EFFECT OF OVARIECTOMY AND PERIODIC IMMOBILIZATION ON SOME INDICES OF LIPID AND CARBOHYDRATE METABOLISM AND OF THYROID FUNCTION IN FEMALE RABBITS

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The dynamics of the glucose tolerance test and of the serum concentrations of cholesterol, phospholipids, and free fatty acids (FFA) was studied for 15 months in female rabbits aged about 1.5 yr at the beginning of the experiments. Some intact and ovariectomized animals were exposed to periodic immobilization in special cages. The immobilization reduced the glucose tolerance and led to the subsequent development of hypercholesteremia. Ovariectomy led to an increase in the blood FFA level and a temporary decrease in the glucose tolerance. In all the experimental rabbits by the end of the experiment the serum cholesterol was raised and the glucose tolerance was lowered relative to the control. In the ovariectomized animals a tendency toward a decrease in the uptake of I^{131} by the thyroid gland was observed, and this tendency was strengthened by a combination of ovariectomy and periodic immobilization.

KEY WORDS: ovariectomy; hypekinesia; thyroid gland; glucose tolerance; free fatty acids; cholesterol.

Among the factors predisposing to the development of atherosclerosis are ovariectomy [1], insufficient motor activity [3, 4], "traumatization" of the CNS [5], and depressed thyroid function [2].

The object of this investigation was to study some indices of carbohydrate and lipid metabolism and of thyroid function in ovariectomized and intact female rabbits immobilized periodically.

EXPERIMENTAL METHOD

Female rabbits aged 1 yr 3 months to 1 yr 6 months were used. Observations continued for 1 yr 3 months, so that by the end of the experiments the animals were aged from 2 years 6 months to 2 yr 9 months. The animals were divided into four groups: control (5 animals), intact + immobilized (6), ovariectomized (8), and ovariectomized + immobilized (5). The immobilization was carried out in special cages [5] for periods of 5 days separated by intervals of 7 days, making a total number of 6 periods of immobilization during the last 3 months of the experiment. Before the experiment began and 1 and 8-9 months after ovariectomy, and again 6 days after the first and last period of immobilization, the serum concentrations of cholesterol [9], phospholipids [11], and free fatty acids (FFA) [6] were determined in the fasting animals. The glucose tolerance test was carried out at the same times. The blood sugar [7, 8, 10] was determined in a fasting state and 1 and 2 h after administration of glucose solution by gastric tube at the rate of 4 g/kg body weight.

At the end of the experiment all the animals received an instramuscular injection of 0.5 μCi I^{131} and the percentage of it taken up by the thyroid gland after 5, 24, and 48 h was determined.

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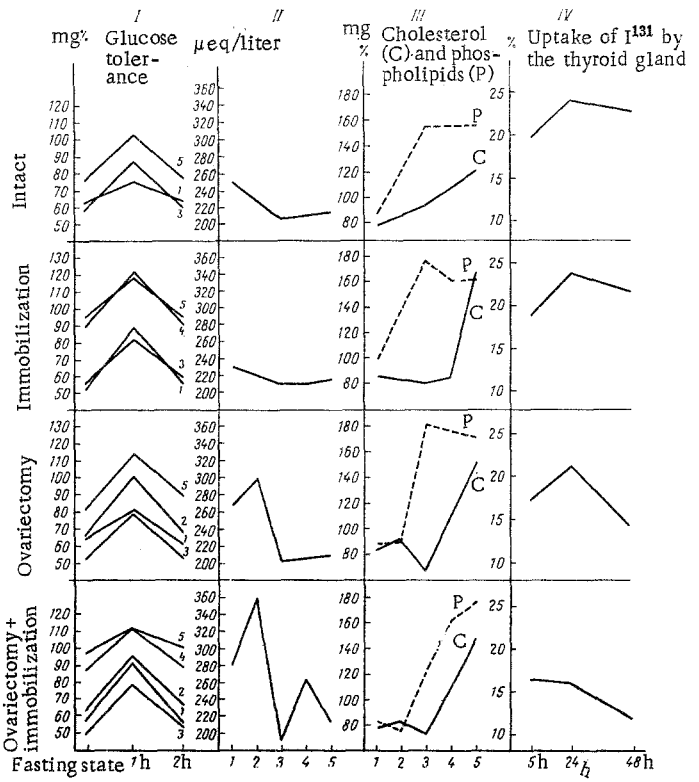

Fig. 1. Glucose tolerance test, serum lipid concentration, and uptake of I^{131} by the thyroid gland in female rabbits subjected to ovariectomy and periodic immobilization: 1) at beginning of experiment; 2) 1 month later; 3) 8-9 months after beginning of experiment (before immobilization); 4) after first immobilization; 5) after last immobilization, at end of experiment.

