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The diagnostic value of tumor markers and endoscopy in patients with gastric disorders

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ABSTRACT

Aim: An endoscopy is mainly used to obtain an early diagnosis confirming or excluding a gastrointestinal cancer, and also to investigate the presence of other gastrointestinal diseases. The most common used tumor markers, namely carbohydrate antigen (CA) 19-9, carcinoembryonic antigen (CEA) and alpha fetoprotein (AFP), are not sufficient for an accurate screening method. Evidence is accumulating that increased serum tumor marker levels can be an urgent indicator of endoscopy in dyspeptic patients.

Materials and Methods: We analyzed serum tumor marker levels of patients who were admitted to Sivrihisar State Hospital with gastrointestinal system symptoms. CA 19-9, CEA and AFP serum levels were examined in forty patients who underwent upper gastrointestinal endoscopy and forty healthy volunteers.

Results: There was no significant difference between serum AFP and CA 19-9 levels of patients group and the control group ($P = 0.218$ and $P = 0.107$, respectively). Serum CEA levels were found to be significantly increased in the patient group ($P < 0.05$). CEA levels of patients with gastritis were significantly higher than in patients with other diagnoses ($P = 0.011$).

Conclusions: Tumor markers cannot detect any kind of digestive system malignancy. Physicians must pay attention to premalignant lesions due to gastric cancer development. We must pay more attention to diagnose gastric malignancy in patients who have increased CEA and CA 19-9 levels.

Key words: *Dyspepsia, endoscopy, tumor markers*

Introduction

Gastrointestinal disorders are common diseases and can be diagnosed by endoscopy as a simple and effective procedure. Endoscopy has become the gold standard diagnostic procedure. The main goal of the endoscopist is the early diagnosis to confirm or exclude gastrointestinal cancer, as well as other gastrointestinal diseases. Alpha fetoprotein (AFP), carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 are used as markers of gastrointestinal malignancies [1]. CA 19-9 and CEA are antigens related with most of epithelial originated cancers, including gastrointestinal cancers [2]. Serum levels of CEA and CA 19-9 are increased in premalignant lesions and early stages of cancer. Also in recent study's measurement of CEA and CA 19-9 in gastric juice by an endogastric capsule, put forth us, we can distinguish between precancerous lesions and cancers or normal cases [3]. The most com-

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mon used tumor markers; CA 19-9, CEA and AFP are not a beneficial screening method [4]. We aimed to investigate the relationship of gastrointestinal disorders diagnosed by endoscopy with the serum tumor marker levels. Evidence of increased serum tumor marker levels can be an urgent indicator of endoscopy in dyspeptic patients. We compared serum tumor marker levels of patients who admitted with gastrointestinal system symptoms and underwent upper gastrointestinal endoscopy with a control group of healthy volunteers.

Materials and Methods

In this study, we compared serum tumor marker levels of patients who were admitted to Sivrihisar State Hospital with gastrointestinal system symptoms and underwent upper gastrointestinal endoscopy with a control group of healthy volunteers. In the control group, only serum tumor marker levels diagnosed and patients did not underwent endoscopy procedure. This study was authorized by the local Ethics Committee (05.01.2013/3). In this way, CA 19-9, CEA and AFP serum levels were examined in forty patients who underwent endoscopy and forty healthy volunteers. Five ml blood samples were taken from all of patients and after 20 min the samples were centrifuged at 5000 RPM for 5 min. The chemiluminometric immunoassay method used. Values above 5 ng/ml for CEA, 37 U/ml for CA 19-9 and 5.5 U/ml for AFP were considered high levels. Demographic data and endoscopy results were collected retrospectively from the database of the endoscopy unit. Patients' symptoms were recorded in an endoscopy request form filled according to the patient's complaints. All endoscopies were performed by the same surgeon using Olympus actera CV-150 processors and a GIF-Q150 endoscope (Olympus Corporation; Tokyo, Japan). A total of 11 patients (6 patients in control group and 5 patients in patients group) were excluded from the study because of gastrointestinal malignancy. Endoscopic diagnoses included gastritis, esophagitis, duodenitis, gastric polyp, gastric ulcer and duodenal ulcer. All diagnoses were confirmed with the histophatological examination of biopsies taken during the endoscopy procedure. Patients' mean age was 49 ± 15.3 (males 52.07 ± 14.1; females 47.16 ± 15.98); 25 patients (62.5%) were females and 15 were males (37.5%). Statistical software SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL, USA) was used to analyze statistical data. The distributions of variables were determined using histograms and Kolmogorov–Smirnov test. Mann–Whitney U-test used as a non-parametric test for statistical evaluation. Differences were considered significant when $P < 0.05$.

