Valley International Journals
Open Access Journal
New Thinking New Innovation

International Journal Of Medical Science And Clinical Inventions
Volume 3 issue 7 2016 page no. 1986-1991 e-ISSN: 2348-991X p-ISSN: 2454-9576
Available Online At: http://valleyinternational.net/index.php/our-jou/ijmsci

Tumor Marker for Diagnosis and Monitoring Response to chemotherapy for Oesophagus Cancer Patients

Ranjit S. Ambad[1], Suryakant Nagtilak[2], Shivkumar Chandraker[3], Dr Madhukar R. Jape[4]

[1]Ph.D Scholar Dept. of Biochemistry Subharti Medical College Meerut.
[2]Professor. Dept. of Biochemistry Subharti Medical College Meerut (UP)
[3]Professor Dept. of Pathology CCM Medical College Durg.
[4]Principal Rama Medical College Hospital & Research center Hapur.
Address for Correspondences: Ranjit Sidram Ambad
Assistant Professor Dept. of Biochemistry, Chandulal Chandrakar Memorial Medical College Durg, (CG)490024

ABSTRACT
Purpose: - To analyze the level of serum Carcinoembryonic antigen (CEA) before and after Different Cycle Of chemotherapy in oesophagus cancer patients.
Methods: - For the study total 120 cases of carcinoma of esophagus of stage I, stage II stage III and Stage IV (before and after different cycle of chemotherapy) were selected. All patients were clinically and histological diagnosed. 42 age and sex matched healthy normal subjects selected as control. CEA activity was measured in the in the serum of control group (n=42) and in patients with esophagus cancer (n=120).
Results: - Mean CEA activity in serum was significantly higher in oesophagus cancer patients as compared to control (p<0.001). After chemotherapy (stage II) the activity of CEA was significantly higher than before chemotherapy (stage I). In stage II (after first cycle of chemotherapy) activity was significantly decreased than stage III (before chemotherapy) and the activity of CEA was significantly decreased in stage IV (after third cycle of chemotherapy) than stage III (after second cycle of chemotherapy).
Conclusion:- Based on the data from our study, it can be stated that serum CEA measurement in plasma may be useful tumor marker in esophageal cancer, its activity might helpful to predict the response of chemotherapy in advance stage of cancer. An initial increased level of CEA before and first cycle of chemotherapy may not indicate tumor progression, but may be represent a transient tumor marker surge phenomenon after second and third cycle of chemotherapy in patients responding to treatment..
Statistically significant change in tumor marker CEA level during the process of treatment in esophageal cancer patients, with a positive response and no established disease progression during study period, near about 12 months after the treatment, point to CEA as an important predictive factor.

Keywords: - CEA, ELISA, Cisplastin, capecitabine esophagus cancer, chemotherapy

Introduction

Oesophagus cancer, cardia cancer and gastric cancer are three of the most commonly seen malignant tumor of gastrointestinal cancer. Oesophagus cancer is start in the inner layer and grows outward. Since two types of cell can line the oesophagus; there are two main types of oesophagus cancer.

1. Squamous cells carcinoma
2. Adenocarcinomas

Squamous cell carcinoma is normally linked with squamous cells. Cancer starting in these cells is called squamous cell carcinoma. This type of cancer can occur anywhere along the oesophagus.

DOI: 10.18535/ijmsci/v3i7.4

Once, squamous cell carcinoma was by far the most common type of oesophagus cancer in worldwide.

The use of tobacco products, including cigarettes, cigars, pipes, and chewing tobacco is a major risk factors for esophagus cancer. The more a person uses tobacco and longer it is used, the higher the cancer risk. Someone who smokes a pack of cigarettes a day or more has atleast twice the chance of getting adenocarcinoma of the oesophagus than a non smoker. The link to squamous cell carcinoma of oesophagus is even stronger. The risk of oesophagus cancer goes down if tobacco use stop. Drinking alcohol also increases the risk of oesophagus cancer. The chance of getting oesophagus cancer goes up with more consumption of alcohol. Combining smoking and alcohol consumption raise the risk of oesophagus cancer much more than using either alone (1).

