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Effect of Diet on Excretion of Estrogens in Pre- and Postmenopausal Women[1]

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Abstract

Fecal, urinary, and plasma estrogens and plasma androgens were studied in healthy pre- and postmenopausal vegetarian and omnivorous women. Dietary histories of the subjects revealed that omnivores consumed a higher percentage of total protein and fat from animal sources. The total 72-hr fecal excretion as measured by dry weight was higher for vegetarians. Preliminary results indicate that vegetarian women excrete 2 to 3 times more estrogens in feces than do omnivores and that omnivores have about 50% higher mean plasma level of unconjugated estrone and estradial than vegetarians. Estriol-3-glucuronide, a compound that is formed upon reabsorption of free estriol from the intestine, is found in lower concentrations in the urine of vegetarians. These data suggest that in vegetarians a greater amount of the biliary estrogens escape reabsorption and are excreted with the feces. The differences in estrogen metabolism may explain the lower incidence of breast cancer in vegetarian women.

Introduction

A number of epidemiological studies have demonstrated a strong positive correlation between the amount of fat and protein in the diet and breast cancer incidence and mortality (2, 3, 5). The incidence of breast cancer is also associated with the reproductive history and urinary estrogen levels of the female population (6). Of all steroid hormones, the estrogens have the most extensive enterohepatic circulation because of the large proportion of estrogens which are excreted with the bile into the intestinal lumen. It is known that intestinal bacterial enzyme activities including deconjugating enzymes are changed by diet (4, 8) and that altering the intestinal microflora by ampicillin causes an increase in the excretion of fecal estrogens (1, 7). It was therefore decided to study if the diet has an effect on estrogen metabolism.

Materials and Methods

Five female groups living in the Boston area have been recruited for this study. The groups are comprised of young and older omnivores and vegetarians and older omnivorous breast cancer patients. In this report, data for the breast cancer patients are not given. Each group consists of 10 to 12 subjects, with the exception of the breast cancer groups which consists of 8 volunteers. This allows for a 2 × 2 factorial design for the healthy volunteers.

Each subject is investigated 4 times at 4-month intervals. In the young subjects aged 20 to 30 years and with normal menstrual cycles, the collection of specimens occurs in midfollicular phase. The preliminary data presented here are the results obtained from samples mainly from the first 3 collection periods and from 7 to 9 subjects in each group.

Careful recording of diet was done in order to allow proper selection of vegetarians who limit their animal food intake.

During the sample collection periods, the subjects collect feces and urine over 72 hr and one blood sample in tubes on each day of the collection period.

Plasma unconjugated estrone and estradiol, urinary conjugated estrone, estradiol, and estriol are determined by a radioimmunological (RIA[2]) method involving chromatographic separation of the estrogens on a Sephadex LH-20 column. In addition, plasma testosterone and androstenedione are assayed by RIA, and E3-3G is determined by direct RIA on diluted urine.

Statistical Methods. Linear contrasts of group means have been used as a measure of the main effects and the interaction term. This allows for the unequal number of observations in the 4 groups. All mean values are geometrical means.

Results

Dietary Composition. Total caloric intake is not significantly different for young *versus* old or omnivore *versus* vegetarian. Vegetarians consume about 43% as much animal calories as omnivores. Older omnivores consume more protein than young omnivores, while older vegetarians consume less than young vegetarians. The interaction term is significant so this reversal does not appear to be due to chance. Vegetarians consume about 33% as much animal protein as omnivores and about 36% as much animal fat.

Thus, in terms of these major dietary measures, the groups do not vary greatly in the total amount consumed, but vegetarians do consume substantially less from animal sources although their intake from animal sources is minimal.

Calculation of the intake of micronutrients revealed that vegetarians consume more iron, vitamin A, thiamine, and ascorbic acid, whereas calcium riboflavin and niacin intake was similar in both diet groups.

Fecal Excretion. Vegetarians' mean 24-hr fecal output, calculated on the basis of dry weight, was twice as high as omnivores. It is also interesting to note that older women in both dietary groups put out significantly lower amounts of feces than their younger counterparts.

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[2] The abbreviations used are: RIA, radioimmunoassay; E3-3G, estriol-3-glucuronide.

Hormone Analysis. The fecal excretion of estrogens is shown in Table 1. The change from a Western to a vegetarian diet results in about 180 and 300% higher fecal excretion values in young and old women, respectively.

