Original Article

Determination of Cancer Antigen CA15-3 and Carcino Embryonic Antigen CEA concentration as Tumor Markers in Patients with Stomach and Colorectal cancers.

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Summary:

Background: Tumor markers are often requested as part of a diagnostic workup, and increased concentrations in serum may suggest malignancy of a particular organ. However, definitive diagnosis is based on histological evaluation of the involved tissue.

Objective: The aim of present study is to evaluated CEA and CA15-3 in order to clarify at least in part their possible use as an early diagnosis tools in sera of patients with stomach, colon and rectum cancers.

Patients and methods: The study was carried out on 61 subjects comprising of 16 patients with colon cancer group (G1), 10 patients with rectum cancer group (G2), 10 patients with stomach cancer group (G3) and 25 normal healthy control The patients were selected, during the period from (February 2010 to January 2011) with age range of (40-55) years. The patients were admitted to Al khadmiya Teaching Hospital, Iraq for treatment. Serum CA15-3 and CEA were measured by enzyme linked immunosorbent assay (ELISA).

Results: The serum value of CA15-3, was highly significant increase ($p \leq 0.001$) in G1 and G2 cancer groups compared to normal healthy subjects. while the serum value of CEA of G1 and G2 was a significant increase ($p \leq 0.05$)compared to control but CA15-3 and CEA in serum of G3 showed no significant difference($p > 0.05$) compared to control.

Conclusions: In this study CA15-3 and CEA could not be of valuable use as diagnostic markers in serum of stomach cancer while in colon and rectal cancers are of useful value.

Keywords: CA15-3, CEA, Tumor markers, Colorectal cancer, stomach cancer.

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Introduction:

Tumor markers are often requested as part of a diagnostic workup, and increased concentrations in serum may suggest malignancy of a particular organ. However, definitive diagnosis is based on histological evaluation of the involved tissue [1]. Cancer antigen CA15-3 is heterogeneous 300 KD glycoprotein antigens was defined by using two monoclonal antibodies 115D8 and DF3 raised against breast carcinoma cells. The diagnostic sensitivity of the CA15-3 for breast carcinoma is low as its elevated levels are also observed in benign breast diseases and in liver cirrhosis, acute and chronic hepatitis. The marker concentrations are also elevated in metastatic cancers of pancreas, ovary, colorectal, lung, stomach, uterus [2].Carcino embryonic antigen (CEA), first described in 1965 by Gold and Freedman, were characterized as a glycoprotein of 200 KD. Subsequent development of a radioimmunoassay (RIA) made it possible to detect very low concentrations of CEA in blood, other body fluids, and also in normal and diseased tissues [3]. Furthermore, linear regression analysis of tumor volume versus gallbladder bile CEA levels in patients with liver metastases predicted that tumors as small as 1cm would produce easily measurable gallbladder bile CEA levels as high as 41 ng / ml[4].Apersistently rising CEA value may be associated with progressive malignant disease and a poor therapeutic response. A declining CEA value is generally indicative of a favorable prognosis and a good response to treatment [5]. Clinical relevance of the CEA assay has been shown in the follow-up management of patients with colorectal, breast, lung, prostatic, pancreatic, and ovarian carcinoma. Follow-up studies of patients with colorectal, breast, and lung carcinoma suggest that the preoperative CEA level has prognostic significance. CEA testing is not recommended as a screening procedure to detect cancer in the general population; however, use of the CEA test as an adjunctive test in predicting prognosis and as a aid in the management of cancer patients has been widely accepted [6]. The aim of present study is to evaluated CEA and CA15-3 in order to clarify at least in part their possible use as an early diagnosis tools in sera of patients with stomach, colon and rectum cancers.

Patients and Methods

The study was carried out on 61 subjects comprising of 16 patients with Colon cancer (G1), 10 patients with rectum

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cancer (G2) , 10 patients with stomach cancer (G3) and 25 normal healthy control. The patients were selected, during the period from (February 2010 to January 2011) with age range of (40-55) years. They were admitted to Al khadmiya Teaching Hospital, Baghdad / Iraq, for treatment.

Blood sample (3ml) was collected left at room temperature and then centrifuge for 15 min. at (3000 rpm). Serum was then separated and freezed until time of analysis.Serum CA15-3 was estimated using an ELISA kit (produced by DrG, Germany)[7] . The concentration of CA15-3 was evaluated from standard curve drawn between standards of CA15-3 provided with the kit and absorbance at 450 nm, (fig1). Serum CEA was estimated using an ELISA kit (produced by DrG, Germany) [8]. The concentration of CEA was evaluated from standard curve drawn between standards of CEA provided with the kit and absorbance at 450 nm, (fig2).Statistical AnalysisThe results were expressed as mean±SD of mean, using Statistical Package for Social Sciences (SPSS) version 19.0 and Microsoft Excel 2010 for data processing and graph construction. Statistical significant difference was ($p \leq 0.05$).and highly significant difference was ($p \leq 0.001$).

Results:

Cancer antigen CA15-3 and carcino embryonic antigen (CEA) in all subjects participated in the study are shown in table 1.The values of serum of colon cancer (G1) , rectum cancer (G2), stomach cancer (G3) and healthy control were shown in table 1. The value for CA15-3 in serum of G1 and G2 showed a highly significant increase compared to normal healthy subjects. but CA15-3 in serum of G3 was within the values for normal healthy subjects. On the other hand, table 1 also showed the serum CEA concentration of patients in the G1, G2, G3 and control groups.The present study showed that the values of CEA in serum of G1 and G2 showed a significant increase compared to control but CEA in serum of G3 showed no significant difference compared to control.

