Increased Circulating Vitamin D and Testosterone Levels in Patients with Cancer

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Abstract

Background: Vitamin D has anticarcinogenic properties and sex steroids play roles in the development of breast cancer, endometrial carcinomas and prostat cancers. In this study, we decided to detect the levels of vitamin D and testosterone in lung and gastric cancer patient.

Patients and Methods: Sixty eight incidental cases with cancer and 20 healthy controls were enrolled the study. Serum samples were collected before the chemotherapy. Serum samples were studied by the way of ELISA with the commercial kit.

Results: Mean plasma 25-OH Vit D concentrations were evaluated. The concentrations were statistically higher in lung cancer and gastric cancer than the controls ($p < .001$, $p = .036$). Interestingly the levels were higher in lung cancer than gastric cancer ($p = .008$). Testosterone levels were statistically significantly higher in lung cancer patients than the controls ($p = .009$).

Conclusion: At the beginning of the study we hypothesied that the concentrations of these steroids are decreased in cancer patients. But the main finding of this study was the high concentrations of Vitamin D and testosterone in cancer patients. This situation can be releated with the 25-hydroxyvitamin D3-24-hydroxylase activity and Vitamin D receptor polymorphism for vitamin D and aromatase enzyme activity for testosterone levels. More studies, about the roles of vitamins and especially androgens on the prognosis of various cancer types are needed.

Key words: Lung neoplasms, stomach neoplasms, testosterone, Vitamin D

Introduction

Vitamin D is a steroid hormone and it is so important for bone health. In addition it has anticarcinogenic properties (1). Vitamin D induces apopitosis of some cancers and it effects tumor invasion and angiogenesis (2). Various epidemiological studies were done about the effects of vitamin D and cancer prognosis. In one study increased vitamin D levels was releated with low mortality rates in patients with cancer (3).

Sex steroids play roles in the development of hormone depent breast cancer, endometrial carcinomas and prostat cancers. A reduction of testosterone levels were detected in patients with lung, stomach and pancreatic carcinoma in various studies and in another study decreased serum testosterone levels were detected in colorectal cancer patients (4). In animal studies the effects of sex hormone on normal lung and lung disease were evaluated (5).

In this study, we decided to detect the levels of vitamin D and testosterone in lung and gastric cancer patient. We tried to evalute the difference of the levels in patient and healthy subjects. We hypothesied that the concentrations of these steroids are decreased in cancer patients.

Materıals and methods

Patients

This is a case control study. Sixty eight cancer patients (all incidental cases) and 20 healthy controls were enrolled between june 2008 and june

2009. The exact diagnosis and the date of diagnosis were determined based on their pathology report. The patients were staged according to the sixth edition of the American Joint Committee (6). The patients were all new diagnosed and chemotherapy naive patients. Serum samples were collected before the chemotherapy and saved at -20 ºC until the time of the study. The patients' and control groups' serum samples were dissolved just before the study and they were studied at Karadeniz Technical University Hematology Laboratory. Serum samples were studied by the way of ENZİME-Linked Immunoabsorbant Assay (ELISA) with the commercial kit. For testing 25-hidroxy vitamin D (25- OH Vit D) , Immundiagnostik 25- OH Vitamin D EIA kit (Immuodiagnostik AG, Stubenwald-Allee 8a, D 64625 Bensheim) was used. For testing the testosterone levels Testo-Easi kit (Biosource Europe S.A. Rese de I'Industine, 8-B-1400 Nivelles- Belgium) was used.

Statistical Analyses

The conformance of data obtained by measurement to normal distribution was investigated in each group by Kolmogorov Smirnov test. The comparisons of the variables conforming to normal distribution were made by Student t-test between the parameters and the means of vitamin D and testosterone. As for the comparisons of the variables not conforming to normal distribution, Mann-Whitney U test was used. The data obtained by measurement were expressed as arithmetic mean ± standard deviation. The significance level was $p < .05$.

Results

Sixty eight patients with cancer and 20 controls were inserted in this trial (a total of 88 participants).There was no statistically significant difference between the patients and the control group with respect to age ($p = .226$). Fourty four of the patients were lung cancer patients and the others were gastric cancer patients. Thirty six patients in lung cancer group were having non small cell pathology. All patients in gastric cancer patient group were in the pathology of adenocarcinoma.

Mean plasma 25-OH Vit D concentrations were evaluated. The concentrations were statistically higher in lung cancer and gastic cancer than the controls ($p< .001$, $p= .036$). Interestingly the levels were higher in lung cancer than gastic cancer ($p= .008$) (Table 1).

Table 1. Mean levels of Vitamin D in groups

	Mean ± SD	**Min-Max**
Lung cancer	52.16 ± 17.87	12-85.7
Gastric cancer	40.02 ± 12.16	16.5-63.1
Controls	28.19 ± 12.11	11.8-53.85
		p<.001*

** Statistically significant*

Testosterone concentrations were evaluated. The levels were statistically significantly higher in lung cancer patients than the controls (p=.009). But no stastistically significance were detected between the gastric cancer and control subjects with respect to the testosterone concentrations (Table 2).

