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Diet and Excretion of Bile Acids[1]

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Abstract

In recent years, salient advances have taken place in the knowledge of the interaction of diets containing high-fat and certain type of fibers and the production of bile acids potentially relevant in the etiology of colon cancer. Other studies also indicate that a high intake of certain dietary fibers, in spite of high dietary fat, not only leads to an increase in stool bulk, thus diluting carcinogens and promoters in the gut, but also modifies the metabolism of these putative substances. These studies thus suggest that both high intake of total fat and low intake of certain fibers may be necessary for the full expression of risk to colon cancer.

Introduction

The etiology of a given disease sometimes may be elucidated by a simple logic. In the case of large bowel cancer, one would obviously consider factors present in the lumen of the large bowel, although one cannot exclude components that are transported to the colon by the circulation. On the basis of that reasoning, it was first suggested that large bowel contents contain tumorigenic compounds, including those that have initiating and promoting activity (16), and that the feces of high- and low-risk populations for large bowel cancer should be examined for possible differences in chemical and bacterial content, since the gut bacteria may play a role in converting an inactive precursor to an active carcinogen (1, 16).

Epidemiological studies indicate that diet is a major etiological factor in large bowel cancer (4, 15). Diets particularly high in total fat and low in fiber, as well as high intake of beef, are generally associated with the incidence of large bowel cancer in humans (2–4, 16). To explain the relationship between dietary fat and fiber and large bowel cancer, it has been hypothesized that a high-fat diet not only changes the composition of bile acids but also modifies the activity of gut microflora which, in turn, produce tumor-promoting substances from bile acids in the lumen of the colon (7, 12). High intake of dietary fiber of certain type not only leads to an increase in stool bulk, thereby diluting carcinogens and promoters (3, 8), but also alters the metabolism of tumorigenic compounds.

Effect of Dietary Fat on Fecal Bile Acid Excretion

Based on the above hypothesis, studies in humans and in animal models were carried out in our laboratory to determine whether changes in the diet can alter the concentration of fecal bile acids and cholesterol metabolites.

Reddy and Wynder (13) investigated fecal bile acids and neutral sterols of various population groups: North Americans consuming a high-fat, mixed western diet; North American Seventh-Day Adventists consuming a diet without meat and moderately low amount of fat; Japanese on a low-fat diet; Chinese consuming low-fat Chinese diet; and strict vegetarians consuming a low-fat vegetarian diet. A significant increase in the excretion of secondary bile acids (deoxycholic acid, lithocholic acid and 12-ketolithocholic acid) and cholesterol metabolites (mainly coprostanol and coprostanone) was observed in North Americans consuming a high-fat mixed western diet, compared with other groups (13). Metabolic studies comparing a high-meat, high-fat diet with a meatless, low-fat diet showed that the former resulted in elevated levels of fecal deoxycholic acid, lithocholic acid, coprostanone, and coprostanol (11). Protein content was essentially the same, but the fat content was altered in these diets. Hentges *et al.* (5) compared diet series in which fat content was kept constant, but protein content altered, consisting of a control diet, a high-beef diet, and a meatless diet. There was no increase in the concentrations of bile acids in the feces of subjects during the high-meat diet. These data indicate that high animal-protein consumption produces no major effect on bile acid excretion. Hill (6), after review of several studies, also concluded that it is the fat, not the protein content, in the meat that determines the effects on the fecal steroids.

Recently, we have undertaken a study in which we compared the fecal excretion of bile acids in healthy subjects consuming a customary high-fat, mixed western diet and an experimental high-fat, high-beef diet. The protein contents of all diets were the same, but the fat content was about 25% higher in experimental diets than in customary mixed western diet. The concentration of total bile acids, as well as secondary bile acids (deoxycholic acid and lithocholic acid) was higher during the period of consumption of experimental high-fat, high-beef diet compared to customary mixed western diet period (Table 1).

In order to understand the specifics of the mechanisms whereby dietary fat influences colon cancer, the effect of type and amount of fat on biliary and fecal bile acid pattern was studied in rats (9). Biliary excretion of cholic acid, β-muricholic acid, ursodeoxycholic acid, and deoxycholic acid was higher in rats fed a diet containing 20% corn oil or 20% lard than in rats fed diets containing 5% corn oil or 5% lard. High-fat (corn oil or lard) intake was also associated with an increased excretion of fecal deoxycholic acid, lithocholic acid, and 12-ketodeoxycholic acid. Type of fat had no effect on biliary and fecal bile acid excretion. The higher biliary and fecal bile acid concentration during the intake of high dietary fat could be the result of increased bile acid synthesis in the liver.

The above studies, both in humans and in animals, have shown the importance of the interaction of high-fat diet and the production of bile acids potentially relevant in the etiology of large bowel cancer (14).

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Effect of Dietary Fiber on Fecal Bile Acid Excretion

It has been postulated that the protective effect of certain dietary fibers may be due to adsorption, dilution, and/or alteration in the metabolism of cocarcinogens, carcinogens, and promoters by the components of the fiber.

Recently, Reddy *et al.* (8) studied the fecal bile acid excretion in healthy controls in Kuopio (Finland), a low-risk population for colon cancer development. The dietary histories indicate that the total fat and protein consumption in Kuopio is quite similar to the New York population but that the consumption of fiber, mainly cereal type, is 3-fold higher in Kuopio compared to the New York population. The concentration of fecal secondary bile acids, mainly deoxycholic acid and lithocholic acid, is decreased in Kuopio but the daily output remained the same in the 2 groups because the dietary intake of fat is the same in Kuopio and New York. The concentration of secondary bile acids was lower in Kuopio, indicating that fecal bulk diluted the bile acids.

