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Consumption of dairy products and basal cell carcinoma: Is there a relationship?

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A B S T R A C T

Background: There are some studies claiming the association of dairy consumption with BCC risks in the general population. In this study, we examined getting the fatty acid C14: 0, C15: 0, C17:0 associated with the amount of the fatty acids in the red blood cell membrane to assess the relationship between them and the risk of BCC.

Methods: This case-control study (40 cases and 40 controls) was conducted with newly diagnosed BCC adults who were recruited from Razi Hospital. To measure fatty acids of red blood cell membrane, fatty acids were extracted and injected to gas chromatography. Case and control groups were matched based on sex, age, and body mass index (BMI). All subjects also completed two 24-hour dietary recalls by nutritionist help, which included two randomly selected days.

Results: Both groups had no significant differences between weight, height, age, sex, and BMI and also macro-and micronutrients intakes. Pentadecanoic acid concentration of red blood cell membrane was higher in BCC patients than in the control group (p=0.04). There was no significant difference in myristic and heptadecanoic acids concentration in the red blood cell membrane between two groups.

Conclusion: Considering that pentadecanoic acid indicates consumption of dairy products, it is likely that consumed greater high fat dairy products in BCC patients seem to be associated with basal cell carcinoma.

Introduction

The prevalence of non-melanoma skin cancer (NMSC) is increasing annually. In the United States, more than one million people who have been treated for the disease are over 65 years in each year [1]. NMSC includes squamous cell carcinoma (SCC) and Basal cell carcinoma (BCC) [2]. The most common type of skin cancer is BCC in most countries of the world. The prevalence of BCC is 900,000 per a year in the United States [2,3]. In Iran, 7000 to 10,000 people are diagnosed with NMSC, and 77% of these patients suffer from BCC [4,5].

BCC occurs in the body areas that are visible, which can be an important factor in quality of life and self-esteem of the patients, and impose a high economic burden to society. On the other hand, this type of cancer is increasing because of raising aging and elderly in any community, and ultraviolet light exposure over the years [1,3,6].

In a prospective study, it was shown that dairy consumption (although low-fat) was correlated with the increased risk of prostate

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cancer [1], while another survey on breast cancer showed that calcium intake in the diet can reduce the incidence of breast cancer after menopause [7]. A study revealed that the amount of serum fatty acid C 15: 0 has a direct relationship with received butter and a total of dairy products, including milk and cream, and serum pentadecanoic acid is considered as an indicator for receiving dairy products [8]. In another study, fatty acids C15: 0 and C17:0 also were as indications of long-term consumption of dairy products in adipose tissue, and serum pentadecanoic acid was as an indicator for receiving dairy products [9]. Wolk et al examined three fatty acids of myristic, pentadecanoic, and heptadecanoic (C 14: 0, C 15: 0, and C 17: 0, respectively) existing in adipose tissue for evaluation of dairy intake, and serum pentadecanoic acid and myristic of adipose tissue were identified as good indicators [10].

Fatty acid intake through diet can demonstrate serum fatty acid composition [8]. In this study, we examined getting the fatty acid C15: 0 and C14: 0 associated with the amount of the fatty acids in the red blood cell membrane to assess the relationship between them and the risk of BCC.

Methods

This is a case-control study conducted on 80 patients referred to Razi Hospital, Tehran, Iran. In this study, the inclusion criteria for cases and controls were no history of nutritional supplements consumed during the last 3 months and no history of any types of cancer. Cases were new BCC patients diagnosed in the hospital. The controls were patients who referred to this hospital for receiving further treatments, except for BCC. Interviews were conducted with two groups on two occasions to get 24-h dietary recall. In addition, patients in both groups were asked demographic questions, taking medications, and medical history; including cardiovascular disease, diabetes, blood pressure, and smoking. Height of subjects was measured using by a stadiometer (seca, clara-700), while hip, shoulder, and heel of patients were leaning against the wall. Subjects were weighted without shoes and with light clothing, standing flat, and fasting using portable electronic digital scale (seca, clara-700). Body mass index (BMI) was calculated as body weight in kilograms (kg) divided by the square of the body height in meters (m^2). Individual matching was carried out based on confounder variables, such as age, sex, and BMI between two groups.

