Assessment of Carcino-embryonic antigen (CEA) in patients with Colorectal Carcinoma (CRC)

Junaid Mahmood Alam¹, Syed Riaz Mahmood², Mohd Azhar Imam³, Aijaz Ahmed⁴, Sarah Sughra Asghar⁵ and Ishrat Sultana⁶

Abstract:

The CEA molecule is an onco-development human tumor marker and bears the cluster differentiation designation of CD66e. It has a molecular weight of 180 kDa. CEA is one of the significant entities to diagnose and monitor solid tumor and the response to therapy, in GIT cancers, especially CRC. Due to substantial clinical importance of CEA for diagnosis, prognosis and treatment, a study was carried out to assess its levels in patients suspected off or diagnosed with GIT cancers, with special reference to colorectal carcinoma (CRC). A total 86 patients, 70 (81.39%) males and 16 (18.60%) females, were included in the study with age range of 36 to 81 years. Out of 70 males, 23 (32.80%) have malignant conditions and exhibited elevated levels of CEA (66 ng/ml to 230 ng/ml; mean = 189+18 ng/ml), whereas 47 have non-malignant complications with normal or non-significant (> 10 ng/ml but < 20 ng/ml) CEA concentrations. Malignant conditions were determined to be pancreatic (13.04%), gastric (26.08%), colorectal (43.47%) and hepatic (17.39%) cancers. In female group, 10 (62.50%) were diagnosed with malignant condition of pancreatic (10%), gastric (20%) and colorectal (70%) cancers with significantly elevated levels of CEA. At present, serial CEA-monitoring is considered the best non-invasive technique for detecting CRC and its recurrence. It is also substantiated that intensive follow-up CEA assays facilitate the identification of treatable recurrence at an early stage.

Key Words: Carcino-embryonic antigen (CEA), Colorectal carcinoma (CRC), gastric carcinoma, Tumor marker.

Introduction:

The CEA molecule is an onco-development human tumor marker¹-⁶. It bears the cluster differentiation designation of CD66e, a subtype of CD66 group of CEA family. It has a molecular weight of 180 kDa²,⁴,¹³,¹⁴. In a series of studies in early 1960s, a tumor component in colon cancer tissue was found that was not present in the corresponding normal tissues⁵. In subsequent years⁵, same antigen was also noted in all GIT tumors derived from endoderm. Later this antigen is designated as Carcino-embryonic antigen (CEA). After nearly 40 years since the discovery of CEA²,⁵,⁶-¹⁰, until now, this tumor marker became one of the significant entities to diagnose and monitor solid tumor and the response to therapy⁸-¹², in GIT cancers, especially CRC¹⁵. Due to an immense importance of CEA in present day diagnostic and health services, a study was carried out to assess its levels in patients suspected off or diagnosed with GIT cancers, with special reference to colorectal carcinoma (CRC).

Methods and Research Design

Selection Criteria

* The study covered the period of August 2001 to August 2003 and includes patients in the age range of 36-81 years. A brief history of Patients was taken with clinical symptoms and signs and initial diagnosis. Patients admitted in wards or visiting OPDs with diagnosis or suspicions of GIT cancers and/or CRC and additional clinical conditions such as gastritis, colitis etc, were selected and classified according to gender.

* Their sub-groups of malignant and non-malignant status was evaluated and classified according to clinical conditions.

* When confirmed, their cancer status was evaluated and classified according to clinical condition.
Sample Collection:
* Blood (5 ml) was collected in clot activated tubes
* Serum was separated and stored at -10°C until analyzed

Analysis and Calculation:
* All CEA analysis was performed in duplicates by Automated ELISA techniques with two -point calibration and controls with definite cut-off values on Elecsys 1010 (Roche Diagnostics, Basil) automated immuno-analyzer.

* For accuracy purpose, CEA values greater than two folds of 10 ng/ml were considered significant. Normal range is between 2.5-5.0 ng/ml.

* All data were statistically compared with student’s t tests with P < 0.01. Data of patients are also presented in the form of percentage occurrence for clarity.

Results:
The results are summarized in Table I-II and Figures 1-4. Briefly, 86 patients, 70 (81.39%) males and 16 (18.60%) females, were included in the study with age range of 36 to 81 years. Out of 70 males, 23 (32.80%) have malignant conditions and exhibited elevated levels of CEA (66 ng/ml to 230 ng/ml; mean = 189±18 ng/ml), whereas 47 have non-malignant complications with normal or non-significant (> 10 ng/ml but < 20 ng/ml) CEA concentrations. Malignant conditions were determined to be pancreatic (13.04%), gastric (26.08%), colorectal (43.47%) and hepatic (17.39%) cancers.