The effect of dietary wheat bran, alfalfa, and pectin at 15% level on the composition of fecal bile acids was studied in rats fed a semipurified diet based on soybean protein, corn starch, dextrose, corn oil, and Alphacel (10). Diets containing wheat bran and alfalfa caused a significant increase in stool weight. The concentration of fecal bile acids, particularly hyodeoxycholic aicd, β-muricholic acid, deoxycholic acid, and lithocholic acid, was lower in rats fed wheat bran compared to those fed a control diet, but the daily output of these bile acids was the same in both groups (Table 2). Alfalfa had no effect on the concentration of fecal bile acids, but the daily excretion of deoxycholic acid, lithocholic acid, and 12-ketolithocholic acid was increased compared to the control diet. Addition of pectin to the diet increased both the concentration and daily output of bile acids.

It is apparent from this study that the fecal excretion of bile acids varies with the type and amount of dietary fiber. The observed differences in fecal bile acid excretion in rats may be explained, in part, on the basis that the different types of nonnutritive fibers and their isolated components bind individual bile acids differently (14). Certain dietary fibers could also affect not only the enterohepatic circulation of bile acids but also the activity of gut microflora which influence the metabolism of bile acids independent from the effects of adsorption.

Table 1

Effect of high-fat, high-beef diet on fecal bile acid excretion in healthy subjects

Healthy subjects were on a high-fat, high-beef diet for 3 months before they were transferred to their customary western diet for 1 month. The protein content was the same in all diets, but the fat content was about 25% higher in high-fat, high-beef diet compared to customary mixed western diet.

Bile acids	Excretion (mg/g dry feces)		
	Customary diet	High-fat, high-beef diet	Customary diet
Cholic acid	0.2 ± 0.04[a]	0.2 ± 0.2	0.1 ± 0.03
Chenodeoxycholic acid	0.2 ± 0.02	0.2 ± 0.03	0.2 ± 0.02
Deoxycholic acid	3.4 ± 0.3[b]	5.3 ± 0.3	3.4 ± 0.1[b]
Lithocholic acid	2.9 ± 0.2[b]	4.7 ± 0.2	3.0 ± 0.1[b]
Ursodeoxycholic acid	0.1 ± 0.02	0.2 ± 0.04	0.1 ± 0.02
Other bile acids	2.8 ± 0.4	3.7 ± 0.4	2.7 ± 0.1
Total bile acids	9.6 ± 0.5[b]	14.3 ± 0.5	9.6 ± 0.3[b]

[a] Average ± S.E. of 15 males and 15 females.
[b] Significantly different from high-fat, high-beef diet ($p < 0.05$).

Table 2

Fecal bile acid excretion in rats fed wheat bran, alfalfa, and pectin

Diet	Hyodeoxycholic acid	β-Muricholic acid	Cholic acid	Deoxycholic acid	Chenodeoxycholic acid	Lithocholic acid	12-Ketolithodeoxycholic acid	Unknown bile acids	Total bile acids
				mg/g dry feces					
Control	0.90 ± 0.14[a]	0.19 ± 0.03	0.25 ± 0.05	1.79 ± 0.30	0.03 ± 0.01	0.44 ± 0.07	0.08 ± 0.02	1.01 ± 0.04	4.92 ± 0.47
Wheat bran	0.54 ± 0.04[b,c]	0.05 ± 0.01[d]	0.18 ± 0.02	1.00 ± 0.04[c]	0.09 ± 0.02	0.27 ± 0.02[c]	0.04 ± 0.01	0.63 ± 0.08[d]	2.90 ± 0.14[d]
Pectin	1.13 ± 0.13	0.36 ± 0.14	0.22 ± 0.02	3.73 ± 0.24[d]	0.11 ± 0.04	1.27 ± 0.16[c]	0.23 ± 0.09	2.34 ± 0.14[d]	9.61 ± 0.32[d]
Alfalfa	0.80 ± 0.06	0.14 ± 0.02	0.29 ± 0.04	1.44 ± 0.14	0.02 ± 0.01	0.37 ± 0.08	0.11 ± 0.03	0.77 ± 0.07[c]	4.02 ± 0.25
				mg/kg body wt/day					
Control	2.99 ± 0.43	0.66 ± 0.12	0.89 ± 0.21	6.01 ± 1.03	0.11 ± 0.03	1.46 ± 0.23	0.28 ± 0.05	3.81 ± 0.30	16.7 ± 1.62
Wheat bran	2.62 ± 0.20	0.25 ± 0.09[d]	0.90 ± 0.15	4.92 ± 0.28	0.45 ± 0.14[c]	1.34 ± 0.14	0.20 ± 0.08	3.07 ± 0.40	14.1 ± 0.77
Pectin	4.86 ± 0.46[c]	1.86 ± 0.93	0.96 ± 0.12	17.1 ± 1.86[d]	0.51 ± 0.24	5.81 ± 0.99[c]	1.18 ± 0.54[c]	10.5 ± 0.76[d]	43.7 ± 3.91[d]
Alfalfa	5.20 ± 0.35[c]	0.94 ± 0.15	1.93 ± 0.25[c]	9.46 ± 1.13[c]	0.14 ± 0.04	2.59 ± 0.48[c]	0.72 ± 0.20[c]	5.17 ± 0.59[c]	26.7 ± 1.80[c]

[a] Mean ± S.E.; $n = 8$.
[b] Significantly different from the control group.
[c] $P < 0.05$.
[d] $P < 0.0001$.

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