Some dilatory factors that have been closely associated with oesophagus cancer are betel nut chewing, hot food and beverages. The incidence rate of oesophagus cancer is 7.6 per 100000 in men and 5.7 per 100000 in women in 2006 but recently 8.63 per 100000 in men and 4.39 per 100000 in women (2, 3, 4).

Oesophagus cancer including squamous cell carcinoma and adenocarcinoma considered as serious malignancy with respect to prognosis and a fetal outcome in the great majority of cases (5, 6). Oesophagus carcinoma affects more than 450000 people worldwide and the incidence rapidly increasing (7). Currently, oesophagus cancer is the eights most common incident cancer in the world because of its extremely aggressive nature and poor survival rate (8, 9). Incidence of oesophagus cancer has increased sharply over the past few decades, both by period and birth cohort. Etiological studies are required to explain the rapid increase of this lethal cancer (10). This oesophagus cancer is 3 to 4 times more common among men than among women (1).

Carcinoembryonic antigen (CEA) is a glycoprotein. It was first identified in 1965 by Gold and Freedman in human colon cancer tissue extracts (11). CEA currently classified under the immunoglobulin super family and functions as an intracellular adhesion molecule. In the recent years CEA has been widely used as a tumor marker in the diagnosis and monitoring of some malignancies (12). Since the 1990s tumor marker including CEA and other have been widely used to monitor oesophagus cancer progression and even to assess the prognosis of oesophagus cancer patients although their specificities have not been satisfactory (13, 14, 15). Therefore, the serum CEA level may be a pertinent index of tumor progression for patients with oesophagus cancer.

In trial of chemotherapy for patients with an oesophagus cancer and who had undergone a noncurative resection, we determined serum CEA levels before and after different cycles of cisplastin based chemotherapy in oesophagus cancer patients. Measurement of CEA in esophageal cancer patients poses a continuing challenge to surgeon. Major predicators of survival are the stage of the tumor at the time of presentation and the extent of the surgical restriction performed [16]. Little emphasis has been given to the value of detection of recurrent disease which has been reliant a crude method such as development of dysphasia or systemic metastases both of which herald the patients' rapid decline. The tumor marker CEA is often elevated in patients with tumor of the gastrointestinal tract [17]. Elevated CEA levels have been used as a marker for recurrent colorectal cancer and prognostic marker for second surgery [18]. CEA has been reported to be beneficial in determining the relapse and the follow up of the response to the chemotherapy or treatment of the patients with gastric and esophageal cancer [19]. , we determined serum CEA levels before and after different cycles of cisplastin based chemotherapy in oesophagus cancer patients.

DOI: 10.18535/ijmsci/v3i7.4

MATERIAL AND METHODS

I. Selection of Patients

For the study total 120 cases of carcinoma of esophagus, 30 each of stage I, Stage II, Stage III and stage IV were selected. All patients were clinically and histological diagnosed. All patients with stage-II, stage-III and stage-IV received chemotherapy including cisplastin, capecitabine, cyclophosphamide, Transtuzumab and doxorubicin. There are 52 males & 68 female of oesophagus cancer. For control total 42 normal healthy age and sex matched persons were selected. Subjects with oesophagus cancer and those without any evidence of any type of cancer participated in this study as listed in table.

II. Collection of samples

5ml blood sample were collected before and after different cycle of chemotherapy in plain bulb from Subharti Medical College, Rama Medical College and Research Centre, Cancer Hospital Delhi, Tata Memorial cancer Hospital Mumbai and Nurgis Dutta Memorial Cancer Hospital Barshi. Serum was separated and used to estimation of Carcinoembryonic antigen (CEA). Serum CEA activity measured by, using commercial kits from accu-bind. On ELISA micro plate Immunoenzymometric assay **(20)**.

