CEA A BIOCHEMICAL MARKER FOR DIAGNOSIS AND PROGNOSIS OF GASTROINTESTINAL CANCER

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ABSTRACT

Serum tumor markers (TM) are widely used for diagnosis and monitoring of treatment of cancer. Carcinoembryonic Antigen (CEA) is one of the most widely investigated tumor markers in gastrointestinal (GI) cancers. Estimation of circulating tumor markers is a non- invasive quantitative method. Serum levels of CEA were studied for diagnosis and prognosis of gastrointestinal malignancies. 140 subjects were undertaken out of which 35 normal and remaining 105 were GI cancer patients. Serum levels of CEA were analyzed by Enzyme Linked Immunosorbent Assay (ELISA). Result of serum CEA levels of the GI cancer patients and normal subjects were analyzed statistically. It was observed that there was significant increase in (P <0.01) in CEA levels of oesophagus, stomach and colon cancer patients as compared to normal subjects. The levels of CEA decreased significantly after the surgery but the decrease in levels of CEA was not up to the levels as normal control subjects.

KEYWORDS

Gastrointestinal Cancer, Tumor marker.

INTRODUCTION: Cancer is a major burden of disease worldwide. Each year, tens of millions of people are diagnosed with cancer around the world, and more than half of the patients eventually die from it. In many countries, cancer ranks the second most common cause of death following cardiovascular diseases. Cancer is a leading cause of death worldwide, accounting for 8.2 million deaths in 2012.[1] In India, GI cancer is third largest group of cancer.[2] Gastric cancer is the fifth most common cancer among males and seventh most common cancer among females in India. The aggressiveness of the disease and need for improvement in therapeutic options is discerned by the fact the cancer is the second most common cause of death globally.[1] The high incidence of local and distant recurrence even in patients with completely resectable gastric cancer indicates the systemic spread of cancer very early in the disease, thus emphasizing the need for multimodality treatment including surgery, radiotherapy, and chemotherapy for treating the disease.

Early detection of cancer is essential for the best chances of cure. Serum tumor markers (TM) are widely used for diagnosis and monitoring of treatment of cancer. TM are considered as the proteins that ideally indicate the presence of malignancy. TM levels are used to find out the response of the treatments to the patients, a decrease or return to the normal level may indicate that the cancer is responding to therapy whereas increase may indicate the cancer is not responding. These markers can be found in tumor cells only,

or in normal cells and over express in malignant cells.[3] Cancer of gastrointestinal (GI) tract is one of the common malignancies in world.

Carcinoembryonic Antigen (CEA) is one of the most widely investigated tumor marker in gastrointestinal (GI) cancers. CEA, an oncofoetal protein, is overexpressed in adenocarcinoma, especially colorectal cancer.[4] Its main application is mostly in gastrointestinal cancers, especially in colorectal malignancy. When CEA levels are positive in patients with gastric carcinoma, they could be useful prognostic indicators.[5] CEA is one of the most widely used tumor markers worldwide and certainly the most frequently used marker in colorectal cancer. Nakane et al.[6] in their study reported that correlation exists between preoperative serum CEA levels and clinic pathologic factor in 865 patients with gastric cancer. Out of 865 patients 249(28.8%) were positive for CEA. The positivity rate was higher in the elderly male patients whose tumors were in the lower third of the stomach. It was also significantly correlated with tumor size, depth of invasion, lymph node metastasis, peritoneal and liver metastasis and cancer stage. Higher the serum CEA levels, the more advance cancer stage and the rate of curative resection decreased. There was a significant difference in patient with CEA levels below 10 μ g/ ml and those with levels exceeding 10 μg/ ml with regard to tumor progression and curability.

Keeping this in view the present study was undertaken to determine quantitative value and sensitivity of CEA levels for diagnosis and prognosis of the gastrointestinal malignancy.

