Effect of Alimentary Hypercholesterolemia in Female Rabbits on Blood Lipid Levels in Their Progeny

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Female rabbits fed cholesterol-rich diet during pregnancy and/or lactation developed hypercholesterolemia and their progeny had higher lipid levels than the progeny of normolipidemic females. The weight of rabbits born from or fed by females with alimentary hypercholesterolemia was lower than normal during the entire observation period (40 weeks). After weaning (at the age of 6 weeks), serum concentrations of cholesterol and triglycerides in the progeny were higher than in adult animals.

Key Words: *alimentary hypercholesterolemia; progeny; cholesterol; pregnancy; lactation*

The role of hereditary factors in lipid metabolism in humans and animals has been extensively studied. Changes in blood content of lipids (hyperlipidemia) in the mother affects cholesterol (CS) homeostasis even if the child does not inherit hyperlipidemia. This problem received little attention, and contradictory results were obtained. We studied the effect of alimentary hypercholesterolemia (HCS) in rabbits during pregnancy and/or lactation on blood lipid levels in the progeny.

MATERIALS AND METHODS

Three groups of rabbits were studied. Group 1 (control, n=8) consisted of the progeny of 4 females fed standard diet; group 2 (n=8) consisted of the progeny of 6 females fed 0.5 g CS daily during the second half (15 days) of pregnancy and during lactation (30 days); and group 3 (n=8) included the progeny of 2 females fed CS in the same dose during lactation.

Serum CS and triglycerides (TG) were measured in females with an AA-II autoanalyzer (Technicon) [2] before experiment and at the end of lactation and in their progeny at the age of 6, 15-20 weeks (period of sexual maturation), and 35-40 weeks (in adult animals). The animals were weighed at the same terms.

Correlations were analyzed by Spearman's test to rule out errors caused by deviations of the distribution from the norm.

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RESULTS

In rabbis fed CS-rich diet, blood CS levels were 3-3.5 times higher in comparison with the control (54.5±14.9 in group 1, 160.3±71.1 in group 2, and 187.0±37.0 mg/dl in group 3). By contrast, serum concentrations of TG in all females were normal (52.2±9.5 in group 1, 61.8±10.6 in group 2, and 57.0±11.0 mg/dl in group 3). Thus, consumption of CS-rich diet during pregnancy and/or lactation led to the development of hypercholesterolemia (HCS) but not hypertriglyceridemia in rabbits.

After 6 weeks serum CS content varied within a wide range in old rabbits (46-249 mg/dl), being higher than in adult animals. In the control, CS content was 86.6±3.4 mg/dl, in group 2 it had a tendency to increase (101.9±10.2), and in group 3 it was lower than in the two former groups (62.2±2.2 mg/dl, $p<0.05$). With aging (15-20 weeks), the level of CS decreased by at least 40%, $p<0.05$, in comparison with the initial level (Fig. 1). A similar time course of CS was observed in group 2. Serum CS

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concentration was the lowest in the progeny of females fed CS only during lactation starting from the age of 6 weeks till weeks 35-40. Serum content of CS in rabbits of both experimental groups, which differed significantly during the first testing, became virtually the same in adult age. At this period the differences between experimental and control groups became obvious: blood CS levels were significantly higher in rabbits born from and/or fed by females with alimentary HCS than in the controls (by 38% in group 1 and by 36% in group 2).

TG concentrations in 6-week-old rabbits were similar in all groups (175.1±12.4 in group 1, 180.3±40.6 in group 2, and 221.4±25.7 mg/dl in group 3); in group 3 there was a trend to increase in comparison with two other groups. Both TG and CS levels were higher in 6-week-old rabbits than in adults (Fig. 2). In group 2, the content of TG at the age of 15-20 weeks was lower and at the age of 35-40 weeks higher than in the control.

Thus, soon after weaning (at the age of 6 weeks), the concentrations of CS and TG were higher in the progeny than in adult animals. This agrees with the data that breast feeding leads to an increase in blood lipid content of sucklings, which gradually decreases with age [7]. In addition, blood concentration of lipids in the progeny depended on the period during which they received CS. In our experiments plasma content of CS was higher and that of TG virtually normal in 6-week-old progeny of females fed CS during pregnancy and lactation. In the progeny of females fed CS only during lactation blood CS level was lower and that of TG higher than in the controls at the same age.

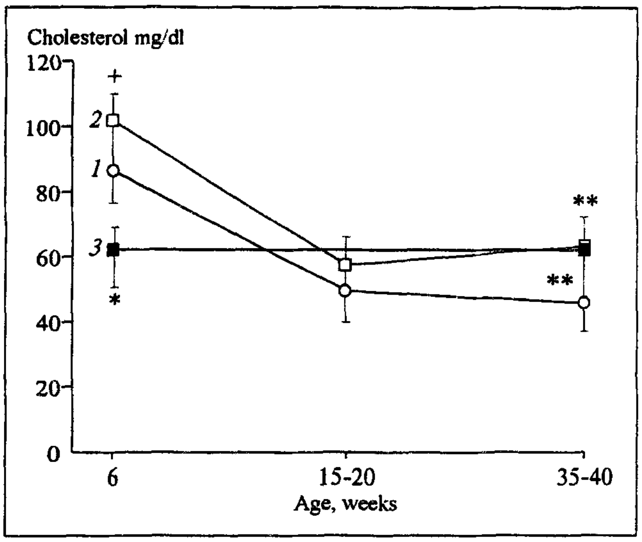

Fig. 1. Effect of alimentary hypercholesterolemia in females during pregnancy and/or lactation on the time course of serum cholesterol content in their progeny. Here and in Figs. 2 and 3: *1*) progeny of normolipidemic females (control); *2*) progeny of females fed cholesterol-rich diet during pregnancy and lactation; *3*) progeny of females fed cholesterol-rich diet during lactation. *$p<0.05$, **$p<0.01$ *vs.* control; +$p<0.05$ between experimental groups.

