KOLO-REKTAL KANSERLİ HASTALARDA LİPİD PROFİLİ

LIPID PROFILE IN THE PATIENTS WITH COLO-RECTAL CANCER.

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Özet

Kolo-rektal kanserde lipid profilini incelemek amacıyla, 46 kolo-rektal kanserli hastada ve 46 sağlıklı kontrol vakasında serum kolesterol, trigliserid, apolipopropein A-1 ve apolipopropein B, yüksek-dansiteli lipoprotein kolesterol, düşük-dansiteli lipoprotein kolesterol ve çok düşük-dansiteli lipoprotein kolesterol düzeyleri incelendi. Hasta grubuna ait serum total kolesterol seviyesi kontrol grubundakinden düşüktü, ancak farklılık istatistiksel olarak anlamlı değildi ($p>0.05$). Benzer şekilde her iki gruptaki serum apolipopropein A-1 ve B seviyeleri arasında da farklılık yoktu. Hasta grubundaki serum trigliserid ($p<0.0001$) ve çok düşük-dansiteli lipoprotein kolesterol düzeyleri ($p<0.001$) kontrol grubundan yüksek; yüksek-dansiteli lipoprotein kolesterol ($p<0.001$) ve düşük-dansiteli lipoprotein kolesterol düzeyleri ($p<0.05$) ise kontrol grubundan düşük olarak bulundu. Hasta grubunda cinsiyet, lokalizasyon ve kanserin evresi yönünden farklılık tesbit edilmedi. Kolo-rektal kanserli hastalarda yüksek-dansiteli lipoprotein kolesterol düzeylerinin düşük, çok düşük-dansiteli lipoprotein kolesterol düzeylerinin ise yüksek olduğu sonucuna varıldı.

Anahtar Kelimeler: *Kolo-rektal kanser, Lipidler, Lipoproteinler.*

Summary

In order to investigate lipid profile in colorectal cancer, this study was conducted in 46 patients with colorectal cancer and in 46 healthy control subjects. Serum cholesterol, triglyceride, apolipopropein A-1 and apolipopropein B, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and very low-density lipoprotein cholesterol levels were quantified in the patient and control group. Serum total cholesterol level obtained in the patient group was lower than that of the control group, but the difference was not statistically significant ($p>0.05$). Like this, serum apolipoprotein A-1 and B concentrations obtained in the patient group were not different from those of the control group. Serum triglyceride ($p<0.0001$) and very low-density lipoprotein cholesterol ($p<0.001$) levels of the patients were higher, and high-density lipoprotein cholesterol ($p<0.001$) and low-density lipoprotein cholesterol ($p< 0.05$) levels of the patients were lower than those of the controls. In the patient group, there were not statistically significant differences with respect to sex, localisation and stage of the cancer. It is concluded that patients with colorectal cancer have low levels of high-density lipoprotein cholesterol and high levels of very low-density lipoprotein cholesterol.

Key words: *Colo-rectal cancer, Lipids, Lipoproteins.*

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Introduction

The positive association between total serum cholesterol level and risk of coronary heart disease is well established (1-3). For many years, much evidence has been accumulated indicating a possible central role of endogenous cholesterol in the pathobiology of cancer. Many alterations occur in the synthesis, uptake, and membrane content of cholesterol. These alterations include changes in chromosome 5, which also carries two genes vital to the biosynthesis and regulation of systemic and cellular cholesterol metabolism, 3-hydroxy-3-methylglutaryl coenzyme A synthase, and 3-hydroxy-3-methylglutaryl coenzyme A reductase. These enzymes are increased in cancer cells for production of cholesterol for new membrane biogenesis and for growth and proliferation. In the body there is a continous exchange of cholesterol between tissues and blood. It is thus conceivable that any substantial alteration of cholesterol metabolism at the cellular level may entail changes in the plasmatic pool of the cholesterol (4-8). So, investigators have begun to deal with the relation between the serum cholesterol level and the incidence of colorectal cancer. While many prospective studies have noted an inverse association between serum cholesterol level and an increased risk for colon cancer (1,2,4,9-11), the others have noted a positive association (3,12). In this study, we aimed to investigate lipid profile in the patients with colorectal cancer in terms of sex, tumor localisation and stage.

