Cyp used in the present study ranges between 2.5 to 20 mg/kg body weight. The dose-dependent alteration in renal cholesterol and phospholipids are similar to what was seen in albino rat brain in our previous study (1). Does Cyp mediate in kidney as well as in brain in a similar way? It needs detailed analysis to understand the site of Cyp interaction as well as the mechanism of action on lipid metabolism and their correlation with cell functions.

B. C. KABI*, Y. N.RAO, B. PARSI AND A. S. CHAKRABARTY

Departments of Biochemistry and Physiology, Maulana Azad Medical College, New Delhi - 110 002

REFERENCES

1. Kabi BC, Rao YN, Parsi B, Chakrabarty AS. Brain cholesterol and phospholipid level in cyproheptadine treated albino rats. *Indian J Physiol Pharmacol* 1993; 37 : 165-166.
2. Schrier RW, Gottschalk CW. Disease of the kidney Vol. 1, 5th edn. Little Brown and Company (London) 1993; 233-260.
3. Vallejo CG, Marco R, Sebastian J. The association of brain hexokinase with mitochondrial membranes and its functional implications. *Eur J Biochem* 1970; 14 : 478-485.
4. Markwel MAK, Has SM, Tolbert NE, Brieber LL. Protien determination in membrane and lipoprotein sample. *Methods in Enzymol* 1981; 72 : 296-303.
5. Folch J. A simple method for isolation and purification of lipid from animal tissue. *J Biol Chem* 1957; 226 : 497-509.
6. Bowman RE, Wolf RC. A rapid and specific method for total serum cholesterol. *Clin Chem* 1962; 8 : 300-309.
7. Mendez J, Franklin B, Gahagan H. Simple manual procedure for determination of serum triglyceride. *Clin Chem* 1975; 21:768-770.
8. Varley H. Practical clinial biochemistry 4th ed. *Arnold Heinman (India)* 1975; 445-450.
9. Chow SA, Fischer LJ. Susceptibility of fetal rat endocrine pancrease to the diabetogenic action of cyproheptadine. *Toxicol Appl Pharmacol* 1986; 84 : 264-277.
10. Chakrabarty AS, Pourany A. Anathanarayanan PH, Subramanian N, Rathinaswamy P, Chakrabarty K. Effect of cyprocreptadine on glucose tolerance, serum insulin and structure of pancreatic islets in rat. *Indian J Exp Biol* 1990; 28 : 721-723.

*Corresponding Author