The differences in lipid levels observed during the early age in the progeny of females with HCS and of normolipidemic females were retained in adult age. Published reports disagree on this point. Plasma level of CS in the progeny of females fed CS during the last 4 days of pregnancy and during lactation was initially higher than in the control but normalized by the age of 11 weeks [8]. In humans, the differences in plasma CS levels in 6-month-old children fed cow milk and formulas with different

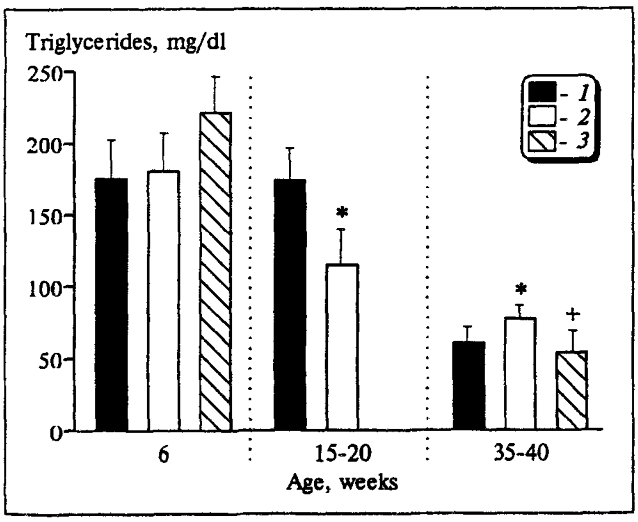

Fig. 2. Effect of alimentary hypercholesterolemia in females during pregnancy and/or lactation on the time course of serum triglyceride content in their progeny.

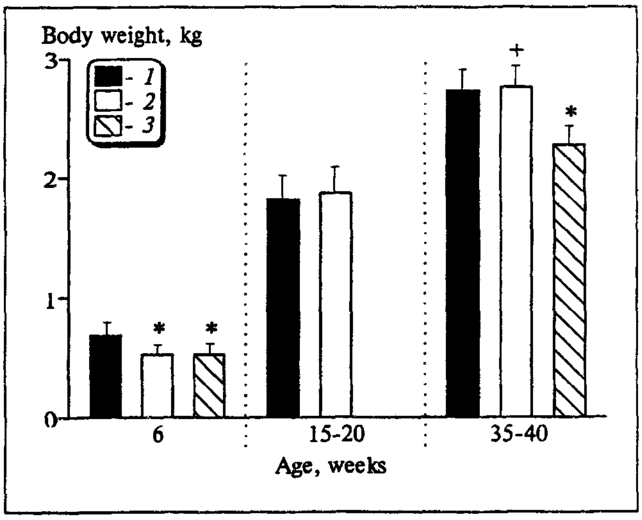

Fig. 3. Effect of alimentary hypercholesterolemia in females during pregnancy and/or lactation on the time course of body weight of their progeny.

content of fat are leveled by the end of the first year of life [3]. However, a longer follow-up showed that at the age of 7-12 years the concentrations of CS in the plasma were lower in children fed low-CS diets during the neonatal period than in those fed diets with higher CS content [4]. High CS consumption at the early stages of development led to an increase in blood CS content in rats which was retained in adult age and affected enzymes regulating CS homeostasis [6]. Similar data were obtained in experiments with baboons. The type of neonatal feeding (breast milk or feeding of formula with different CS content) did not alter serum CS concentrations at the age of 7-8 years but changed the rate of CS metabolism and the volume of fast-metabolized pool of CS [5]. Previously we showed that the reaction to acute lipid loading was changed in rabbits born from females fed CS during the second half of pregnancy and/or during lactation [1]; this change indicates deep restructuring of lipid metabolism which is not always manifested by serum level alterations after an overnight fast.

Moreover, alimentary HCS in females during pregnancy and/or lactation affected the development of the progeny, specifically, the weight. At the age of 6 weeks the rabbits in groups 2 and 3 weighed less (0.519±0.030 and 0.521±0.016 kg, respectively) than the controls (0.679±0.030). Later, all animals gained weight and by 35-40 weeks rabbits in group 2 did not differ from the control by this parameter, while in group 3 the mean body weight was still lower than in two other groups (Fig. 3).

CS levels in the blood of mothers and progeny at the age of 6 weeks were in negative correlation (r=-0.300, p<0.02), but this relationship disappeared with age. Severity of HCS in the mother also influenced her progeny's weight at early (6 weeks) and adult (35-40 weeks) age; these values were inversely related (r=-0.351 and -0.520, respectively, p<0.01). Study of relationship between lipid level and body weight of the progeny showed that blood CS concentration in 6-week-old rabbits positively correlated with their body weight (r=0.280, p<0.05). This relationship persisted over the entire follow-up period (r=0.389, p<0.05). On the other hand, we observed no relationship between blood CS levels in rabbits aged 6 weeks and in older animals, while body weight of adult rabbits positively correlated with this parameter in early age (r=0.707 and 0.572 in 6-week-old rabbits, on the one hand, and of 15-20 and 35-40 weeks, respectively, on the other, p<0.005).

These results demonstrate the effect of alimentary HCS in females during pregnancy and/or lactation on the development and lipid metabolism of their progeny.

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