Table I. *Serum Cholesterol, Triglyceride, Apo A-1 and B, HDL, LDL and VLDL Cholesterol Levels Measured For Men, For Women and For Both Sexes Combined in the Patients and Controls.*

	Patient Group			Control Group		
	Men	Women	Total	Men	Women	Total
Cholesterol (mg/dl)	156.50 ± 29.14	139.72 ± 61.60	152.55 ± 40.97	178.12 ± 46.93	163.42 ± 50.12	170.96 ± 43.32
TG (mg/dl)	170.00 ± 49.42	147.76 ± 46.90	154.28 ± 46.68 *	93.11 ± 40.33	74.11 ± 33.70	83.90 ± 26.68
Apo A-1 (mg/dl)	132.18 ± 18.12	123.82 ± 9.09	128.25 ± 11.74	127.28 ± 24.02	120.12 ± 20.12	123.11 ± 21.02
Apo B (mg/dl)	105.00 ± 21.08	101.08 ± 19.59	102.52 ± 19.66	99.18 ± 88.78	90.12 ± 78.11	94.65 ± 83.48
HDL (mg/dl)	28.23 ± 9.02	31.59 ± 10.29	30.34 ± 9.84 **	39.42 ± 9.43	38.27 ± 17.97	39.14 ± 10.34
LDL (mg/dl)	99.82 ± 26.07	100.01 ± 22.46	96.26 ± 30.43***	131.12 ± 37.73	106.99 ±31.49	117.53 ± 33.83
VLDL (mg/dl)	34.68 ± 16.10	29.55 ± 12.38	30.20 ± 18.05 **	25.44 ± 9.12	15.41 ± 8.19	19.72 ± 6.50

* $p<0.0001$, ** $p<0.001$, *** $p<0.05$, when compared to control group (total group).

Materials and Methods

In order to investigate lipid profile in colorectal cancer, this study was conducted in 46 patients with colorectal cancer (16 males, 30 females) with a mean age of 53.57 ± 16.00 years (range 21-75 years) and in 46 healthy control subjects (11 males, 35 females) with a mean age of 52.07 ± 12.07 years (range 18-70 years). The patients were diagnosed by colonoscopic biopsies or by histopathologic examination of the specimens removed at the operation. Eighteen of the cancers localised in colon, 26 in rectum and 2 both in colon and rectum. Six of the patients did not undergo an operation. Of the patients that had been operated on, 14 were in stage IV, 10 were in Stage III, and 16 were in Stage II. After overnight fast of at least 12 h, blood samples were taken from the patient and control subjects. Serum was seperated from the blood samples after allowing to clot for at least half an hour at room temperature. Then, the serum samples were frozen at -70°C until assayed, which in all cases was within 2 months. At the time of sampling, no patient and control cases were receiving any drug known to affect lipid metabolism. We quantified serum cholesterol and triglyceride (TG) levels by using enzymatic methods (Cholesterol, Cat no: 16083, Trace; Triglycerides, Cat no: 16935, Trace) with a Hitachi 717 autoanalyzer (Hitachi Ltd, Japan). Serum Apolipoprotein (Apo) A-1 and B concentrations were determined immunoturbidimetrically (Incstar Corporation, Cat no: 86059, 86060, USA). High-density lipoprotein (HDL) cholesterol was determined by cholesterol oxidase after sodium phosphotungstate precipitation of low-density lipoprotein (LDL) cholesterol and very low-density lipoprotein (VLDL) cholesterol (Chol HDL, Sclavo, cat no: 81430). VLDL and LDL cholesterols were calculated as TG / 5 and cholesterol - (HDL chol + TG / 5), respectively, if TG was < 400 mg / dl (13). We used the unpaired Student's t test to assess the differences between the colorectal cancer group and the control group with respect to each of the variable measured. A p value lower than 0.05 was taken as significant. For correlation analysis, a linear regression test was used.

