

The Effects of Pluronic F68 on Cholesterol Absorption

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Background and Significance: The solubilization of cholesterol and fats by bile salts to form micelles is a key step in lipid metabolism. Pluronic F68 (Poloxamer 188), a hydrophilic detergent used in artificial blood in humans, has been proposed to compete with bile salts for the solubilization of cholesterol, altering the interaction of micelles with the brush border membrane and resulting in reduced uptake of cholesterol (but not fatty acids) by enterocytes. The primary aim of our study is to determine the effect of Pluronic F68 on intestinal uptake and lymphatic transport of fatty acids and cholesterol in bile duct intact animals.

Methods: Adult rats were prepared via the lymph fistula method. Following surgery, an infusion of lipids was prepared containing tritium labeled triglyceride, ¹⁴C labeled cholesterol, and phosphatidylcholine. Along with the lipids, each rat was infused with a 19mM solution of NaTC, F68, or 2:1 F68: NaTC at a rate of 3 mL/hr for a total of 6 hours, with lymph collected every hour. The small intestine, cecum, and large intestine were removed and washed with sodium taurocholate in normal saline, which was then collected. Finally, lipid from the mucosa of the intestine was extracted by the Folch method. An aliquot of each washing, along with an aliquot from each sample of lymph and of the extracted lipid, was taken for radioactive determination by scintillation spectrometry.

Results: We observed significantly lower cholesterol levels in the lymph of F68 treated animals versus the controls (NaTC) ($P < 0.001$). There was no significant difference in luminal cholesterol levels between F68 and control rats, while there was significantly lower levels of cholesterol in the mucosa of the F68 group versus control ($P < 0.001$). F68 led to significantly lower levels of triglyceride in the lymph compared to control rats ($P = 0.023$). However, there was no significant difference between triglyceride levels for 2:1 F68:NaTC and control rats, while the 2:1 F68:NaTC rats still showed a significant reduction in lymph cholesterol levels ($P = 0.002$) compared to controls.

Discussion: F68 is very effective in reducing cholesterol absorption in rats, and, when titrated with NaTC, does not significantly decrease absorption of triglycerides. Treatment of F68 lowers cholesterol levels in the lymph and mucosa, without having a significant effect on luminal cholesterol levels. This may be due to cholesterol being transported to the portal blood supply- a possibility with exciting potential for treatment of hypercholesterolemia.