

RESEARCH COMMUNICATION

Tumor Markers and Biochemical Parameters in Colon Cancer Patients Before and After Chemotherapy

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Abstract

Objectives: Tumor markers and biochemical parameters were investigated in patients suffering from colon cancer and in volunteer healthy persons. **Design and Methods:** Biochemical analyses of erythrocyte enzymes and serum values for series of established tumor markers were conducted for 40 patients diagnosed with colon cancer, before and after chemotherapy, and 29 healthy volunteers between 2008 and 2009. **Results:** Activities of catalase and carbonic anhydrase were lower in sick than healthy groups ($p<0.05$) before and after chemotherapy, while alkaline phosphatase and creatinine were increased. The patients with colon cancer showed significant ($p<0.05$) elevation of CRP, fibrinogen, CA125, AFP, and decrease in ferritin, before but not after therapy. **Conclusion:** The results obtaining from this investigation can be useful for colon cancer risk assessment.

Keywords: Colon cancer - ALT - AST - carbonic anhydrase - catalase

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Introduction

Of all patients with colorectal carcinoma, an estimated 2- 6% are below 40 years of age. Several reports have described the poor prognostic factors for the survival in young patients with colorectal carcinoma (Turkiewicz et al., 2001). Malignant tumours arising in the colorectal mucosal epithelium destroy extracellular matrices such as the basement membrane, eventually becoming advanced cancers metastasizing to the liver and other distant organs (Liotta,1986).

Carcinoembryonic antigen (CEA) is a 180 kDa oncofetal glycoprotein and a well-known soluble tumor marker. Although its presence in normal tissues is mainly limited to the large intestine, it is overexpressed in most gastrointestinal malignancies, lung cancer, breast cancer and thyroid cancer (Thompson et al., 1991; Ojima et al., 2006). Cancer antigen (CA)-15.3 is a tumor marker detectable in the serum, which recognizes a mucinous antigen of MUC-1 glycoprotein, initially recognized by the monoclonal antibodies DF3 and 115D8, but later cloned and characterized as CD227 (Symeonidis et al., 2004).

C-reactive protein (CRP) is an acute-phase reactant and a known indicator of the malignant potential of tumors. C-reactive protein (CRP) is a sensitive but nonspecific systemic marker of inflammation. CRP is produced mainly in the liver along with other acute-phase proteins in response to cytokines released by phagocytes during infection, trauma, surgery, burns, tissue infarction, advanced cancer and chronic inflammatory conditions (Otterness, 1994; Gabay and Kushner, 1999; Gan et al., 2004; Pepys, 2005; Konstantinos et al., 2008; Demir et

al., 2010).

It is known that when oxidative stress increases, damage may occur in the DNA sequence leading to cancer and other diseases as a result of the deterioration in the balance between free radicals and antioxidants (Halliwell, 2007). Antioxidant potential in all cases of gastrointestinal tract cancer has been unbalanced which has led to increase in reactive oxygen species action and enhancement of lipid peroxidation and cancer procoagulant generation. Catalase subsequently reacts with hydrogen peroxide which was produced by SOD, and decomposes it into water and molecular oxygen (Skrzydowska et al., 2003; Hwang et al., 2007; Demir et al., 2010).

CA is a member of the alfa-family of carbonic anhydrases of zinc metalloenzymes that catalyze the reversible hydration of carbon dioxide to carbonic acid (Sly and Hu, 1995; Demir et al., 2010).

In this investigation, we aimed to determine possible changes of some tumor markers (CEA, CA125, CA19-9, CA15-3 and AFP) before and after chemotherapy and some biochemical parameters (glucose, albumin, globulin, ferritin, ALT, AST, CRP, LDH, creatinin, alkaline phosphatase, amylase, fibrinogen, carbonic anhydrase and catalase) in a series of colon cancers in a relatively high incidence region of Van, Turkey.

