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Original article

Fatty acid intake and erythrocyte fatty acid profile in women with breast, ovarian and cervical cancers

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SUMMARY

Aim: To assess dietary fat and fatty acid (FA) intakes and to correlate it with red blood cell (RBC) FA composition in women with newly diagnosed breast, cervical and ovarian cancer.

Methods: 185 women who were newly diagnosed with breast, cervical or ovarian cancer were recruited for the study and dietary information was obtained using food frequency questionnaires. RBC fatty acid composition was analyzed in a subset of 96 women with cancers (35 breast cancer, 31 cervical cancer and 30 ovarian cancer) and 56 age-matched controls.

Results: Subjects with malignancies were seen to consume lower amounts of fat and higher amounts of carbohydrates compared with controls. While the intakes of saturated fatty acids (SFA) were similar across the groups, The intakes of PUFA, specifically linoleic acid (LA, 18:2 n-6) and long chain n-3 PUFA (LC n-3 PUFA) were significantly lower ($p < 0.05$) in the cancer groups. Correspondingly, RBC fatty acid profile in all cancer groups showed significantly lower levels of LA compared to controls. Furthermore, the calculated activity of Δ6-desaturase (D6D) using the precursor-product ratio was significantly higher in cancer groups compared to controls. Subjects with breast cancer had lower levels of RBC docosahexaenoic acid (DHA, 22:6 n-3), and all three groups had higher levels of docosapentaenoic acid (DPA, 22:5 n-3) as compared to controls. Calculated activity of Δ4-desaturase (D4D) was found to be significantly lower in cancer groups.

Conclusion: The study shows a good correlation between dietary PUFA intakes and RBC PUFA composition, and suggests that elongation of fatty acids is significantly affected in cancer such that it favours the formation of pro-inflammatory n-6 PUFA while repressing the formation of anti-inflammatory n-3 PUFAs.

1. Introduction

There have been many studies that suggest that dietary fat and fatty acid (FA) composition could play a key role in tumour development and cancer [1,2]. Several studies suggest that high saturated fatty acid (SFA) diets lead to increased risk of breast cancer. Animal studies also suggest that diets rich in n-6 polyunsaturated fatty acids (n-6 PUFA) stimulate mammary tumour development whereas diets rich in n-3 PUFA appear to inhibit it [3]. Epidemiological studies provide ambiguous data about the relationship between n-6 and n-3 PUFA intake and cancer incidence. Although most epidemiological studies depend on the use of food questionnaires to gather dietary intake data, increasing numbers of researchers are attempting to obtain more objective data such as the fatty acid composition of plasma or red blood cells (RBC)

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phospholipids, which can serve as useful indices of dietary intakes of PUFA [4,5].

Incidences of cancers are on the rise in developing countries and India is no exception [6]. This has been attributed to multiple factors including changes in dietary habits, lifestyle modifications as well as to increased life expectancy. However there are very few studies looking into the role of diets, especially that of dietary fats in the aetiology of cancers in India.

This study was aimed at understanding the role of dietary FA and RBC membrane FA composition in Indian women with incident cancers of the breast, cervix or ovary.

2. Subjects and methods

One hundred and eighty five naïve patients diagnosed with carcinomas of the breast (n = 49), cervix (n = 51) and ovary (n = 85) at Kidwai Memorial Institute of Oncology, Bangalore, India, formed the study group. Controls belonging to the same socioeconomic strata as the patients, were selected from age-matched groups. Since there were many women of similar ages in the three study groups, only 56 controls were required to match them all.

2.1. Dietary intake

Habitual dietary intake for the preceding 3 months was assessed using a pretested, interviewer-administered, food frequency questionnaire (FFQ), adapted from one developed earlier for urban south Indian adults [7]. This FFQ uses standard food measures to quantify the portion size of each food item, and nutrient composition of foods was calculated using Indian food conversion tables [8], or from the USDA food composition data (USDA ARS; http://www.nal.usda.gov/fnic/foodcomp/search/). This FFQ has earlier been validated against 24-h food recalls [9].

