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LETTER TO THE EDITOR

EFFECT OF NIFEDIPINE ON CARBOHYDRATE METABOLISM IN RATS

Sir,

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It has been reported that long term nifedipine therapy produces hyperglycemia (1, 2) but others (3) could not find any significant effect on blood glucose or glucose tolerance test in normal individuals, though glucose tolerance in non-insulin dependent diabetics was impaired. Donnelly et al (4) published contravertical data including some early impairment of glucose tolerance which improved after long term treatment. We therefore studied the effect of nifedipine on carbohydrate metabolism in rats.

In all the studies Wistar strain albino rats (150-200 g) of either sex were used in groups (6 rats/group).

Blood sugar and glycogen content in organs- Nifedipine dissloved in a vehicle containing polyethylene glycol 400, ethenol and saline (15:15:70) given ip in the dose of 0.5, 2.5, 5 and 10 mg/kg for a period of 3 weeks; controls received vehicle in the same volume. At the end of 3 weeks blood sample was collected from renal artery under ether anaesthesia and blood sugar (5) and glycogen content of the heart, liver and skeletal muscle was estimated (6).

Glucose uptake of diaphragm- Rats fasted for 24 hours were sacrificed. Half diaphragm was transferred to incubation media containing nifedipine in concentration of 100 ug/100 ml, while the other half served as control. Glucose uptake of isolated diaphragm was estimated (7).

Alloxan induced hyperglycemia - One group received nifedipine (2.5 mg/kg ip) for 3 weeks while the other (control) received vehicle only. Alloxan (150 mg/kg) was injected sc 2 days prior to sacrificing animals. After 3 weeks of nifedipine treatment blood was collected from renal artery after 24 hours fasting under ether anaesthesia for estimation of blood sugar (5).

TABLE I : Effect of nifedipine (given ip for 3 weeks) on blood sugar and glycogen content of liver in rats.

Sr. No.	*No. of animals*	*Dose of nefedipine mg/kg*	*Blood sugar mg%*	*Glycogen content µg/100 mg of tissue*
1.	10	—	84±2.24	1965±77.8
2.	6	0.5	111±3.29*	2792±63.76**
3.	6	2.5	114±1.8*	2901±109.4**
4.	6	5.0	116±2.1*	3290±87**

All value are mean ±S.E.M. *P<0.05, **P<0.01.

Nifedipine produced significant hyperglycemia but rise in blood sugar was not dose dependent (Table I). Nifedipine also increased blood sugar in rats rendered hyperglycemic by alloxon (193 ± 10.7 and 224 ± 9.3 mg%, n = 6, p < 0.05). Nifedipine

TABLE II : Glucose uptake in rat diaphragm under aerobic condition.

Dose of nifedipine 100 ug/100 ml of medium
n = 6 (in each group)
Glucose uptake mg/gm of wet tissue

Incubation time in minutes	*Control*	*In presence of nifedipine*
15	0.84±0.038	0.81±0.035
30	1.53±0.06	1.48±0.073
60	2.55±0.163	2.57±0.133

± S.E.M., P> 0.05

significantly increased liver glycogen (Table I) in dose dependent manner. Glycogen content of heart (173 ± 5 ug/100 mg, n = 6) or skeletal muscle (185 ± 4.5 ug/100 mg, n = 6) was not altered. Glucose uptake of diaphragm was not altered by nifedipine (Table II).

We observed that nifedipine produced hyperglycemia in rats after chronic treatment which was only moderate and it was also not dose dependent. Nifedipine also increased the liver glycogen content without altering that in heart or skeletal muscle. The rise in blood sugar could be due to alteration in insulin secretion impairment of entry of calcium ion in Beta cells of Langerhan's by nifedipine could lead to subsequent inhibition of insulin release (8, 9, 10). There was some potentiation of diabetogenic action of alloxan after nifedipine treatment indicating some direct action on carbohydrate metabolism. But this does not explain increase in liver glycogen level. Possibly, action of insulin in liver is still adequate even after moderate inhibition of insulin release or else, hyperglycemia is more due to a direct peripheral action rather than due to inhibition of insulin release.

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