EXPERIMENTAL RESULTS AND DISCUSSION

In the intact rabbits (Fig. 1) toward the end of the period of observation the fasting blood level was raised ($P < 0.05$); 1 and 2 h after glucose loading, the blood cholesterol concentration also was raised ($P < 0.01$).

In the intact animals 6 days after the first immobilization the blood sugar was raised in the fasting state and 1 and 2 h after glucose loading ($P < 0.01$). However, there was no change in the lipid concentration by this time. Not until two months later was the cholesterol concentration and the cholesterol/phospholipids ratio increased ($P < 0.01$), while the carbohydrate metabolism remained distrubed. The serum FFA level in the fasting state was practically unchanged in this group of animals throughout the experiment. It is important to emphasize that by the end of the experiment the blood sugar and cholesterol concentrations of these rabbits were higher ($P < 0.05$) than in the control animals at the same time.

Ovariectomy without immobilization led after 1 month to a raised blood sugar concentration 1 h after glucose loading ($P < 0.05$) and a tendency for the FFA level to rise ($P = 0.06$). However, after 9 months the glucose tolerance test and the FFA concentration were back to normal. Only at the end of the experiment was the blood sugar of these rabbits raised in the fasting state and after glucose loading, in conjunction with hypercholesteremia ($P < 0.01$). Though the cholesterol concentration was significantly higher ($P < 0.05$) than in the rabbits of the control group, the blood sugar concentration, after glucose loading, was not.

If ovariectomy was combined with immobilization, an increase ($P < 0.05$) in the blood sugar level was observed after the first immobilization in a fasting state and 1 and 2 h after glucose loading, together with elevation of the serum cholesterol and FFA levels. By the end of the experiment the changes in the carbohydrate and lipid metabolism were still mainly present but the cholesterol concentration was higher still ($P < 0.05$) and the FFA concentration lower ($P < 0.05$) than at the previous period of investigation.

No significant differences in the uptake of I^{131} by the thyroid gland between the experimental and control animals could be found. Only a tendency was seen for the thyroid activity to decrease in the ovariectomized animals, whether immobilized or not.

Staining of the aorta in toto with Scharlach Red revealed no atherosclerotic changes. They evidently develop later [5]. The results give evidence of the role of stressor situations in the formation of disturbances of carbohydrate and lipid metabolism. Considering that the disturbance of the glucose tolerance test in the rabbits appeared immediately after immobilization, whereas hypercholesteremia was observed later, it can be postulated that the disturbance of carbohydrate tolerance is one of the factors leading to hypercholesteremia. Disturbance of the glucose tolerance test in the animals not immobilized was not accompanied by elevation of the serum FFA level. Consequently, an increase in lipolysis was probably not the cause of the disturbance of the carbohydrate tolerance during immobilization. Soon after ovariectomy, besides lov ing of the glucose tolerance, some increase in the serum FFA concentration was observed. The possibility cannot be ruled out that the sex hormones have an inhibitory effect on lipolysis (direct or via the CNS, especially the hypothalamus). Restoration of the normal blood FFA level 8-9 months after ovariectomy possibly reflects compensatory and adaptive reactions of the body to prolonged estrogen deficiency.

Some decrease in glucose tolerance and increase in the blood cholesterol concentration was noted even in the intact animals at the end of the period of observation, probably on account of the age dynamics of these parameters. However, in all the experimental animals by the end of the experiment the blood sugar and cholesterol concentrations were significantly higher than in the control.

Since no clear changes in I^{131} uptake by the thyroid gland were observed in the experimental animals, lowering of the function of this gland could hardly have played a significant role in the genesis of the changes in lipid and carbohydrate metabolism under the experimental conditions used. However, the tendency toward a decrease in I^{131} uptake by the thyroid gland at the end of the experiment coincided with the hypercholesteremia.

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