Table 2. Mean levels of Testosterone in groups

	Mean ± SD	**Min-Max**
Lung cancer	14.09 ± 5.51	0.35-25
Gastric cancer	11.60 ± 5.99	0.80-18.20
Controls	9.27 ± 5.71	0.06-18.10
		P=.01*

** Statistically significant*

Median age was 62 (range 39-75) in lung cancer group. The patients were classified into two groups according to the age. There were no statistically significant difference for vitamin D and testosterone levels among the classifiying the age. With respect to metastasis status, the concentrations of vitamin D and testosterone were not statistically signifcantly different in metastatic and nonmetastatic patients. According to the histological properties vitamin D levels were not different between groups. But testosterone levels were statistically significatly higher in adenocarcinoma histology. Mean testosterone level was 21.25 in adenocarcinoma group and in non-adenocarcinoma group the level was 13.50 (p=.001) (Table 3).

In gastric cancer patients there were no stastisticaly significant differences in the disrubition of age and metastasis by Vitamin D and testosterone levels. With respect to gender testosterone levels were lower in women ($p= .001$) (Table 4).

Table 3. Relationship between variables and mean levels of Vitamin D and testosterone in lung cancer patients

Variables	Vitamin D Mean ± SD / p		Testosterone Mean ± SD / p	
Age				
< 50 y	58.6 ± 8.00	0.312	12.26 ± 2.64	0.319
≥ 50 y	50.95 ± 19.01		14.41 ± 5.84	
Gender				
Male	53.02 ± 17.07	0.644	13.78 ± 5.54	0.187
Famale	45.50 ± 24.58		17.05 ± 4.87	
Hystological type				
Small cell	49.03 ± 20.54	0.692	13.48 ± 7.56	0.357
Non-small cell	52.86 ± 17.47		12.25 ± 5.04	
Hystological subtype				
Adenocarcinoma	46.90 ± 17.62	0.191	17.41 ± 4.84	0.026*
Others	54.45 ± 17.57		13.34 ± 5.01	
Metastasis				
Precence	49.00 ± 18.51	0.279	15.17 ± 6.17	0.144
Absence	55.67 ± 17.86		13.41 ± 5.01	

**Statistically significant*

Table 4. Relationship between variables and mean levels of Vitamin D and testosterone in gastric cancer patients

Variables	Vitamin D Mean ± SD / p		Testosterone (pl) Mean ± SD / p	
Age		0.062		0.897
< 50 y	48.50 ± 15.33		11.71 ± 5.20	
? 50 y	37.22 ± 10.23		11.26 ± 6.83	
Gender		0.747		0.001*
Male	39.21 ± 9.87		14.74 ± 2.48	
Female	41.56 ± 16.31		2.19 ± 1.20	
Metastasis		0.891		0.661
Presence	40.60 ± 12.70		13.90 ± 1.74	
Absence	40.43 ± 12.58		10.25 ± 7.06	

** statistically significant*

Discussion

The main finding of this study was the high concentrations of vitamin D and testosterone in cancer patients. Vitamin D has effects on the development of different types of cancers. Vitamin D can supress cell proliferation, invasion, angiogenesis and it can stimulate apopitosis (7). In vitro studies showed that high levels of vitamin D inhibits the metastatic spread (8). In another study circulating 25-OH Vit D levels were associated with the prognosis of the non small cell lung cancer (9). But in this study we found high levels of Vitamin D in lung cancer patients. The concentrations were higher than the healthy subjects. This result was not compatible with the studies in the literature.

Why our lung cancer patients' Vitamin D levels are higher? This situation can be releated with the 25-hydroxyvitamin D3-24-hydroxylase (CYP24) activity. In vitro studies showed that non small cell carcinoma cell lines can express this enzyme (10). Increased CYP24 expression can effect the activity of 1,25 dihydroxyvitamin D3 and Vitamin D3 cannot play a potent role for antiproliferative activity in this patient group (11). Another explanation about the high levels may be the best care of the patients. Because in our country when the cancer was diagnosed overfeeding starts. This means the relatives of the patients make them to eat and drink more dairy products and the patients take vitamin pills out of order.

Vitamin D levels were detected higher in gastric cancer patients. The try of overfeeding is same as lung cancer. In addition it can be releated with the metabolic transformation of 25-OH Vit D to 1,25 dihydroxyvitamin D3. In a study mean plasma 25-OH Vit D concentrations were detected higher in colorectal cancer patients (12). But

the concentrations were not evaluated in gastric cancer patient. We evaluated and we found high levels. One hypothyse about this problem, malign cells may protect theirselves from the activity of Vitamin D by decreased Vitamin D receptor expession and conversion of 25-OH Vit D to 1,25 dihydroxyvitamin D (13).

Sex steroids play roles in the development of hormone depent breast, endometrial carcinomas and prostat cancers. Sex steroid receptors were found in lung cancer tissues in prevous studies (14,15,16). In a study the level of estradiol was higher and the testoserone level was detected lower in patients with lung cancer. In this study it was suggested that aromatase enzyme was releasing from the lung cancer tissue and turning the androgen to estrogen (17). In our study we found increased testosteron levels and it may be releated with the problem in aromatase activity.

Finally, in this area more studies are needed, especially the roles of androgens and its relation with the prognosis of the lung cancer.

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