The plasma estrogen levels are lower in the vegetarian women as compared to the omnivores (Table 2).

The preliminary analysis of urinary estrogens does not indicate significant differences between the dietary groups. However, E3-3G, an estrogen conjugate formed from estriol upon reabsorption from the intestine, is lower in vegetarians. The young omnivores excrete 29.7 nmol/24 hr compared to 21.3 nmol for vegetarians. The difference is approaching statistical significance. The importance of this finding rests upon the fact that E3-3G is a good direct marker for intestinal estrogen reabsorption because of the exclusive synthesis of this compound by the intestinal tissue.

The levels of 2 androgens were measured in the plasma. The results show a reversal of diet effect from young to old women which is statistically significant (Table 3). The androgens in young vegetarian women are higher than in young omnivores, but the older vegetarians have lower androgen values than the old omnivores.

Discussion

It has been demonstrated repeatedly that interruption of the enterohepatic circulation of the estrogens caused by various mechanisms results in a decrease of the excretion of E3-3G in urine (9, 10). In vegetarian women, the excretion of "immunoreactive" E3-3G is approaching a significant decrease in the small group of samples so far tested, suggesting that the vegetarian diet may have a similar effect as, *e.g.*, administration of ampicillin. Ampicillin administration causes a huge increase in unconjugated and conjugated estrogens in feces (1, 7) which is believed to be due, at least partly, to a decrease in bacterial β-glucuronidase activity necessary for the hydrolysis of the biliary estrogen conjugates before the estrogen moiety is absorbed. A vegetarian diet has been shown to result in a decrease in bacterial β-glucuronidase activity in feces (4, 6); hence, the high amount of estrogens in feces of vegetarians as compared to omnivores may occur by the same mechanism. In these studies, only the unconjugated estrogens in feces were studied, but it has been shown previously that about 98% of the fecal estrogens are unconjugated (1). Whether this is also true for vegetarians is not known. The reason for the high excretion of unconjugated estrogens in feces in addition to conjugated estrogens after ampicillin administration may result from hydrolysis of estrogen conjugates in the lower colon, a site where absorption is very poor.

The greatly increased fecal excretion of estrogens in vegetarians seems to result in a lowering of the plasma estrogens as compared to omnivores; however, the difference is not statistically significant in this small sample. The omnivores have 57% (mean for estrone and estradiol in both groups) higher plasma estrogens than the vegetarians.

The postmenopausal women living in Boston have higher estradiol values than expected. Simultaneous repetition of the assay with 3 different antisera and using a number of samples from Finnish postmenopausal women revealed that the values are true ones and that the Finnish women had considerably lower values. The incidence of mammary cancer is much lower in Finland, but whether this is related to this observation remains to be established. The small number of observations is now being extended, and the women with the highest plasma estradiol values are being investigated further.

Thus, all results point to a definite difference in the enterohepatic metabolism of estrogens in vegetarian women as compared to omnivorous women which ultimately may lead to a decrease of the biologically active unconjugated estrogens in plasma. Whether such a decrease may explain the difference in incidence of breast cancer in vegetarians and omnivores remains to be established.

Table 1
Fecal excretion of estrogens[a]

	nmol/24 hr					
	Young women (mid-follicular phase)			Old women (postmenopausal)		
	Estrone	Estradiol	Estriol	Estrone	Estradiol	Estriol
Omnivorous	0.45[b]	0.44	0.38	0.27	0.33	0.31
Vegetarian	1.64	1.31	1.70	0.50	0.50	0.48

[a] Influence of age and diet is statistically significant for all estrogens.
[b] Geometric mean.

Table 2
Plasma unconjugated estrogens in young and postmenopausal omnivorous and vegetarian women

	nmol/liter			
	Young women (mid-follicular phase)		Old women (postmenopausal)	
	Estrone	Estradiol	Estrone	Estradiol
Omnivorous	0.47	0.46	0.38	0.32
Vegetarian	0.27	0.35	0.27	0.26

Table 3
Androgens in plasma in young and postmenopausal omnivorous and vegetarian women[a]

	nmol/liter			
	Young women (mid-follicular phase)		Old women (postmenopausal)	
	Androstenedione	Testosterone	Androstenedione	Testosterone
Omnivorous	3.9	1.2	2.1	0.76
Vegetarian	4.5	1.5	1.2	0.47

[a] Effect of age is statistically significant. The reversal of diet from young to old women is statistically significant.

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