After 8 to 12 hours fasting, 5 ml of blood was obtained, and blood serum was separated. Serum was stored in 500 microliter vials, transferred to the freezer -80 °C, and injected to gas chromatography after extraction. Fatty acids were extracted from red blood cells, and put in the vials. Fatty acids were extracted from samples by methanol HPLC-grade, N-HexaneHPLC-grade, and bornorifluride (BTF) [11, 12]. Fatty acids extracted from all samples were measured using gas chromatograph (YL-instrument-Korea YL-6500) one by one. The percent of three fatty acids of a subject (C 14: 0, C 15: 0, C 17: 0) was calculated by the total fatty acids in the blood of the same subject. Two 24-hour recalls were randomly taken in different working days. All recalls were made by dietitian, and data was transferred to the program N4. Recalls and their authenticity were confirmed again by another person. The mean calories, protein, carbohydrates, and fat were compared separately and in terms of calcium, phosphorus, and magnesium in the two groups.

The sample size for this study was calculated based on the formula, $N= 2\ [(Z_{1-\alpha/2}\ \ Z_{1-\beta})^{2} \times S^2]/d^2$ where $\alpha = 0.05$ (type 1 error) and $\beta=0.20$ (type 2 error). RBCs fatty acids were determined as main variable. Variance of RBCs fatty acids was 1.04 [13], and difference in mean of this variable was 0.78. The formula estimated that 28 participants were required for each group.

Data were analyzed using SPSS (Inc, Chicago, IL, USA) version 20. Distribution of variables was evaluated by Kolmogorov-Smirnov test. To compare mean dietary intake between case and control groups, Student s t-test and chi square test was used for continuous and categorical variables, respectively. Means of dietary intakes were adjusted for age, BMI, and sex. The statistical significant level was considered 0.05. Continuous variables were expressed as mean± SEMs and categorical variables as number (percentage). If p-value were less than 0.05 in any analysis, it is demonstrated significant result.

This study was approved by ethical committee of Tehran University of Medical Science. The written informed consent was taken from all subjects.

Results

In this study, 80 participants were investigated in case and control groups according to macro and micronutrients, and the fatty acids in the red blood cell membrane. Table1 shows that there was no significant difference between both groups according to demographic characteristics of participants (age, weight, sex, height, and BMI).

Table 2 shows that there was no significant difference between cases and controls in the mean intake of energy, carbohydrates, protein, and various types of fats. The mean intake of some micronutrients (magnesium, phosphorus, and calcium) was not significantly different between two groups.

In Table 3, three fatty acids (myristic, pentadecanoic, and heptadecanoic), as an indicator of long-term consumption of dairy products, were examines in the red blood cell membrane in both groups studied. The percent of myristic (C 14:0) and heptadecanoic (C 17:0) acids existing in the red blood cell membrane than the total fatty acids in the red blood cell membrane was calculated, and no significant difference was seen between both groups, while the percent of pentadecanoic acid (C 15:0) in the red blood cell membrane was significantly different in two groups. In other words, the amount of pentadecanoic acid was significantly higher in BCC patient than controls (p=0.04).

Discussion

To the best of our knowledge, this was the first study on the intake of dairy products (the amount of myristic, pentadecanoic, and heptadecanoic acids) and the risk of BCC. Studies showed that there is a relationship between higher consumption of dairy products (milk, butter, and cream) and risk of BCC. However, this relationship may be due to high intake of high fat dairy products. To prove this hypothesis, more investigations are required. In our study, the pentadecanoic acid existing in the red blood cell membrane was higher in BCC patients than healthy controls. This indicates greater consumption of dairy products in the cases. However, the intake of dairy products reported in 24-hour recalls was not significantly different between two groups. On the other hand, myristic and heptadecanoic acids in the red blood cell membrane were not significantly different between two groups. The mean intake of energy, carbohydrates, protein, and all types of fats, as well as the mean intake of some micronutrients (magnesium, phosphorus, and calcium) were not significantly different between two groups.

Table 1. Demographic characteristics and medical history of Basal Cell Carcinoma and control group#

Demographic characteristics		BCC	Control	P-value
Sex (%)	**Male**	28 (68%)	13 (31.7%)	0.18¶
	Female	21 (51.2%)	20 (48.8%)	
Age (years)		57.76±1.56	54.05±1.16	0.06*
Weight (kg)		72.39±1.94	72.48±2.46	0.98*
Height (cm)		167.76±1.59	166.30±1.36	o.49*
BMI (kg/m^2)		26. 02±0.74	25.74±0.67	0.78*

Mean ± SE; ¶ Chi-square test; *Independent sample t-test

Table 2. Energy, macronutrients and some micronutrients intakes of BCC subjects and control group#