III.Treatment

According to the protocol, 63.82% (30 patients out of 47) of the patients completed three cycle of chemotherapy included the cisplastin, 5-FU. All the chemotherapy regimens were used under standard protocol.

The combination of cisplastin (60-100 mg/m^2) and 5-FU (750-1000 mg/m^2) given by continuous infusion for 4-5 days after second stage.

IV. Follow Up

Overall 47 patients were followed up at time of admitted in hospital and after discharge by hospital. Out of 10 patients were lost to follow up. The follow up system consisted of measurement of serum CEA level after chemotherapy countinely 3 months intervals for first 6 month and at 6 month intervals thereafter. The follow up program included, clinical examination, hematological analysis, tumor marker and enzyme assay at each check up. Criteria for the establishment of recurrent disease included histological conformation or disease evident radiological with subsequent clinical progression and supportive biochemical data. The follow up end date was 14th December 2015. All survival patients followed up for at least 27 months. Seven patients died during the follow up period.

Data were expressed as mean ±SD. Mean values were assessed for significance by unpaired student –t test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 21.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.0001$ were considered statistically significant.

TABLE1: Distribution for control and patients

	Number of subjects (male/female)	**Age-range (years)**
Control	42(25/17)	25-60
Oesophagus cancer	120 (52/68)	25-60
Stage I	30(13/17)	25-60
Stage II	30(13/17)	25-60
Stage III	30(13/17)	25-60
Stage IV	30(13/17)	25-60

TABLE 2: Comparison of CEA, activity in control with 0esophagus cancer

Tumor Marker	No. Of cases	Mean ± SD	No. of cases (Value> normal)	'p' Value
CEA Control	42	1.55 ± 0.30		
CEA	47	7.33 ± 1.12	30 (100%)	<0.001

All Values are expressed in IU/L, "P" Value <0.001.

DOI: 10.18535/ijmsci/v3i7.4

RESULTS

As shown in Table 2 mean CEA activity (mean±SD) in control using commercial kits from accu-bind on ELISA micro plate Immunoenzymometric assay was 1.55±0.30. Serum CEA activity of oesophagus cancer patients was 7.33 ± 1.12. CEA level was significantly higher in oesophagus cancer patients than control ($p<0.001$).

Table 3 shown that mean CEA level (mean±SD) in control using commercial kits from accu-bind on ELISA micro plate Immunoenzymometric assay was 1.55±0.30. CEA level in oesophagus cancer patients before chemotherapy (Stage I) was 17.33 ± 1.12. CEA level was significantly higher in oesophagus cancer patients than control ($p<0.001$). After first, Second and third cycle of chemotherapy CEA level was 8.01± 2.64, 2.56±0.23, and 1.44±0.43 respectively. CEA level was significantly decreased after different cycles of chemotherapy than before chemotherapy (<0.001). After first and second cycle of chemotherapy CEA level was significantly increased than control group but after third cycle of chemotherapy CEA level was normal.

Table 3: Comparison of CEA activity in oesophagus cancer patients before (stage I) and after first cycle of chemotherapy (stage II) with control group.

	No. Of Cases	Mean ±SD	p-value
Control	42	1.55 ± 0.30	-
Before Chemotherapy (stage I)	30	17.33 ± 2.44	< 0.001*
After first cycle of Chemotherapy (stage II)	30	8.01±2.64	< 0.001**
After Second cycle of Chemotherapy (stage III)	30	2.56±0.23	<0.001$
After Second cycle of Chemotherapy (stage IV)	30	1.44±0.43	<0.001$$

(All Values are expressed in IU/L) * Control vs Stage-I, ** Stage I vs Stage II, $ Stage II vs Stage III and $$ Stage III vs Stage IV

DISCUSSION

Knowledge of diagnostic and prognostic factors are essential for the management of individual patients and these factors should be taken into account in the design of randomised trials and in interpreting the result of such trials.

