Effect Of Pregnancy And Lactation On Lipoprotein And Cholesterol Metabolism In The Rat

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Abstract

Origins of hyperlipidemia and cholestasis that occur during pregnancy were investigated by examining expression of key elements related to plasma and hepatic cholesterol metabolism during pregnancy, lactation, and post-lactation in the rat model. Among major findings were: during pregnancy, the activities of hepatic 3-hydroxy-3-methylglutaryl coenzyme A reductase, acyl coenzyme A:cholesterol acyltransferase, acyl coenzyme A:diacylglycerol acyltransferase, cholesterol 7\textsubscript{a}-hydroxylase, cholesterol ester hydrolases, low density lipoprotein receptors, LRP, and mdr2 were significantly lower or similar to non-pregnant controls while SR-B1 was elevated. Once lactation began, reductase, cholesterol acyltransferase, 7\textsubscript{a}-hydroxylase activities, low density lipoprotein receptors, and mdr2 increased while SR-B1 decreased. In later stages of lactation most hepatic elements returned to near control levels. Plasma cholesterol levels were higher than control at birth and during lactation with increase in LDL-size particles. By 24 h post-lactation, plasma triglycerides were 3.7-fold higher while cholesterol remained unchanged. Very large lipoproteins were present while LDL-size particles were now absent. Hepatic cholesterol acyltransferase had decreased to 27\% of control while diacylglycerol acyltransferase increased 3-fold and low density lipoprotein receptors doubled. Most elements were normalized 3 weeks after weaning except for LRP and low density lipoprotein receptors which were elevated. These studies provide an integrated picture of expression of key elements of hepatic and plasma cholesterol metabolism during pregnancy and lactation and advance understanding of hyperlipidemia and cholestasis during these states.

Keywords

Liver; ACAT, cholesterol 7\textsubscript{a}-hydroxylase; SR-B1; mdr2, LDL receptor; LRP; apolipoproteins; DGAT; cholesterol ester hydrolases