	BCC	Control	P-value*
Total energy (kcal)	2537.65±146.68	2246.55±234.98	0.27
Total carbohydrate (g)	327.32±23.78	320±27.55	0.86
Total protein (g)	68.85±3.33	68.90±4.99	0.99
Total fat(g)	80.82±6.02	85.49±8.09	0.65
Saturated fat(g)	20.22±1.91	17.57±1.55	0.36
Mono fat (g)	32.00±3.98	29.63±2.84	0.62
Poly fat (g)	30.41±3.36	36.06±6.39	0.39
Cholesterol (mg)	115.37±39.94	120.42±11.65	0.74
Oleic fat (g)	19.56±2.06	23.24±2.2	0.26
Linolenic fat (g)	2.47±1.33	1.33±0.39	0.54
Linoleic (g)	28.47±3.19	34.27±21.18	0.37
DHA (g)	0.02±0.01	0.001±0.00	0.39
EPA (g)	0.01±0.00	0.00±0.00	0.43
Magnesium	242.39±77.50	238.85±64.48	0.49
phosphor(mg)	2033.09±149.80	1954.79±467.85	0.11
Calcium(mg)	630.73±74.41	502.37±52.89	0.05

Mean±SE; *Independent sample t-test; BCC= Basal Cell Carcinoma

Table 3. Myristic, heptadecanoic and pentadecanoic acid of red blood cell membrane in Basal Cell Carcinoma and control group#

Saturated fatty acids	BCC	Control	P-value*
C 14:0(%)	0.03±0.01	0.04±0.01	0.82
C 15:0(%)	0.05±0.01	0.02±0.01	0.04*
C 17:0(%)	0.03±0.01	0.03±0.01	0.98

Mean±SE; *Independent sample t-test; BCC= Basal Cell Carcinoma

Another study revealed that the amount of the fatty acid C:15:0 is directly related to the intake of butter, milk, cream, and ice cream, and it was found that pentadecanoic acid is an indicator of intake of dairy products, but there was no significant relationship between the pentadecanoic acid and cheese consumed. These findings were analyzed using gas chromatography. A study examined a hypothesis on pentadecanoic and heptadecanoic acids (C 15:0 and C 17:0, respectively) indicating long term consumption of dairy products in communities with high intake of dairy products. Only pentadecanoic acid was proposed as an indicator of intake of dairy products [9]. Another study investigated three fatty acids (myristic, pentadecanoic, and heptadecanoic acids) in the adipose tissue for intake of dairy products, and it was shown that myristic and pentadecanoic acids of the adipose tissue are identified as good indicators [10]. According to above studies, serum pentadecanoic acid is an appropriate indicator of intake of dairy products, especially high fat dairy products. In our study, a significant difference seen between two groups by the percent of pentadecanoic acid in the red blood cell membrane confirmed that consumption of dairy products in BCC patients was higher despite of not reporting higher intake of dairy products. Considering that pentadecanoic acid indicates consumption of dairy products, such as ice cream, butter, cream, and milk, it is likely that BCC patients consumed greater high fat dairy products. A cohort study examined the effect of dairy products on incidence of prostate, lung, and colon cancers. The risk of prostate cancer was higher in people who consumed greater high fat dairy products. Consumption of low fat dairy products had poor relationship with risk of prostate cancer. Long term use of calcium supplements had no effect on the risk of the cancer. Also, other products in dairy can cause cancer, for example insulin-like growth and hormonal factors in dairy. High calcium intake can affect turnover of $1,25(OH)_2D$ [14], which cannot be effective in three cancers mentioned, but can increase the risk of BCC. Two general mechanisms involved promotion of ca^{+2} increase in cells exposed to growth factors and signals promote cell death. In other way it is not the ca^{+2} increase but the intracellular ca^{+2} empty that result apoptosis [15]. On the other hand apoptosis can be started by engagement of "death receptors" by cytokines (such a tumor necrosis factor), toxin, oxidative stress, growth factor insufficiencies and calcium influx through plasma membrane channel or release from the endoplasmic reticulum. Calcium as a messenger could coordinate mitochondrial-endoplasmic reticulum(ER) interactions that drive apoptosis. Binding cytochrome c to the insP3 receptor occurs early in a cell death and enhances calcium release from ER resulting large increase in cytoplasmic free calcium concentration [16].

Conclusion

In summary, in our study, sample size was small (40 cases and 40 controls). According to complexity in the use of gas chromatography, an expert was required. The study on fat intake by 24-hour recalls was simultaneously done with examination of on fat intake in the red blood cell membrane. The procedure enhances the accuracy because the recalls have lower accuracy than cellular examinations. It is suggested to conduct a study with larger sample size or cohort design to obtain generalizable results.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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