Serum tumor markers have been used in aiding the diagnosis of gastrointestinal cancers for a long time. Previous studies reported that the elevated serum values reflect the increased secretion of tumor antigens by tumor itself [21]. However mild elevation of serum tumor marker level in a number of early-stage of cancer has been always difficult to justify as many benign pathologies may frequent because such changes. The clinical use of tumor markers is much more beneficial in determination of prognosis assessing response to treatment and detection of early recurrence [22,23].

Carcinoembryonic antigen (CEA) is used predicting & in monitoring patients with advanced cancer. Tumor markers alone cannot be used to asses response, but could be used to confirm complete response – serum tumor markers have been used in aiding the diagnosis of gastrointestinal cancers for a long time. Previous studies reported that the elevated serum values reflect the increased secretion of tumor antigen of tumor itself. However mild elevation of serum tumor markers level in a number of early stage cancers has always been difficult to justify as many benign pathologies may frequently cause such changes. The clinical use of tumor markers is much more beneficial in determination of prognosis is assessing response to treatment & detection of early recurrences [24].

In the study various tumor markers such as CEA has been investigated in the serum of gastric adenocarcinomas to markers. Llyas Tuncer show the serum CEA level was found to be higher in 70% cases in both cases [25]. CEA is one of the most reliable tumor associated markers used for

DOI: 10.18535/ijmsci/v3i7.4

the detection of malignancy serum CEA level are used for cancer detection determination of cancer stage recurrence ,& evolution of cancer therapy, especially in patients with colorectal cancer. **Gion et. Al [26] ,** reported that CEA was positive in 27% of the patients with oespohagas cancer. In the same study it has been reported that the positivity rate of CEA was correlated with the stage of the disease.

In our study the activity of total CEA in stage I before chemotherapy was significantly higher than control (before esophagus cancer) but after first, second and third cycle of chemotherapy activity of total CEA was significantly decreased.

CONCLUSION

Based on the data from our study, it can be stated that serum CEA measurement in plasma may be useful tumor marker in esophageal cancer, its activity might helpful to predict the response of chemotherapy in advance stage of cancer. An initial increased level of CEA before and first cycle of chemotherapy may not indicate tumor progression, but may be represent a transient tumor marker surge phenomenon after second and third cycle of chemotherapy in patients responding to treatment..

Statistically significant change in tumor marker CEA level during the process of treatment in esophageal cancer patients, with a positive response and no established disease progression during study period, near about 12 months after the treatment, point to CEA as an important predictive factor.

References

1. American cancer society. Cancer facts and figures 2015. Atlanta Ga: American cancer society 2015.
2. A Gallo Charel Cha. Updates on esophageal and gastric worked gastroenterol 2006, 12 (20) 3237-3242.
3. P Ghadirian food habits and oesophagus cancer: an overview. Cancer detects prev. 16, 163-8(1992).
4. Cummings LC, cooper GS. Descriptive epidemiology of oesophageal carcinoma in the Ohio cancer registry. Cancer detects prev 2008; 32: 87-92.
5. Retraction: The candidate tumor suppressor gene ECRG4 inhibits cancer cells migration and invasion in oesophageal carcinoma. J Exp clin cancer Res 2011; 30: 19.
6. Esophageal cancer: epidemiology pathogenesis and prevention. Nat. clin Pract Gastroenternal Hepatal 2008; 5: 517-526.
7. Pennathur A, Gibson MK, Jobe BA, Luketich JD. Oesophageal carcinoma. Lancet 2013; 381: 400-412.
8. Mao WM, Zheng WH, Ling ZQ. Epidemiologic risk factor for oesophageal cancer development. Asian Pae J cancer Prev 2011; 12: 2461-2466.
9. Enzinger PC, Mayer RJ, Esophageal cancer. N Engl J med. 2003; 349: 2241-2252.
10. Lepage C, Rochet B, Jooste V, Faivre J, Coleman MP. Continuing rapid increase in oesophageal adenocarcinoma in England and Wales. Am J Gastroenternal 2008; 103: 2694-2699.
11. Staab HJ, Anderer FA, Brummendorf T, Hornung A, Fisher R. Prognostic value of preoperative serum CEA level compared to clinical staging: II stomach cancer Br J. cancer 1982; 45: 718-727.
12. Ren JQ, Liv JW, Chen ZT, Liu SJ, Huang SJ, Huang A, Hong JS. Prognostic value of the lymph node ratio in stage II colorectal cancer. Chin J cancer 2012; 31: 241-247.
13. Ohkura H. Tumor markers in monitoring response to chemotherapy for patients with gastric cancer. Jpn J clin oncol 1999; 29: 525-526.
14. Yamao T, Kai S, Kazami A, Koizumi K, Handa T, Takemoto N, Maruyama M. tumor marker CEA, CA19-9, and CA125 in monitoring of response to systemic chemotherapy in patients with advanced

