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ORIGINAL ARTICLE

Nutrition and prostate cancer

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Summary

Purpose: *Since an association between prostate cancer and some foods or food groups like meat, milk and dairy products, tomato foods, and allium vegetables, has been suggested, we analyzed the possibility that some food items or some food groups could be related to prostate cancer in some other way and not only through their nutrients. The purpose of this study was to test some hypotheses about diet as risk factor for prostate cancer.*

Methods: *This case-control study comprised 101 cases of prostate cancer and 202 hospital controls individually matched for age (± 2 years), hospital admission and place of residence. Dietary information of 150 food items was obtained by a quantitative history approach.*

Results: *Multivariate logistic regression analysis indicated as risk factors for prostate cancer high intake of fruit, processed meat, fish (most frequently canned) and butter. High intake of chicken, potato and rice exhibited a protective effect.*

Conclusion: *These results support the hypothesis that consumption of meat and fat play a role in the development of prostate cancer. The findings that consumption of processed meat only (not fresh) and fish increased the risk of prostate cancer, as well as the protective effect of chicken, potato and rice consumption should be corroborated by other investigators.*

Key words: case-control study, diet, prostate cancer

Introduction

Several years ago we published the results relating to dietary and some other factors and prostate cancer, obtained in a case-control study carried out in Serbia [1,2]. A quantitative dietary history was used to estimate the average daily intake of various nutrients. According to the results obtained, risk factors for prostate cancer were high intake of proteins, saturated fatty acids, fibers, vitamin B12 and retinol equivalents. Protective effect was found for high intake of α-tocopherol, calcium and iron.

Since an association between prostate cancer and some foods or food groups such as meat, milk and dairy products, tomato foods and allium vegetables, have been suggested [3-5], we reanalyzed our data having in mind the possibility that some food items or some food groups could be related to prostate cancer in some other way and not only through their nutrients which we had analyzed.

Methods

The study was conducted in two towns of central Serbia (Serbia and Montenegro) during the period 1990-1994. The study group comprised 101 patients with histologically confirmed prostate cancer. For each case, two hospital controls (202 controls in total) were chosen from among patients confirmed as having neither prostate cancer nor other prostate diseases. Those with other malignancies were also excluded. Cases and controls were individually matched for age (± 2 years), hospital admission and place of residence. Demographic, epidemiological and dietary data were obtained using a standard questionnaire. Dietary information was obtained by a quantitative history approach in which subjects were asked about their usual frequency of intake and portion size of a list of 150 food items including alcoholic beverages. The technique was similar to the one used by Jain and associates [6], although somewhat modified and adapted to suit the Serbian di-

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et. More detailed description of material and methods is presented elsewhere [1,2].

Foods were classified into 21 groups: cereals without rice, rice, milk and dairy products, eggs, fresh meat, processed meat, chicken, fish, cruciferous vegetables, green leafy vegetables, legumes, potato, allium vegetables, other vegetables, fruit, butter, margarine, sugar, alcohol, coffee.

Statistical analysis

For statistical analysis of data univariate and multivariate conditional logistic regression methods were used [7,8]. For case-control comparison two approaches were applied: a) medians of average daily intake of the control group were used as a basis for comparison; and b) terciles of average daily intake of the control group were used as a basis for comparison. A test for linear trend of risk was calculated as proposed by Breslow and Day [7]. Results are presented only for foods and food groups, which were, in at least one of the analyses, related to prostate cancer at the level of ≤ 0.10. Since there were significant differences between cases and controls in the total energy intake, in the analysis all variables were adjusted to energy.

Results

Medians of average daily food intake

According to univariate logistic regression analysis, when medians of average daily intake of foods and food groups were compared (Table 1), higher than median consumption of milk and dairy products, fruit, processed meat, fish (fresh and processed) and butter were positively related to prostate cancer. Inverse relationship was found for consumption of cruciferous vegetables, tomato foods, potato, rice, fresh meat and chicken.