Results

Forty six patients with colorectal cancer and 46 healthy control cases were included in the study. Serum cholesterol, TG, apo A-1 and B, HDL, LDL and VLDL cholesterol levels measured for men, for women and for both sexes combined in the patients and controls are summarized in Table I. As shown in Table I, mean serum cholesterol level obtained in the patient group was lower than that of the control group, but the difference was not statistically significant ($p>0.05$). Like this, serum apo A-1 and B concentrations obtained in the patient group were not different from those of the control group. There were statistically significant differences between serum TG ($p<0.0001$), HDL cholesterol ($p<0.001$), LDL cholesterol ($p<0.05$) and VLDL cholesterol ($p<0.001$) levels obtained in the patient and control group. In the patient group, we compared all these measurements obtained in men with those obtained in women, and those obtained in the patients with colon cancer with those obtained in the patients with rectal cancer, and did not find any statistically significant difference.

Table II. *Breakdown of the Cancer Cases By Localization of the Tumor.*

	Colon	Rectum
Cholesterol (mg/dl)	151.62 ± 45.24	155.72 ± 35.37 n.s.
TG (mg/dl)	139.12 ± 42.80	154.66 ± 35.84 n.s.
Apo A-1 (mg/dl)	126.12 ± 12.03	129.42 ± 32.00 n.s.
Apo B (mg/dl)	109.33 ±19.50	101.88 ± 11.62 n.s.
HDL (mg/dl)	28.36 ± 11.28	31.26 ± 11.79 n.s.
LDL (mg/dl)	115.25 ± 28.91	109.88 ± 27.42 n.s.
VLDL (mg/dl)	25.14 ± 9.43	28.20 ± 8.00 n.s.

n.s.: not significant

Table III. *Breakdown of the Cancer Cases By Stage.*

	Stage II	Stage III	Stage IV
Cholesterol (mg/dl)	158.11 ±42.19	142.00 ± 28.95	165.20 ± 57.22
TG (mg/dl)	148.40 ± 42.68	150.20 ± 33.86	181.75 ± 24.90
Apo A-1 (mg/dl)	122.60 ± 22.12	126.73 ± 20.18	132.00 ± 28.18
Apo B (mg/dl)	108.83 ± 12.05	99.25 ± 6.84	110.00 ± 26.87
HDL (mg/dl)	35.58 ± 10.53	28.20 ± 9.88	26.28 ± 10.59
LDL (mg/dl)	127.26 ± 23.66	91.25 ± 19.01	111.26 ± 36.81
VLDL (mg/dl)	29.68 ± 8.53	30.04 ± 6.77	24.84 ± 11.69

There was not any correlation between any two stages with respect to parameters studied.

Similarly, a breakdown of the cancer cases by stage showed that there were no statistically significant differences among the measurements of the Stage II, III and IV groups. Breakdown of the cancer cases by localization of the tumor and by stage are summarized in Table II and III, respectively. In the patient group, analysis of the data revealed that mean serum cholesterol level was positively correlated with serum TG ($r = 0.58$, $p<0.001$), LDL cholesterol ($r=0.81$, $p<0.0001$), VLDL cholesterol ($r=0.58$, $p<0.001$) and HDL cholesterol ($r=0.37$, $p<0.05$) levels. Serum TG level was positively correlated with serum cholesterol ($r=0.58$, $p<0.001$). There was not any correlation between serum HDL cholesterol and VLDL cholesterol level.

