THE EFFECTS OF MEDROXYPROGESTERONE ACETATE ON CARBOHYDRATE METABOLISM: MEASUREMENT OF GLUCOSE, GLYCOGEN. PYRUVATE, AND LACTATE AFTER 1-MONTH OF TREATMENT IN FEMALE RATS

by

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The effects of oral contraceptives on various parameters of metabolism have been extensively studied during the past decade. Conflicting reports have appeared in the literature and it has now become important for investigators to study the effects of the individual estrogens and progestogens in order to resolve these problems. Spellacy *et al.*, (1972) have shown the changes in carbohydrate metabolism in women treated with medroxyprogesterone acetate for one year. Obviously, the mechanisms involved in mediating the changes so reported cannot be done in human beings and animal studies are called for. This report deals with the effects of an injectable, long acting progestogen, medroxyprogesterone acetate (6α-methyl-17-acetoxy progesteron) on glucose, glycogen, pyruvic acid, and lactic acid in female rats measured after one month period of treatment.

Material and Methods

Female albino rats weighing between 200-250 g. body weight were used in all the experiments. To the experimental group a single dose of 30 mg. of medroxyprogesterone acetate was injected intramuscularly. Two days before sacrifice oral glucose tolerance tests was carried out. After one month of treatment, overnight fasted animals under light ether anaesthesia were killed and pyruvic acid and lactic acid in blood and liver were estimated. Liver glycogen was also determined. In the control group, all the assays were performed without medroxyprogesterone acetate treatment.

Oral Glucose Tolerance Test: Fasting blood glucose level was determined by taking the blood from the tail. After taking the fasting blood sample, 0.8 ml. of 50% glucose was administered. Repeat blood samples were then drawn at 1, 1.5, 2, and 3 hours and glucose level determined.

Glucose: The blood for glucose determination was placed in tubes containing fluoride, to inhibit glycolysis, and potassium oxalate as an anticoagulant. These were mixed well and glucose content was measured in duplicate by the method of Nelson (1944).

Pyruvic acid in the liver and blood was determined by the method of Wootton (1964).

Lactic acid was determined by the method of Barker and Summerson (1941).

Glycogen: Liver glycogen was deter-

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mined by the method of Montgomery (1957).

Results

Glucose tolerance was not deteriorated ($p>.05$) in medroxyprogesterone acetate treated rats and it was similar to the control rats (Table 1).

TABLE I

Blood Glucose Values in mg/100 ml. in Controls and Medroxyprogesterone Acetate Treated Female Rats

(Values are mean ± S.D. Figures in parenthesis indicate the number of animals studied)

Group	Fasting	Time in Hours			
		1	1.5	2	3
Controls (10)	76.2 ± 3.6	128.3 ± 4.6	112.1 ± 6.2	95.2 ± 9.8	74.3 ± 4.3
1 month treated (10)	76.3 ± 4.2	128.4 ± 3.9	118.8 ± 6.5	94.4 ± 8.8	78.1 ± 4.2

There was no significant change ($p>0.05$) in pyruvic acid and lactic acid levels in blood and liver of medroxyprogesterone acetate treated rats as compared to control rats (Table 2).

TABLE II

Lactic Acid and Pyruvic Acid in Blood and Liver of Controls and Medroxyprogesterone Acetate Treated Female Rats

(Values are mean ± SD. Figures in parenthesis indicate the number of animals studied)

Group	Blood		Liver	
	Lactic acid mg/100 ml.	Pyruvic acid mg/100 ml.	Lactic acid mg/100 g	Pyruvic acid mg/100 g
Controls (10)	33.8 ± 4.2	1.22 ± 0.13	173 ± 47	7.5 ± 1.2
1 month treated (10)	37.2 ± 3.6	1.46 ± 0.48	158 ± 50	8.8 ± 4.2

There was a significant decrease ($p<.01$) in liver glycogen in medroxyprogesterone treated animals when compared with that of controls (Table 3).

TABLE III

Glycogen Content in the Liver of Controls and Medroxyprogesterone Acetate Treated Female Rats

(Values are menn ± SD. Figures in parenthesis indicate the number of animals studied)

Group	Glycogen content (mg/g of liver)
Controls (10)	7.84 ± 1.4
1 month treated (10)	2.1 ± 0.21

Discussion

The literature dealing with the metabolic effects of medroxyprogesterone has been reviewed by Spellacy *et al.*, (1970). The current results are important for several reasons. First, these data confirm the fact that this particular progestogen has an adverse effect on carbohydrate metabolism, although the mechanism of action is still obscure. Secondly, it appears that the duration of treatment is important as there is no change in blood glucose level after one month of treatment. Also, there is no change in pyruvic acid and lactic acid in blood and liver of animals treated with medroxyprogesterone acetate for one month. It may be possible that there may be a deteriora-

tion of glucose tolerance and changes in pyruvic acid and lactic acid when the duration of treatment is increased as reported by Spellacy *et al* (1972). He reported that increase in blood glucose and plasma insulin levels are more significant after one year of treatment of women with medroxyprogesterone acetate than six months of treatment. The subjects had a normal glucose curve after 6 months of therapy but an "abnormal" one after one year. Thirdly, there is a significant decrease in liver glycogen in the experimental animals than those of controls. So, the decrease in liver glycogen in the medroxyprogesterone acetate treated animals may be due to decreased rate of production rather than increased rate of degradation because there is no change in blood glucose level in the experimental rats. Also, there is no change in pyruvic acid and lactic acid in the blood and liver of medroxyprogesterone acetate treated rats.

Summary

The carbohydrate metabolism of female rats receiving intramuscular injections of medroxyprogesterone acetate was prospectively investigated during one month of treatment. There was a significant decrease in liver glycogen, but no change in pyruvic acid and lactic acid in blood and liver of medroxyprogesterone acetate treated rats than those of controls. Deterioration of oral glucose tolerance did not occur in rats after one month of treatment.

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