DOI: 10.18535/ijmsci/v3i7.4

gastric cancer. Jpn J clin oncol 1999; 29: 550-555.
15. Takahashi Y, Takeuchi T, Sakamoto J, Touge T, Mai M, Ohkura H, Kodaria S, Okajima K, Nakazato H. The usefulness of CEA and CA19-9 in monitoring for recurrence in gastric cancer patients: a prospective clinical study. Gastric cancer 2003; 6: 142-145.
16. Demeester TR, Zaninotto G, Johansson KK. Selective Therapeutic approach to cancer of the lower esophagus and cardia. J Thorac cardiovasc. Surg 1988; 95: 42-54.
17. Gold P, Freedom SO. Demonstration of tumor specific antigen in human colonic carcinoma by immunological tolerance absorption techniques. J Exp Med. 1965; 121: 439-462.
18. Wanebo HJ, Rao B, Pinsky CM. et al. Preparative CEA level as a prognostic indicator in colorectal cancer NEJM. 1978; 299: 448-451.
19. Ial chenko NA, Lagutin VD, Lavik MN, Musin II. The clinica information value of an immunoenzyme study of the tumor markers CA 19-9, CEA and AFP in cancer of the stomach pancreas, colon and rectum. Vopr Onkol 1991; 37: 921-4.
20. Masao Tomita, ahiroyoshi,Ayabe, kaqtsunobu, Kawahara, Yutaka, Tagawa, Akihiro, Nakumura, Nobufumi Sasaki, Takao Takahasmi Estimation of CEA. (Acta med. Nagasaki 38:158-160).
21. Pasane PA, Eskelinen M, Partanen K, Pikkarainen P, Pentilla I, Alhavo E. clinical value of serum tumor marker CEA, CA50, and CA242 in distinction between malignant versus benign disease causing jaundice and cholestasis, results from a prospective study. Anticancer Res 1992; 12: 1689-94.
22. Bann PA, Cohen MI, Widerlite L, Negent JL, Mathews MJ, Minna JD. Simultaneous and plasma immuno reactive CEA in 108 patients undergoing gastroscopy. Gastroenterology 1979;76: 734-41.
23. N.R. Hazari, V.S.Hatalkar. Study of glutathione-s-transferase in gastrointestinal cancer. Int.J of recent trends and technology August 2015; 16(1): 10-12.
24. Carcinoembryonic Antigens of the Human Digestive System. J Exp Med 183:387; 1968.
25. IlyasTuncer, HalukDulger, Ismail Uygan, Mustafa, Cetin, Ramazan, eastern Journal of Medicine:72- 78,9- 2004.
26. Gion M Tremolada C, Mione R, della Palma P, Dittadi R, Zari C, Nosadini A et al Tumor markers in serum of patients with primary squamous cell carcinoma of the esophagus tumor: 489-93,751989

DOI: 10.18535/ijmsci/v3i7.4