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Concordant Hamster-to-Rat Liver Xenotransplantation Leads to Hyperlipidemia

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DIFFERENT species have adapted in different ways to their environment through the variation of specific metabolic parameters. For example, hamsters, unlike rats, are able to adjust their metabolism when they are subjected to extreme temperatures, modifying the mobilization of fat and regulating its storage.[1] Knowing that the liver plays a primary role in lipid metabolism, we performed liver transplantation between hamsters and rats to determine what effects this might have in recipient cholesterol and trygliceride levels.

MATERIALS AND METHODS

Golden Syrian hamsters were the donors and LEW rats were the recipients of the orthotopic liver transplant. Syngeneic (LEW to LEW) liver transplants were controls. Both xenogeneic and syngeneic recipients received 1 mg/kg/d of tacrolimus and a 10-day treatment with mycophenolate mofetil 10 at mg/kg/d. Recipients' body weight was registered weekly as well as the serum levels of cholesterol and tryglicerides after a 4-hour fast. Cholesterol concentration in bile was also measured in xenogeneic and syngeneic recipients.

RESULTS

Naive rats had a serum cholesterol level of 91.17 ± 17.93 mg/dL and a trygliceride level of 92.17 ± 16.8 mg/dL. Naive hamsters had a higher serum cholesterol and trygliceride levels of 173.5 ± 40.3 mg/dL and 125 ± 14.5 mg/dL, respectively. Both cholesterol and trygliceride serum levels in xenogeneic recipients were highly elevated during the first weeks posttransplantation. While hypercholesterolemia recovered to normal values after 3 weeks, hypertrygliceridemia persisted significantly at high levels throughout the observation period (Table 1). Liver histology from representative xenograft recipients at 2 and 8 weeks posttransplantation revealed a normal lobule architecture. Similarly, serum AST and total bilirubin levels were within normal ranges. The body weight of the rats receiving a hamster liver stayed significantly below that of syngeneic controls. Cholesterol level in bile of naive hamsters was half of that in naive rats (12 ± 2.53 vs. 21.83 ± 3.13, respectively). After xenotransplantation, biliary cholesterol levels remained diminished, as in naive hamsters.

DISCUSSION

The rate of fat utilization and deposition in normal hamster is 200% of that in normal rats.[1] This peculiar trait in hamsters has allowed them to survive in extremely cold and arid environments. Liver xenotransplantation from hamster to rat resulted in transient hypercholesterolemia and sustained hypertrygliceridemia, which did not correlate with body weight gain. The initial hypercholesterolemia may be partially explained by the diminished biliary cholesterol excretion that follows xenogeneic liver transplantation. Syngeneic controls and liver function tests, together with histologic examination of liver xenografts, ruled out that the observed hyperlipidemia was an effect of immunosuppression or liver dysfunction. We propose that the sustained hypertrygliceridemia may be due to an inefficient activity of the rat lipoprotein lipase present on the endothelial cells in dealing with hamsters apoproteins, present in VLDL produced by the new hamster liver. Clearly, even in concordant liver xenotransplantation there are metabolic incompatibilities that must be further explored before we engage in clinical xenotransplantation.

REFERENCE

1. Borer KT: In Siegel HI (ed): The Hamster—Reproduction and Behavior. New York: Plenum; 1985, p 363

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Table 1. Serum Cholesterol and Trygliceride Levels Following Syngeneic and Xenogeneic Liver Transplantation

	Week 1	Week 2	Week 3	Week 4	Week 8
Syngeneic					
Chol (mg/dL)	95.8 ± 21.4	114.6 ± 21.0	131.2 ± 30.2	113.4 ± 19.1	123.8 ± 33.0
Tg (mg/dL)	118.3 ± 32.1	147.1 ± 42.9	126.7 ± 37.4	102.2 ± 40.3	121.2 ± 49.7
Xenogeneic					
Chol (mg/dL)	**252 ± 30.0**	**227.5 ± 55.6**	155 ± 12.9	127.3 ± 26.5	111 ± 19
Tg (mg/dL)	**350 ± 94.1**	**277.5 ± 55.0**	**252.5 ± 42.7**	**229 ± 45.1**	**306.2 ± 87.5**

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