Discussion

A potential inverse correlation between serum cholesterol levels and cancer incidence and mortality has been observed in several epidemiologic studies in patients with colon cancer (1,2,4,9-11). Until now these studies have not explained whether the association is due to a metabolic or nutritional effect of the cancer on the serum cholesterol level or reflects a causal relationship between low serum cholesterol level and colon cancer (1,4-9). Neugut and associates (1) determined serum cholesterol levels in patients with adenomatous polyps and colon cancer. The mean serum cholesterol level of the patients with colon cancer was lower than that of the control group and of the patients with adenomatous polyps. So, they concluded that the low serum cholesterol level was probably a result of metabolic changes due to the disease process. Because if low serum cholesterol levels were a causal agent for colon carcinoma, one would expect that the same relationship that held for the malignancy would be found for the precursor lesion. Further, studies that showed a negative association between serum cholesterol and cancer found that this inverse relation diminished or disappeared when cases of cancer diagnosed in the first 2 to 7 years of follow - up were eliminated from the analysis. This finding suggests that the inverse association between the serum cholesterol level and colorectal cancer could be attributable to metabolic effects of cancer undetected at the baseline examination (9). Of the studies that have investigated serum cholesterol levels in the patients with colorectal cancer and have found an inverse relation, Neugut (1), Neaton (2), Kreger (10), and Burnstein (11) have found total serum cholesterol levels as lower than those of the controls. In a recent study of Dessi and associates (4), an increase of about twofold of cholesterol content was observed in tumor tissues compared with the normal tissues. HDL cholesterol, of which function is to maintain normal cell cholesterol homeostasis by removing excess cholesterol from intracellular pools, was markedly reduced. Because during proliferative processes cholesterol accumulates in proliferating tissues, the observed decrease in HDL may be caused by a reduced release of cholesterol from proliferating cells to HDL. Similarly, Bayerdörffer (9) and Kritchevsky (14) found lower HDL cholesterol and higher LDL cholesterol and VLDL cholesterol levels in patients with colorectal adenomas. Their analyses indicated that HDL cholesterol is the lipoprotein most strongly associated with the frequency of colorectal adenoma. In contrast, Törnberg (12) and Mannes (3) showed a positive association between serum cholesterol or beta-lipoprotein levels and the subsequent risk of cancers of the colon and the rectum. In the present study, serum total cholesterol level obtained in the patient group was lower than that of the control group but the difference was not significant. Serum triglyceride and VLDL cholesterol levels were higher and serum LDL cholesterol and HDL cholesterol levels were lower than those of the control group. Because serum apo A-1 and B concentrations reflect the serum lipoprotein values more accurately, we determined both of them but we failed to find any association between two groups. The association between the serum VLDL cholesterol level and colorectal cancer has not been much studied. It has been reported that the HDL cholesterol level is inversely related to the VLDL cholesterol level (9). Our study did not confirm this finding. A role for triglyceride-rich VLDL cholesterol has been described for coronary heart disease, suggesting that such an association may also

(2,10) or positive association (12) tends to be found among men only. We determined serum lipoprotein levels in men, in women, and in both sexes combined in the patient and the control group, and found that the changes affected both men and women. In a study of Chyou and associates (15), 7716 Japanese American men were examined and tasted for serum cholesterol. After 22 years, 1380 incident cancer cases were identified. Of the site specific cancers, only colon cancer cases had a significantly low mean serum cholesterol values. We wondered if there is a difference between all these measurements obtained in the patients with colon cancer and those obtained in the patients with rectal cancer, and compared these values, but did not find any statistically significant difference. In the present study, the measurements of the patients in Stage II, III and IV were compared with each other, and no statistically significant difference was found. Neugut et al (1) compared the serum cholesterol level measured in the Dukes 'B group with that measured in the Dukes 'A group and found that the serum cholesterol level in Dukes 'B group was lower than the other. We conclude that patients with colorectal cancer have lower levels of HDL cholesterol and higher levels of VLDL cholesterol.

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