Table (1): Serum CA15-3 and CEA in patients with colon, rectum and stomach cancer groups.

Parameter Group	CA15-3 U/ml mean±SD	P	CEA ng/ml mean±SD	P
Control N=25	18.18 ±4.42		3.68±0.98	
G1 N=16	33.39 ±1.76	P≤0.001	5.63±1.36	P≤0.05
G2 N=10	32.28±2.75	P≤0.001	5.90±0.88	P≤0.05
G3 N=10	19.82 ±1.28	P>0.05	2.66±1.03	P>0.05

Discussion:

Salto in(1990) who claimed that the CA15-3 antigen is an immunohistochemical marker for colorectal carcinoma[9]. CA15-3 antigen is not specific for the breast, and other tumors may give increased concentration in serum of patients with colorectal, lung, ovary, pancreas and liver cancers[10].The present study demonstrated that CA15-3 together with CEA, is a well known useful clinical tool for diagnosis of patients with colorectal cancers.

The results of present study are in agreement with reported data claimed elevated in the levels of serum CA15-3 antigen in patients groups of colorectal cancer [11]. CA- reactive antibodies 115D8 and Df3 detect individual antigen that are present in human primary epithelial carcinoma. Ninety-three percent of 140 human epithelial primary tumors reacted with monoclonal antibodies 115D8 or Df3, including breast, ovarian, lung, and also colon and gastric carcinoma. In general, changes in tumor markers accurately and consistently reflected changes in disease status but the pertinent issue, whether the use of tumor markers in clinical practice will lead to more effective treatment remain controversial.CA15-3 is a marker of distant metastasis in breast carcinoma with high specificity and moderate sensitivity.[12]Recent study showed that carcino embryonic antigen (CEA) is the most significant in prognosis and diagnosis of colorectal cancer and they are linked to tumor growth and metastasis as well as other tumor properties [13]. Carcino embryonic antigen (CEA) is one of the first tumors markers to be identified and characterized. Since its discovery. CEA has been evaluated in a wide range of malignancies including breast cancer, and historically, has been considered the standard to which new serum markers are compared[14] Carcino embryonic antigen plays an important role in tumor metastasis, especially to liver, where it mediates tumor cells adhesion to new site, in colorectal cancer however, its concentration is increased and the general distribution of the molecules on the cell surface is also altered. CEA is considered as one of the most clinically significant tumor markers for colorectal cancer, providing information on prognosis, tumor recurrence, and metastasis [15].Locker and co-worker found that CEA is the best serum marker for colorectal cancer carcinoma, but it has low sensitivity makes it suitable for monitoring than diagnosis less than 10% of patients with early stage colorectal cancer have an elevated CEA. This value rises to about 70% in patients with metastatic disease[16]. In conclusion CA 15-3 and CEA are considerably specific tumor markers in diagnosis and especially monitoring of patients with colorectal cancer. On the other hand CA15-3 and CEA could not be of valuable use as diagnostic of patients with stomach cancer.

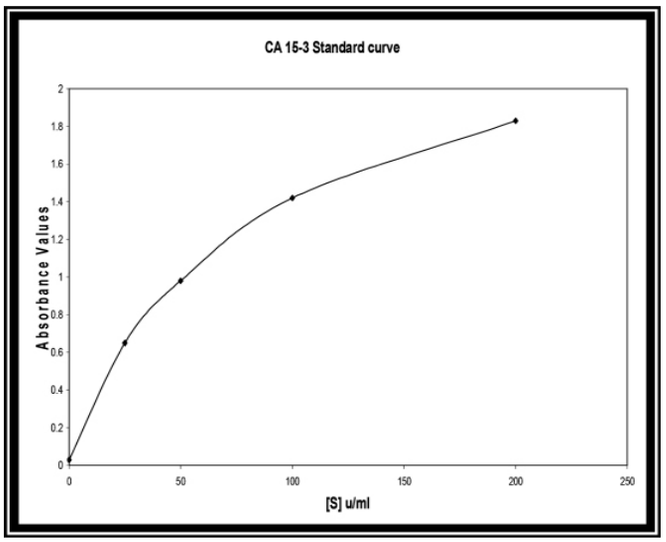

Fig. (1): Standard curve of CA 15-3 Concentration.

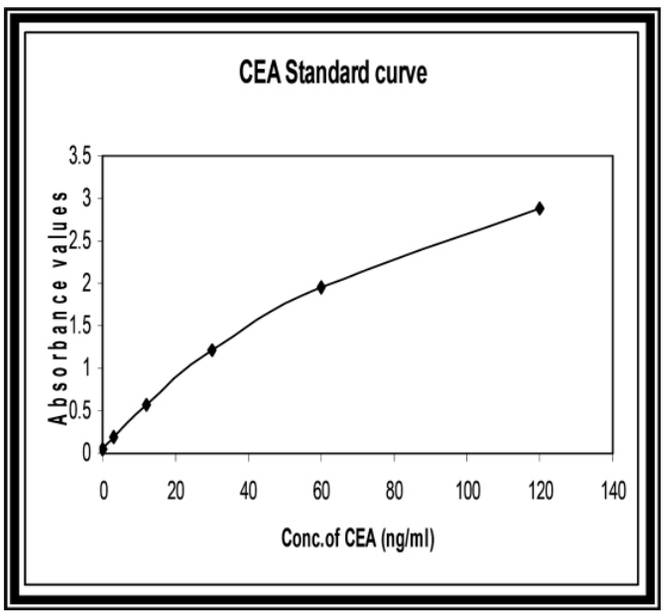

Fig. (2): Standard curve of CEA Concentration.

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