Dietary Cholesterol Affects Lipid Metabolism in Rabbits

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Summary and Implications

Effects of dietary cholesterol (0 (control), 1, 2, 4 or 8 g cholesterol/kg diet for 12 wks) on lipid contents and fatty acid compositions in red blood cell (RBC) membranes and plasma of rabbits and pathological changes and lipid oxidation in their livers were determined. Contents of total lipid and unsaturated fatty acids in RBC membrane and plasma of rabbits fed ≥4 g and ≥2 g dosages, respectively, were significantly higher ($P < 0.05$) than those of the control, and their increases were dosage-dependent. Accumulations of neutral lipids in centrolobular regions of livers in rabbits fed ≥ 2 g were dosage-dependent. Lipid oxidation in liver of rabbits fed 8 g was >2 times higher ($P < 0.05$) than those fed lower dosages. The results indicated that dietary cholesterol can modify lipid metabolisms of rabbits, including biosynthesis and transportation of lipids and fatty acids and incorporation of fatty acid into RBC membranes.

Introduction

Dietary cholesterol is linked to many lipid-associated disorders such as atherosclerosis and other cardio-vascular diseases. Dietary cholesterol are suggested to induce changes in fatty acid compositions and cholesterol/phospholipid ratio in cell membrane and, consequently, its physicochemical properties including membrane fluidity. Membrane fluidity mainly depends on fatty acid compositions, their degree of unsaturation, phospholipid classes, and cholesterol/phospholipid ratios. Increased cholesterol/phospholipid ratio in lipoproteins, platelets, and erythrocyte, endothelium and liver cell membranes is one of typical metabolic disorders during the development of atherosclerosis. Changes in fatty acid composition and membrane fluidity of other cells such as immune cells can affect the cell functions, resulting in the development of various disorders and diseases. However, little attention has been paid to the effect of cholesterol on lipids metabolism such as changes in lipid content and fatty acid composition although the effect of dietary lipids on cholesterol metabolism has been extensively studied.

The objective of this study was to determine the effect of dietary cholesterol in low-fat diet on lipid contents and fatty acid compositions of plasma and red blood cell (RBC) membranes, and pathological changes and lipid oxidation in the liver of rabbits.

Materials and Methods

- A total of 30 (3-month-old) male New Zealand White (NZW) rabbits (pathogen free) were used.
- The dosages of dietary cholesterol were 0 (control), 1, 2, 4 or 8 g cholesterol/kg basal diet.
- Rabbits were continuously fed the same diet for additional 12 wks (totally 13 wks).
- Blood samples were taken from the ear vein every two weeks to collect plasma and RBC membrane.
- At the end of feeding trial, liver samples were collected and analyzed for pathological legions and lipid oxidation.

Results and Discussion

- Total cholesterol contents in rabbit RBC membrane increased proportionally as dietary cholesterol dosages increased.
- Total lipid contents in RBC membrane of rabbits fed 4 and 8 g cholesterol dosages were > 2 times higher compared to that of the control after the feeding trial.
- Total lipid content in plasma of rabbits fed 2, 4, and 8 g cholesterol dosages had approximately 7, 18, and 25 times greater than the control.
- Large amounts of neutral lipids were accumulated in the livers of the rabbits fed > 2 g cholesterol and their accumulations were dose-dependent.
- The TBARS values in the liver of rabbits fed 8 g cholesterol dosage had 2.7 times higher TBARS values than that of the control.

Conclusion

Dietary cholesterol caused modification in total lipid contents and fatty acid compositions in RBC membrane and plasma of rabbits probably by inducing changes in lipid metabolisms including lipid and fatty acid biosynthesis, unsaturation and relocation processes of certain fatty acids to prevent loss of membrane fluidity caused by increased incorporation of cholesterol.

Table 1. Total cholesterol contents in RBC membrane and TBARS values in liver of rabbits fed diets with different dietary cholesterol dosages for 12 weeks*

Dietary Cholesterol dosage g/kg diet	Total cholesterol content in RBC membrane mg/g RBC	TBARS value nmol MDA/g tissue
0	0.34^{z}	15.60^{x}
1	0.61^{yz}	19.01^{x}
2	1.03^{y}	18.89^{x}
4	2.61^{x}	21.21^{x}
8	4.04^{w}	42.29^{w}
SEM	0.26	8.12

*Rabbits were fed with the same diets during the 1-week adaptation period.
$^{w\text{-}z}$Means with different superscript in the same column are significantly different ($P < 0.05$).

Table 2. Total lipid contents in RBC membrane of rabbits fed diets with different dietary cholesterol dosages during the 12 wks of experimental period

Dietary Cholesterol	Feeding period (Wk)			
(g/kg diet)	0	6	12	SEM
	---------- % lipid ----------			
0	0.37	0.40^{y}	0.43^{y}	0.02
1	0.38^{b}	0.41^{aby}	0.44^{ay}	0.01
2	0.40^{b}	0.45^{by}	0.58^{ay}	0.03
4	0.34^{c}	0.63^{bx}	1.02^{ax}	0.05
8	0.33^{c}	0.71^{bw}	1.29^{aw}	0.08
SEM	0.02	0.02	0.08	

*Rabbits were fed with the same diets during the 1-week adaptation period.
$^{a\text{-}c}$Means with different superscript in the same row are significantly different ($P < 0.05$). n = 6.
$^{w\text{-}z}$Means with different superscript in the same column are significantly different ($P < 0.05$).

Table 3. Total lipid contents in plasma of rabbits fed diets with different dietary cholesterol dosages during the 12 wks of experimental period*

Dietary Cholesterol	Feeding period (Wk)			
(g/kg diet)	0	6	12	SEM
	---------- g/100 mL plasma ----------			
0	2.64	2.33^{z}	2.30^{z}	0.22
1	2.40	4.83^{z}	4.20^{z}	0.86
2	2.63^{b}	20.43^{ay}	15.93^{ay}	2.21
4	2.53^{b}	37.53^{ax}	42.30^{ax}	3.74
8	2.46^{b}	51.78^{aw}	57.03^{aw}	3.47
SEM	0.20	3.59	4.62	

*Rabbits were fed with the same diets during the 1-week adaptation period.$^{a\text{-}b}$Means with different superscript in the same row are significantly different ($P < 0.05$). n = 6.
$^{w\text{-}z}$Means with different superscript in the same column significantly differ at $P < 0.05$.

Figure 1. Degrees of vacuolar degeneration in hepatocytes of rabbits fed with different levels of dietary cholesterol after 12 weeks of feeding trial. 1a, rabbits fed with 8 g cholesterol/kg diet: Characterized as diffuse severe vacuolation of hepatocytes throughout all areas of hepatic lobules with marked swelling of the hepatocytes. Also, showed lipid deposition and eccentric nuclei; 1b rabbits fed with 4 g cholesterol/kg diet: Moderate vacuolation of cells in the periacinar and midzonal areas of the hepatic lobules. Affected cells have diffuse vacuolation of the cytoplasm; 1c: rabbits fed with 2 g cholesterol/kg diet. Mild vacuolation of hepatocytes in the periacinar and midzonal areas of the hepatic lobules; 1d, rabbits fed 1 g cholesterol/kg diet: Mild vacuolation of hepatocytes in the periacinar region of the hepatic lobules. Hepatocytes of rabbits from control diet were similar to those in Figure 1d. 160x H&E staining.