Materials and Methods

In this study totally 40 patients diagnosed with colon cancer and 29 healthy volunteers between 2008 and 2009 used as material for examinations in Yuzuncu Yil University, Faculty of Medicine, Department of Medical

Table 1. Erythrocyte Activities of Catalase , Carbonic Anhydrase and some Tumor Markers

Parameters	Patient/Control groups	Healthy control groups	Before chemotherapy	After chemotherapy
Glucose mg/dL	40/29	93.21±5.48 [§]	115.99±46.99 [#]	118.07±37.89
Creatinin mg/dL	40	0.69±0.14	0.89±0.56 [#]	0.75±0.31*
LDH U/L	40	386.57±66.58	371.69±96.09	405.27±140.28
AST U/L	40	20.20±5.39 [§]	21.72±9.02	29.48±22.63*
ALT U/L	40	18.19±7.31	22.05±12.99	22.09±15.13
Albumin g/dL	40	4.63±0.39 [§]	3.71±0.57 [#]	3.45±0.84
Globulin g/dL	40	2.59±0.22	3.38±0.52 [#]	2.91±0.56*
Amylase U/L	40	56.79±11.31	72.34±35.40	58.32±28.33*
Alkaline Phosphatase U/L	40	158.49±38.23 [§]	278.28±199.45 [#]	249.68±149.93
CA-125 U/mL	40	11.20±4.36	22.85±18.17 [#]	9.51±30.45*
CA15-3 U/mL	40	15.44±7.64 [§]	32.25±15.55 [#]	27.24±8.75*
CA19-9 U/mL	40	57.95±5.79	175.60±258.69 [#]	57.21±178.18*
CEA ng/mL	40	1.30±0.83 [§]	171.97±251.13 [#]	16.80±42.94*
AFP IU/mL	40	2.03±0.85	47.66±78.57	1.51±1.41*
Ferritin ng/mL	40	287.86±55.60 [§]	54.78±63.22 [#]	590.26±256.59*
CRP mg/L	40	3.38±1.06 [§]	150.75±117.95 [#]	26.52±43.60*
Fibrinogen mg/dL	40	290.59±52.40 [§]	230.62±3.09 [#]	723.00±22.07*
Catalase (EU/gHg) ⁻¹	40	95.11±24.74 [§]	27.52±21.04 [#]	14.91±13.55*
Carbonic anhydrase (EU/gHg) ⁻¹	40	3.52±2.60 [§]	2.14±1.07 [#]	1.15±0.60*
Glucose mg/dL	40/29	93.21±5.48 [§]	115.99±46.99 [#]	118.07±37.89
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*patients compared before and after chemotherapy (p<0.05); # compared before chemotherapy for patients and healthy person group (p<0.05); § compared after chemotherapy for patients and healthy person group (p<0.05).

Oncology. Venous blood samples of colon cancer were obtained from the antecubital fossa veins the lung cancer in accordance with the guidelines set out in the Declaration of Helsinki. Consent was given by family members of all the patients included in this work. The study was also approved by the local ethics committee.

Biochemical Analysis

Biochemical analysis of the erythrocyte CAT activity was performed using a method described by Aebi in the Biochemistry Laboratory of the Chemistry Department, Faculty of Science, Yuzuncu Yil University. Briefly, the supernatant (0.1 ml) was added to a quartz sink containing 2.95 ml of 19 mmol/l H₂O₂ solution prepared in potassium phosphate buffer (0.05 M, pH 7.00). The change in absorbance was monitored at 240 nm for five minutes using a spectrophotometer (Shimadzu UV-1201, Japan). CA activity was assayed by hydration of CO₂, measured by the method of Rickli and Wilbur-Anderson with bromothymol blue as the indicator (Rickli et al., 1964).

All serum markers obtained from serum samples and some biochemical parameters were determined by Modular equipment P800 and Roche/Hitachi apparatus

in the Biochemical and Hormone Laboratory.

Serum was used for the calculation of CRP by Dade Behring marker BN II. Model Nefolometer equipment with hsCRP apparatus.. CRP in serum was measured by using a latex photometric immunoassay (Eiken Co., Ltd., Tokyo, Japan).

Fibrinogen measurement: The blood samples were added the tube with sodium citrate and then it was centrifuged at 3000 rpm for 10 minutes. The quantitative level of fibrinogen in the blood plasma was determined according to Clauss Kloting method using fibrinogen determination apparatus containing dry and specific heparin inhibitory frozen in STA Compact set.