When all these variables were included in the model of multivariate logistic regression analysis, risk factors for prostate cancer were consumption of fruit, processed meat, fish and butter. Consumption of potato and rice showed a protective effect (Table 2).

Terciles of average food intake

When terciles of average daily intake of the same foods and food groups were compared, with low intake as the reference group (Table 3), univariate analysis showed that consumption of milk and dairy products, fruit, processed meat and fish were risk factors for pros-

Table 1. Odds ratios for prostate cancer according to median of average daily intake of selected food groups

Food group (grams)	*Level of median intake of controls*	*Number of cases whose intake was*		*Odds ratios (95% CI)**
		≤ Md	*> Md*	
Cruciferous vegetables	263.8	67	34	0.60 (0.35-1.02)
Tomato foods	114.3	68	33	0.59 (0.34-1.04)
Potato foods	158.9	75	26	0.39 (0.22-0.68)
Fruit	120.6	39	62	2.87 (1.60-5.14)
Rice	48.5	73	28	0.43 (0.25-0.75)
Fresh meat	165.5	67	34	0.59 (0.35-1.01)
Processed meat	14.3	43	58	2.69 (1.54-4.70)
Chicken	70.8	72	29	0.46 (0.27-0.78)
Fish	1.5	32	69	2.51 (1.49-4.22)
Milk and dairy products	271.6	39	62	1.96 (1.17-3.29)
Butter	3.6	32	69	4.72 (2.48-8.99)

*According to univariate logistic regression analysis. 95% CI: 95% confidence interval, Md: median

Table 2. Risk factors for prostate cancer - multivariate analysis (cases were divided according to median intake of controls)

Food group	*B*	*Standard error*	*p-value*	*Odds ratio*	*95% CI*
Potato	-0.7625	0.3555	0.0320	0.47	0.23-0.94
Rice	-0.7187	0.3516	0.0409	0.49	0.24-0.97
Fruit	1.1644	0.3406	0.0006	3.20	1.64-6.24
Processed meat	0.8153	0.3247	0.0121	2.26	1.20-4.27
Fish	0.5680	0.2952	0.0543	1.76	0.99-3.15
Butter	1.3788	0.3701	0.0002	3.97	1.92-8.20

95% CI: 95% confidence interval

Table 3. Odds ratios for prostate cancer according to terciles of average daily intake of selected food groups

Food group (grams)	*Terciles*	*No. of cases*	*Odds ratio* (95% CI)*	*Odds ratio** (95% CI)*
Cruciferous vegetables	1	45		
	2	34	0.82 (0.46-1.46)	
	3	22	0.58 (0.30-1.12)	
p-value		0.02		
Tomato foods	1	40		
	2	41	1.07 (0.60-1.90)	
	3	20	0.59 (0.29-1.19)	
p-value		0.02		
Potato foods	1	49		
	2	42	0.86 (0.50-1.48)	1.14 (0.61-2.14)
	3	10	0.23 (0.11-0.52)	0.35 (0.13-0.93)
p-value		<0.01	<0.01	
Fruit	1	25		
	2	34	1.80 (0.94-3.45)	1.72 (0.86-3.45)
	3	42	3.91 (1.84-8.34)	3.94 (1.73-8.98)
p-value		<0.01	<0.01	
Rice	1	48		
	2	33	0.69 (0.39-1.20)	
	3	20	0.46 (0.24-0.90)	
p-value		<0.01		
Fresh meat	1	47		
	2	41	0.93 (0.53-1.63)	
	3	13	0.31 (0.15-0.65)	
p-value		<0.01		
Processed meat	1	18		
	2	38	2.11 (1.08-4.12)	1.90 (0.93-3.85)
	3	45	4.04 (1.97-8.31)	3.99 (1.81-8.78)
p-value		<0.01	<0.01	
Chicken	1	53		
	2	39	0.83 (0.48-1.43)	0.72 (0.40-1.29)
	3	9	0.19 (0.08-0.43)	0.18 (0.07-0.43)
p-value		<0.01	<0.01	
Fish	1	29		
	2	21	1.25 (0.64-2.45)	0.99 (0.48-2.02)
	3	51	2.60 (1.45-4.65)	2.17 (1.14-4.12)
p-value		<0.01	<0.01	
Milk and dairy products	1	28		
	2	33	1.26 (0.68-2.34)	
	3	40	1.87 (0.99-3.54)	
p-value		<0.05		