Results

There was no significant difference between the serum AFP and CA 19-9 levels of patients group and control group ($P = 0.218$ and $P = 0.107$, respectively). Serum CEA levels were found to be significantly in-

Table 1. Serum AFP, CEA and CA 19-9 levels of patients group and controls group.

	Mean±SD (Min-Max)		*P*
	Patients group	Controls group	
AFP (U/ml)	3.27±1.8 (0.89-8.78)	2.63±1.11 (0.69-5.06)	0.218
CEA (ng/ml)	2.77±3.47 (0.5-22)	1.65±1.35 (0.5-7.78)	0.020
CA 19-9 (U/ml)	4.99±5.69 (2-23.72)	9.86±15.3 (2-71.7)	0.107

SD: Standard derivation, Min: Minimum, Max: Maximum, AFP: Alpha fetoprotein, CEA: Carcinoembryonic antigen, CA 19-9: Carbohydrate antigen 19-9

Table 2. Comparison of endoscopic diagnosis and serum tumor marker levels.

	Gastritis		Esophagitis		Duodenitis	
	Mean±SD	*P*	Mean±SD	*P*	Mean±SD	*P*
AFP (U/ml)	3.39±1.72	0.369	3.23±1.87	0.903	3.12±1.96	0.440
CEA (ng/ml)	3.25±3.93	0.011	2.20±1.23	0.828	2.54±1.79	0.785
CA 19-9 (U/ml)	4.35±5.27	0.148	4.10±5.36	0.113	5.20±5.44	0.736

SD: Standard derivation, AFP: Alpha fetoprotein, CEA: Carcinoembryonic antigen, CA 19-9: Carbohydrate antigen 19-9

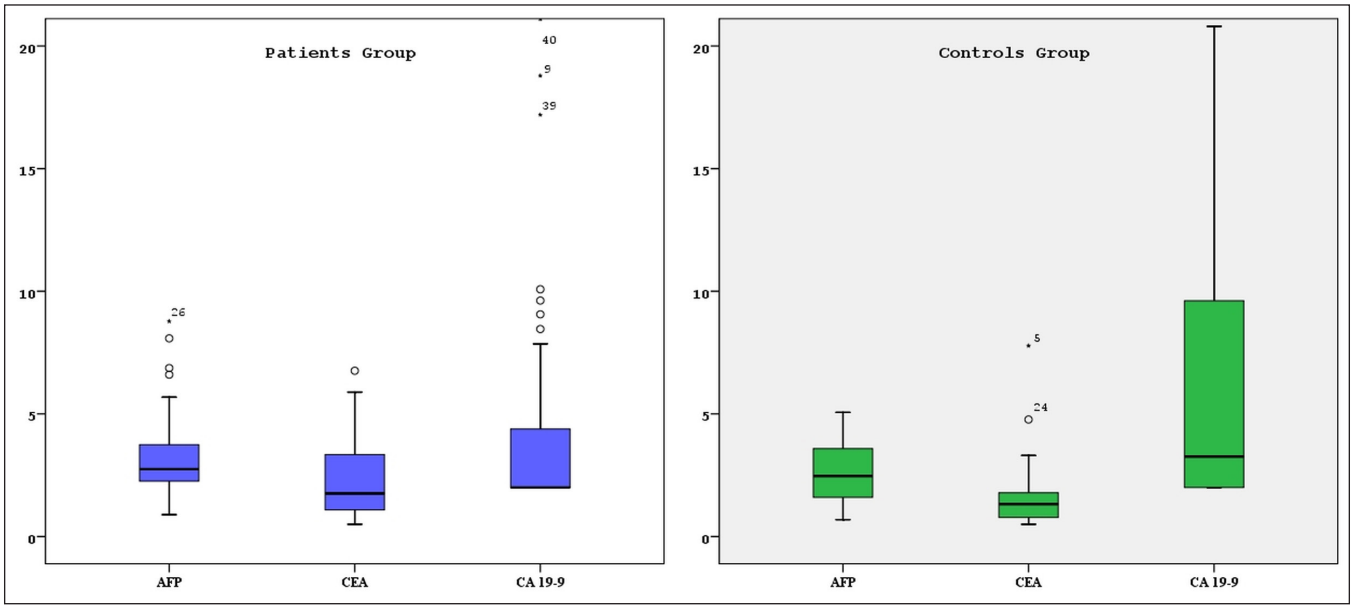

Figure 1. Distribution of serum tumor marker levels of patients group and control group.