2.2. RBC membrane fatty acid profile

5 ml of peripheral blood was sampled from patients after establishing the diagnosis and before they received any form of treatment and also from controls. RBCs were separated, and FA in the erythrocyte membranes was analyzed using gas chromatography with a flame ionization detector (Varian 3800; Varian, Palo Alto, CA, USA). Briefly, the procedure followed involved the extraction of total lipids, and transmethylation of all fatty acids from this fraction using BF3-methanol. The fatty acid methyl esters were then separated by chain length and degree of saturation by injection onto a 50 m, 0.2 mm capillary column (FAME, Varian) with nitrogen as carrier gas. Based on the internal standard (C17:0), total fatty acid content of the samples was calculated and each identified fatty acid was expressed as a percentage of the total fatty acids. Desaturase activities were calculated based on product-to-precursor ratios as follows:

Delta 9-desaturase (D9D) activity = 18:1 n-9/18:0

Delta 6-desaturase (D6D n-6) activity = (18:3 n-6 + 20:3 n-6 + 20:4 n-6)/18:2 n-6

Delta 4-desaturase (D4D n-3) activity = 22:5 n-3/22:6 n-3

2.3. Statistical analysis

All data are presented as mean ± SD when normally distributed and as median (quartile 1, quartile 3) when not normally distributed. All normally distributed data were compared between the 4 group ANOVA and the rest by non-parametric Kruskall Wallis Test. The stars indicate values that are significantly different from controls when compared using post-hoc students T-test. Correlations between dietary fat and fatty acid and RBC FA were calculated on the total data using Spearman's correlation coefficient. The odds ratio for being in the cancer group vs the control group among the tertiles of the various enzyme activities were computed using logistic regression and presented as OR (95% Confidence interval). Statistical significance was considered at $p < 0.05$ and all analyses were performed using SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

3. Results

Table 1 gives the intakes of all the macronutrients and fatty acids. No significant difference was seen in the intakes of total calories between the four groups, however the controls were seen to consume significantly higher levels of both protein and fat and lower amounts of carbohydrates. Consumption of SFA did not vary between the groups; however the intakes of linoleic acid (LA) as well as long chain (LC) n-3 PUFA was significantly lower in all three cancer groups.

Food group analysis (Table 2) showed that these differences were mainly due to higher intakes of cereals and lower intakes of legumes in women with ovarian and cervical cancers. These women were also seen to consume lower amounts of fats and oils although this did not reach statistical significance.

Table 1
Daily intake of macronutrients and fatty acids by subjects with cancer compared to controls.

Consumption per day	Control	Breast cancer	Ovarian cancer	Cervical cancer
	N = 56	N = 49	N = 85	N = 51
Energy (kcal)	2140 ± 519	2367 ± 671	2061 ± 469	2214 ± 599
Protein (%E)	12.5 ± 1.1	11.8 ± 1.3*	11.9 ± 1.1*	11.8 ± 1.2*
Fat (%E)	26.0 ± 4.8	21.0 ± 4.7*	22.0 ± 5.1*	22.0 ± 4.4*
Carbohydrates (%E)	61.0 ± 5.4	67.0 ± 5.4*	65.0 ± 6.6*	65.0 ± 5.1*
SFA (%E)	8.8 ± 1.4	7.9 ± 2.6	8.5 ± 3.0	8.9 ± 2.5
MUFA (%E)	6.4 ± 1.4	6.0 ± 1.5	6.8 ± 1.7	7.0 ± 1.8
PUFA (%E)	8.5 ± 2.2	5.2 ± 2.8	5.10 ± 2.6	4.42 ± 1.8
LA (%E)	8.2 ± 2.2	4.9 ± 2.8*	4.8 ± 2.6*	4.1 ± 1.8*
ALNA (%E)	0.24 ± 0.05	0.22 ± 0.04	0.22 ± 0.05	0.22 ± 0.05
LC n-3 PUFA (mg)	0.030 ± 0.03	0.014 ± 0.02*	0.017 ± 0.03*	0.017 ± 0.02*

%E – energy%, SFA – saturated fatty acids, MUFA – monounsaturated fatty acids, PUFA – polyunsaturated fatty acids, LA – linoleic acid, ALNA – α-linolenic acid, LC n-3 PUFA – long chain n-3
All values represented as mean ± SD. *$P < 0.05$.

Table 2
Food group composition of diet.

Intakes (g/day)	Control	Breast cancer	Ovarian cancer	Cervical cancer
Cereals	268 ± 110	387 ± 126*	319 ± 102*	362 ± 133*
Legumes	68 ± 21	60 ± 23	53 ± 19*	45 ± 12*
Vegetables	136 ± 47	138 ± 72	114 ± 45	140 ± 48
Nuts	22 ± 12	16 ± 10*	18 ± 10	20 ± 9
Fats and oils	26 ± 8	24 ± 12	21 ± 8	21 ± 7
Fruits	121 ± 108	72 ± 55*	71 ± 54*	63 ± 46*
Milk and milk products	316 ± 157	345 ± 218	301 ± 185	333 ± 190*
Fish and fish products	4.9 ± 6.4	1.8 ± 4.1*	2.0 ± 6.0*	1.7 ± 3.1*
Meat and poultry	23 ± 18	19 ± 28	17 ± 20	17 ± 13

All values represented as mean ± SD. *$P < 0.05$.

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