* According to univariate logistic regression analysis - adjusted to energy, ** Variables significantly related to prostate cancer after adjustment for possible confounders: energy, potato foods, fruit, rice, fresh meat, processed meat, chicken, fish and milk and dairy products. p-value for linear trend of odds ratio. 95% CI: 95% confidence interval

tate cancer. Consumption of potato, rice, fresh meat and chicken were inversely related to prostate cancer. All these associations were found only for the high intake of named foods and food groups. There was no significant relationship between prostate cancer and intake of cruciferous vegetables and tomato. Consumption of butter could not be divided into terciles.

When variables significantly related to prostate cancer according to univariate analysis (all variables with the exception of cruciferous vegetables and tomato foods) were included in the model of multivariate logistic regression analysis, risk factors for prostate cancer appeared to be intake of fruit, processed meat and fish (Table 4). Protective effect was found for intake of

Table 4. Risk factors for prostate cancer - multivariate analysis (cases were divided at each tercile level of control)

Food group	*B*	*Standard error*	*p-value*	*Odds ratio*	*95% CI*
Fruit	0.6848	0.2103	0.0011	1.98	1.31-2.99
Processed meat	0.6363	0.2044	0.0015	1.89	1.27-2.80
Chicken	-0.7343	0.1968	0.0002	0.48	0.33-0.71
Fish	0.3871	0.1643	0.0185	1.47	1.07-2.03

95% CI: 95% confidence interval

chicken. Consumption of potato, rice and chicken were significantly collinear at 0.01 levels, for both ways of categorization of food intake, i.e., categorization according to median value and according to terciles.

Discussion

According to the results of both analyses performed in this study, with medians and with terciles of food intake, risk factors for prostate cancer appeared to be consumption of processed meat and fish and intake of fruit.

Meat and fat intake

Many epidemiological studies report that diet high in meat possibly increases the risk of prostate cancer [9,10]. In the present study only intake of processed meat was risk factor for prostate cancer. Consumption of fresh meat was a protective factor although this association was not an independent one. It is a fact that processed meat (salami, sausages, bacon, ham, manufactured luncheon meats, mortadella) contain more fat than fresh meat. Fat intake, analyzed as total fat, saturated fat and/or animal fat, has long been suggested as the major risk factor for prostate cancer, although the data were inconsistent [9]. However, according to Kolonel et al. [10], such an association has diminished in recent years as more epidemiological evidence has been obtained. High consumption of butter –found to be risk factor for prostate cancer in the present study– supports the hypothesis that animal fat is associated with increased risk of this malignant tumor. The association of prostate cancer with diet high in meat has been also considered as an indirect proof of the importance of fat consumption in the occurrence of prostate cancer. However, there is also a possibility that the mode of processing meat incorporates factors related to development of this malignancy. The protective effect of high consumption of chicken could be attributed to the assumption that those who eat a lot of chicken do not eat high quantity of meat, either fresh or processed.

Fish intake

Data about a relationship between fish intake and risk of prostate cancer are neither numerous nor consistent [4,11-13]. In Serbia fish has not been frequently consumed, especially before one or even two decades. When consumed, it was more frequently canned, not fresh. Processed fish, similarly as processed meat, could increase the risk of prostate cancer through factors incorporated in the mode of processing.