MATERIALS & METHODS: This study was carried out in Department of Biochemistry at SMS, Medical College Jaipur. Blood samples were collected from the cancer patients admitted in Gastrology and Surgery Department of SMS,

Hospital Jaipur. The present study was carried out on 140 subjects of either sex, out of which 35 were normal adults having no symptoms of any disease and the rest 105 were the patients admitted in the wards of Gastro logy and Surgery Departments. There were 37, 30 and 38 patients in the study who had oesophagus, stomach and colon cancer respectively. At the time of their admissions the patients were found suffering from different types of GI malignancy as evidenced by clinical as well as histopathological observation. 80 patients did not come for their treatments continuously for various reasons. In fact only 25 patients remained for follow up studies. The same 25 patients were studied for before and after surgery. Socio economic status, habitat, habits (smoking, alcoholic addiction, chewing, drug, food), Physical activities, History of present illness, Family history and complaint with duration of the illness of the patient and normal subject were recorded before study.

Fasting blood samples were collected from antecubital vain of healthy control and gastro intestinal cancer patients before and after surgery in plain vials. The blood was allowed to clot at room temperature and serum was separated after centrifuging. The serum samples were stored at -20^{0}C until analysis.

The marker CEA was analysed by sandwich ELISA method supplied by Syntron Bioresearch, catalog – 3110-96.[7,8]

Dispensed 50 µl of each reference standard, control and test samples in to the numbered wells and then dispensed 50 µl enzyme conjugate in each well (horse radish per oxidase). The wells were incubated at 37^{0}C for 30 minutes. The incubated mixture was decanted thoroughly. The micro wells were washed 5 times and dried. 50 µl of substrate reagent A (acetate buffer and hydrogen per oxide) and substrate reagent B (3 3' 5 5' tetra methyl benzidine) were dispensed in wells. The wells were incubated at room temperature for 15 minutes. The reaction was stopped by adding 50 µl of stopping solution (1N HCl). The absorbance of each well was read at 450 nm against the substrate blank within 30 min after stopping the reaction.

A standard curve was prepared relating colour intensity to the concentration of CEA. Statistical significance was tested by student's t –test and paired t –test. P <0.05 and P <0.01 were considered significant and highly significant respectively.

RESULTS: Mean values of serum and Carcinoembryonic Antigen (CEA) of normal subjects and gastrointestinal cancer patients are given in Table 1. The mean value of CEA in normal control group was 1.95 ng/ml whereas these values were 4.54, 4.68 and 4.85 ng/ml in oesophagus, stomach and colon respectively. It is obvious from the table that CEA levels increased highly significantly (P<0.01) in

gastrointestinal cancer patients as compared to normal subjects. Minimum and maximum CEA values in normal group were ranged between 1-3 ng/ml while these values were varying between 3.13 to 6.32, 3.01 to 5.76 and 3.20 to 5.89 ng/ml in oesophagus, stomach and colon cancer patients respectively. Higher elevated values of CEA in different cases of GI cancer patients than the normal control group can also be seen in Fig. 1.
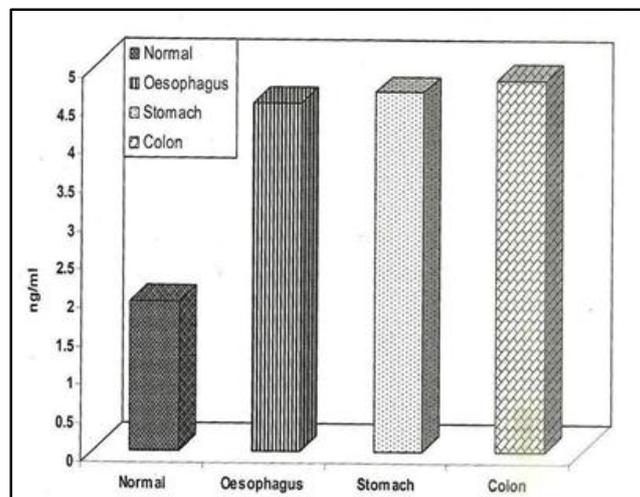
Fig. 1: Serum CEA levels in normal and different GI cancer patients
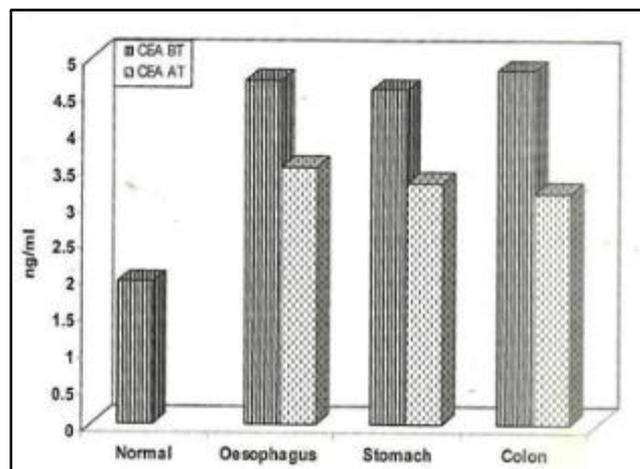
Fig. 2: Serum CEA levels in different GI cancer patients before and after treatments