creased in the patient group (P < 0.05) (Table 1). The diagnoses were as follows: 29 (72.5%) patients had gastritis, 18 patients (45%) had esophagitis and 11 patients (27.5%) had duodenitis. Serum AFP levels were above the upper limit in 5 patients; the maximum level was 8.78 U/ml. Serum CEA level was found high in 4 patients; the maximum level was 22 ng/ml. All CA 19-9 levels of the patients were in the normal range. In controls group; serum CEA level was high in only 1 patient with 7.78 ng/ml, serum CA 19-9 level was high in two patient and highest level of CA 19-9 was 71.7 U/ml (Figure 1).

The most frequent diagnosis was gastritis, which was found in 29 (72.5%) patients. Esophagitis was diagnosed in 18 (45%) patients and duodenitis was found in 11 (27.5%) 11 patients. The serum AFP and CA 19-9 levels of patients with gastritis did not show any statistical difference (P>0.05). CEA levels of patients with gastritis were significantly higher than in patients with other diagnoses (P=0.011). There was no significant difference in the serum tumor marker levels of patients evaluated with esophagitis or duodenitis (P>0.05) (Table 2).

Discussion

Gastric cancer is currently one of the most common gastrointestinal system malignancies. The delay in its diagnosis is a serious problem, because the major prognostic factor of gastric cancer is the tumor stage. After surgical treatment, the 5-year survival of Stage IV gastric cancer is not more than 7% [5]. At the present time delayed diagnosis of gastric cancer has brought out advanced stages. Thus, even though tumor markers cannot be used for diagnosis of digestive tract malignancies when increased levels of tumor markers are identified, additional investigations considering that possibility should be carry out immediately [4]. Levels of serum tumor markers including AFP, CEA and CA 19-9 can be found high in most of gastrointestinal malignancies. However, tumor markers have a low specificity and sensitivity between 60% and 90% for diagnoses [6]. Nevertheless, patients with increased serum CA 19-9 levels are suspected of biliary tract malignancies such as pancreatic cancer, cholangiocarcinoma and gallbladder cancer, and levels of CA 19-9 can also be found associated to pancreatitis, cholangitis and chronic liver diseases [7]. At the time of first diagnosis, serum levels of CEA and CA 19-9 in patients diagnosed with gastric cancer have been reported in 11.8%-37% and 18%-45% of patients, respectively [8-13]. Serum CEA levels increase in some benign diseases such as gastritis, bronchitis and cirrhosis, and also in smokers [14]. In this study, there was a significant difference between patients who were diagnosed with gastritis and the control group, a finding consistent with the literature [14]. Serum tumor markers levels of the gastric mucosa are elevated in patients diagnosed with chronic gastritis and intestinal metaplasia [15]. Farinati et al. determined increased CA 19-9 levels of gastric juice in

both gastric cancer and chronic atrophic gastritis [16]. Before the development of gastric cancer, often premalignant changes occur in gastric mucosa. These lesions tend to be asymptomatic. Atrophic gastritis, intestinal metaplasia and dysplasia are reported as premalignant gastric lesions with increased gastric malignancy risk in a large cohort study in the Netherlands. de Vries et al. reported the time from first diagnosis of atrophic gastritis to gastric cancer development as nearly 19 months [17]. Patients with premalignant gastric lesion should be inspected frequently during the follow-up. Endoscopic follow-up with histopathological correlation is a recommended procedure. Helicobacter pylori gastritis is a preconditioned disease for gastric malignancy. In fact, the most common cause of chronic gastritis is H. pylori infection. Thus, H. pylori has an intense relationship with gastric cancer development trough gastritis. Patients in which H. pylori was identified in gastric biopsy must have an eradication treatment without delay. However, it is not recommended to apply this treatment in premalignant lesions without histopathological identification. In conclusion, tumor markers cannot detect any kind of digestive system malignancy. Physicians must pay attention to premalignant lesions due to gastric cancer development. We must remain skeptical of the diagnosis of gastric malignancy in patients with increased CEA and CA 19-9 levels.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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