Statistical Analysis

The results were expressed as the Mean ± Standard deviation (SD). One-way ANOVA was used for the comparison of mean values of the groups. Then, Student-t test, Mann-Whitney U test, Kruskal-Wallis test and Shapiro-Wilk test was used to determine the difference between groups. A P-value<0.05 was considered statistically significant. Statistical analyses were carried out using the SPSS® statistical software package (SPSS

for Windows version 13.0, SPSS Inc., Chicago, Illinois, USA).

Results

Data are summarized in Table 1. Activities of catalase and carbonic anhydrase were lower in sick and healthy groups ($p < 0.05$) before and after chemotherapy, while alkaline phosphatase and creatinine were increased. The patients with colon cancer showed significant ($p < 0.05$) elevation of CRP, fibrinogen, CA125, AFP, and decrease in ferritin, before but not after therapy. As to glucose level for patients (both before and after chemotherapy) it was higher in patient than healthy groups ($p < 0.05$).

Discussion

Colorectal cancer (CRC) is the third most common cancer worldwide with an estimated one million new cases and a half million deaths each year (Parkin et al., 2005; Arnold et al., 2005). Many surgeons feel that operative exploration is sufficient to guide subsequent treatment in colon cancer (Barton et al., 2002). Earlier studies have shown elevated levels of CA 19-9 in patients with advanced colorectal cancer (Koprowski et al., 1981). The patients with colon cancer (before and after chemotherapy) and healthy persons were showed significant value by statistically ($p < 0.05$) for CA125.

CA 15-3 has been considered more specific than other tumor markers, such as carcinoembryonic antigen (CEA) and CA-125 as a diagnostic and prognostic index of the disease (Symeonidis et al., 2004). Increased serum CA-15.3 levels have also been reported in patients with various solid tumors of epithelial cell origin, such as in 45% of the patients with ovarian cancer, in 25% of those with lung cancer, in 30% of hepatocellular carcinoma, in 20–25% of colon cancer etc. (Colomer et al., 1989). For sick people (both before and after chemotherapy) and healthy volunteer persons; there were found an important significant as statistically for CA15-3 ($p < 0.05$).

CRP concentrations between colorectal cancer patients and healthy controls, and have reported at least 10-fold higher concentrations in the cancer patients (Zaloudik et al., 1999; McMillan et al., 2002; Engwegen et al., 2006; Dymicka-Piekarska et al., 2007; Tsilidis et al., 2008). In addition, CRP levels in patients with colorectal cancer are correlated with tumor stage (Nozoe et al., 1998). The patients with colon cancer and healthy persons were showed significant value by statistically ($p < 0.05$) for CRP.

Several reports had indicated that preoperation LDH levels did not predict the OS for colorectal carcinoma in the multivariate analysis (Kemeny and Braun, 1983; Lin et al., 2005). For LDH, there was not found any important significant value in terms of statistically for patients suffered from colon cancer (before and after chemotherapy) and healthy persons ($p > 0.05$).

AST formerly was called serum glutamic oxaloacetic transaminase (SGOT). Previous studies reported that smoking and alcohol usage increased the risk of esophageal cancer multiplicatively (Kimm et al., 2010). Alanine transaminase or ALT is a transaminase enzyme

(EC 2.6.1.2). It is also called serum glutamic pyruvic transaminase (SGPT) or alanine aminotransferase (ALT). ALT is found in serum and in various bodily tissues, but is most commonly associated with the liver. It catalyzes the two parts of the alanine cycle (Demir et al., 2010). Before and after chemotherapy in patients and healthy persons; it was found a significant at high degree for AST and amylase ($p < 0.05$), but for ALT ($p > 0.05$).

The most important antioxidant enzyme systems against the toxic effects of free radicals are as follows: superoxidodismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR) and sulfhydryl compounds (Cobanoglu et al., 2010). The activities catalase for sick and healthy groups were found as significantly in terms of statistically ($p < 0.05$) before and after chemotherapy.

Carbonic anhydrase (CA), a highly active carbonic anhydrase, is a novel tumor-associated protein. This tumor marker has been evaluated in several types of solid tumors (Zavada et al., 1993). The CO_2 level is important in low pH. High partial CO_2 pressures were measured in solid tumors until the early 1960s (Gullino et al., 1965). The activities carbonic anhydrase for sick and healthy groups were found as significantly in terms of statistically ($p < 0.05$) before and after chemotherapy.

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