Mean value of CEA before and after treatments are presented in Table 2. It is obvious from the table that the values of CEA indicate the decreasing trend 4.71 to 3.53, 4.58 to 3.31 and 4.85 to 3.18 ng/ml in oesophagus, stomach and colon cancer patients respectively. Decrease of CEA levels of different GI cancer patients after the treatment can be seen in Fig. 2.

Sl. No.	Subjects	No. of cases	Mean±SE (ng/ml)	Range (ng/ml)		CI(p=0.01) (ng/ml)		Compared to normal	
				Min.	Max.	Lower	Upper	t-stat	p-value
1.	Normal (Control)	35	1.95±0.089	1.00	3.00	1.83	2.06	-	-
2.	Oesophagus cancer	37	4.54±0.130	3.13	6.32	4.37	4.71	16.24	<0.01

3.	Stomach cancer	30	4.68±0.135	3.01	5.76	4.50	4.88	17.34	<0.01
4.	Colon cancer	38	4.85±0.130	3.20	5.89	4.68	5.02	18.09	<0.01

Table 1: Serum CEA levels in normal subjects and gastro intestinal cancer patients

Sl. No.	Subjects	No. of cases	Before treatment Mean±SE (ng/ml)	After treatment Mean±SE (ng/ml)	Paired t-stat	p-value
1.	Normal (Control)	35	1.95±0.89	-	-	-
2.	Oesophagus cancer	8	4.71±0.310	3.53±0.280	4.077	0.021
3.	Stomach cancer	7	4.58±0.210	3.31±0.331	4.374	0.023
4.	Colon cancer	10	4.85±0.264	3.18±0.189	6.025	<0.01

Table 2: Serum CEA levels in gastro-intestinal cancer patients before and after treated conditions

DISCUSSIONS: It was observed that there was significant increase in (P <0.01) in CEA levels of oesophagus, stomach and colon cancer patients as compared to the normal subjects. CEA is an oncofoetal antigen. The oncofoetal antigens are so named because they are normally produced during embryonic development and decreased soon after birth. Cancer cells tend to dedifferentiate or revert to a more immature tissue and begin to produce fetal antigens again. Oncofoetal antigens are very nonspecific and expressed by a wide number of cancer types. Kim et al[5] suggested that preoperative serum CEA levels may have a predictive value in determining prognostic information for patients with gastric cancer. The increase in CEA levels closely resembles the findings of Fornes, N.M. Tanka, M. and Falcao and Shimizu, et al.[9,10] Patients with preoperative elevated CEA represent a risk group with need of consistent post-operative follow – up. In gastric cancer patients, the preoperative and postoperative assay of CEA levels has predictive value in determining cancer stage progression and recurrence.

CONCLUSION: It can be concluded from the study that there was significant increase in CEA levels of oesophagus, stomach and colon cancer patients as compared to normal subjects.[11] Higher CEA levels indicate additional therapy compared to those with normal subjects. The study reveals that preoperative serum CEA levels are important prognostic marker for gastro intestinal malignancy. The levels of CEA decreased significantly after the treatments of oesophagus, stomach and colon cancer patients but the decrease in levels of CEA was not up to the levels as normal control subjects hold. The CEA can be used as an early detector or good prognostic indicator of GI cancers in India.

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