Fruit intake

How to explain that in the present study high intake of fruit increased the risk of prostate cancer? Evidence of the effect of diets high in fruits on prostate cancer risk is inconsistent [14-17]. However, recently great attention has been paid to the role of phyto-oestrogens in the development of numerous chronic diseases, including prostate cancer. Actually, there are some epidemiological data showing that phyto-oestrogens, especially isoflavonoids, present mainly in soybeans and soy products, and to a lesser extent lignans (present in fruit, vegetables, whole grains and some other plants) have preventive effect on the development of several cancers (breast, gastric, colon, endometrial and some others), cardiovascular diseases and osteoporosis. Because of the structural similarity of phyto-oestrogens to endogenous oestrogens it has been hypothesized that phyto-oestrogens exert hormonal or anti-hormonal effects relevant to the risk of hormone-dependent diseases [18]. The effect of steroid oestrogens on the development of prostate cancer is not clear enough, although they have beneficial effect in the treatment of this malignant tumor. If phyto-oestrogens are protective for breast cancer because they have an anti-hormonal, anti-oestrogen effect [19,20] it seems more plausible that they could be risk factors for prostate cancer rather than preventing its development. Soybeans and soy products are not frequently present in Serbian diet and lignans are probably the most frequent phyto-oestrogens consumed in our population. The relation between prostate cancer

and lignans has not been a subject of many studies, and in a recent Nordic nested case-control study there was no significant association between prostate cancer and serum enterolactone [21] as a probable biomarker for exposure to lignan-containing foods [22]. Evidently, more research is needed to clarify the possible effect of phyto-oestrogens on human health.

Vegetables intake

Although the pattern of association between prostate cancer and consumption of vegetables is not clear enough [9], it has been accepted that diets high in vegetables possibly decrease the risk of this malignant tumor [9]. A protective effect has been related to intake of cruciferous vegetables [23], legumes [24], orange-yellow vegetables [24], allium vegetables [3,12] and tomato foods [3,15,25,26]. In the present study cases consumed lower quantity of potato, cruciferous vegetables and tomato foods than their controls, but independent inverse relationship with prostate cancer was found only for consumption of potato.

In this study consumption of chicken, potato and rice was inversely related to prostate cancer. However, since chicken is commonly eaten with potato and rice it is difficult to attribute protective effect to any one of them.

Milk and dairy products intake

Diet high in milk and diary products have been found as a risk factor for prostate cancer in several studies [17,27]. In the present study high intake of milk and dairy products was a risk factor for prostate cancer, but this association disappeared after adjustment for possible confounding variables. Takeda and Sato [5] suggested that the sharp increase of prostate cancer mortality in Japan after the Second World War, could be attributed to milk, which contains considerable amounts of estrogens and saturated fat, the consumption of which has recently increased rapidly in Japan. They stated that in recent years milk from pregnant cows has been frequently used. As a consequence, milk nowadays contains higher quantity of estrogens than 100 years ago. However, as already mentioned, there was not enough data to support the role of estrogens in the development of prostate cancer. Association between prostate cancer and oestrogens either was not found or it was an inverse one [28,29]. On the basis of some epidemiological studies it has been suggested that fat may be the constituent responsible for association between prostate cancer and dairy products, although this association was not found in a large American cohort study [30]. Milk and dairy products are also the most common dietary source of calcium. Giovannucci et al. [31] proposed that calcium could increase the risk of prostate cancer by suppressing the circulating levels of dihydroxyvitamin D, which, in turn, decreases prostate cancer risk. Data about the effect of calcium intake on the risk of prostate cancer are inconsistent. High calcium intake was found to be risk factor for prostate cancer in some studies [31,32], but in others this relationship was not present [33], and in our study it was even inverse [2].

The present study has some disadvantages, like other case-control studies, the most important one being related to the accuracy of recall of past exposure. But since controls were chosen from among hospital patients it could be expected that incomplete and/or inaccurate data about diet were equally distributed in the compared groups. In the present investigation the number of cases was relatively small, and a larger study on the same subject would be desirable.

Conclusion

The results obtained in the present study support the hypothesis that consumption of meat and fat plays a role in the development of prostate cancer. The findings that consumption of processed meat only (not fresh) and consumption of fish (most frequently canned) increased the risk of prostate cancer, as well as the findings that consumption of chicken, potato and rice decreased the risk of prostate cancer, should be corroborated by other investigators.

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