In female group, 10 (62.50%) were diagnosed with malignant condition of pancreatic (10%), gastric (20%) and colorectal (70%) cancers. Non-malignant conditions were found to be hepatitis, cirrhosis, pancreatitis (acute and obstructive) and gastritis. In present study all malignant conditions, either metastasizing or not, showed significantly elevated levels of CEA. In male-malignant cancer patients’ groups, average CEA values were 92±20 ng/ml, 118±21 ng/ml, 192±16 ng/ml and 76±5 ng/ml for pancreatic, gastric, colorectal and hepatic cancers, respectively. Similarly in females elevated levels of CEA were noted in pancreatic (69 ng/ml), gastric (139±22 ng/ml) and CRC (141±16 ng/ml).

<table>
<thead>
<tr>
<th>Table I: Registry of male patients diagnosed with malignant and non-malignant conditions and assessed for serum CEA concentrations.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Conditions</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Elevated levels</td>
</tr>
<tr>
<td>I) Pancreatic cancer</td>
</tr>
<tr>
<td>II) Gastric cancer</td>
</tr>
<tr>
<td>III) Colorectal cancer</td>
</tr>
<tr>
<td>IV) Hepatic cancer</td>
</tr>
<tr>
<td>Normal levels</td>
</tr>
<tr>
<td>I) Hepatitis</td>
</tr>
<tr>
<td>II) Cirrhosis</td>
</tr>
<tr>
<td>III) Pancreatitis</td>
</tr>
<tr>
<td>IV) Gastritis</td>
</tr>
</tbody>
</table>
Table II: Registry of Female patients diagnosed with malignant and non-malignant conditions and assessed for serum CEA concentrations.

<table>
<thead>
<tr>
<th>Type of Conditions</th>
<th>No of patients [Total n = 16]</th>
<th>%</th>
<th>Age group (Yrs)</th>
<th>Malignant</th>
<th>CEA conc [ng/ml]</th>
<th>A) Disease other than malignancy</th>
<th>B) Non-malignant tumor a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated levels</td>
<td>10 [10/16]</td>
<td>62.50</td>
<td>56-81</td>
<td>---</td>
<td>124 ± 16</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>I) Pancreatic cancer</td>
<td>01 [01/10]</td>
<td>10.00</td>
<td>70</td>
<td>Yes</td>
<td>69.00</td>
<td>----</td>
<td>---</td>
</tr>
<tr>
<td>II) Gastric cancer</td>
<td>02 [02/10]</td>
<td>20.00</td>
<td>51,70</td>
<td>Yes</td>
<td>139 ± 22</td>
<td>----</td>
<td>---</td>
</tr>
<tr>
<td>III) Colorectal cancer</td>
<td>07 [07/10]</td>
<td>70.00</td>
<td>50-81</td>
<td>Yes</td>
<td>141 ± 16</td>
<td>----</td>
<td>---</td>
</tr>
<tr>
<td>Normal levels</td>
<td>06 [06/16]</td>
<td>37.50</td>
<td>36-78</td>
<td>---</td>
<td>4.7 ± 1.6</td>
<td>4.7 ± 1.6</td>
<td></td>
</tr>
<tr>
<td>I) Hepatitis</td>
<td>01 [01/06]</td>
<td>16.66</td>
<td>36</td>
<td>Nil</td>
<td>----</td>
<td>----</td>
<td>A + B</td>
</tr>
<tr>
<td>II) Cirrhosis</td>
<td>---</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>III) Pancreatitis</td>
<td>02 [02/06]</td>
<td>33.33</td>
<td>51,78</td>
<td>Nil</td>
<td>----</td>
<td>----</td>
<td>A</td>
</tr>
<tr>
<td>IV) Gastritis</td>
<td>03 [03/06]</td>
<td>50.00</td>
<td>66,71,76</td>
<td>Nil</td>
<td>----</td>
<td>----</td>
<td>A + B</td>
</tr>
</tbody>
</table>

Fig 1: Percent distribution of malignant conditions in male patients (n=23)

Hepatic cancer 17.39% (n=4)  
Pancreatic cancer 13.04% (n=3)  
Colorectal cancer 43.47% (n=10)  
Gastric cancer 26.08% (n=6)

Fig 2: Percent distribution of malignant conditions in female Patients (n=10)

Colorectal cancer 70% (n=7)  
Pancreatic cancer 10% (n=1)  
Gastric cancer 20% (n=2)

Fig 3: Percent distribution of non-malignant conditions in male Patients (n=47)

Gastritis 55.31% (n=26)  
Hepatitis 10.6% (n=5)  
Cirrhosis 21.27% (n=10)  
Pancreatitis 12.76% (n=6)

Fig 4: Percent distribution of non-malignant conditions in female patients (n = 6)

Gastritis 50% (n=3)  
Hepatitis 16.66% (n=1)  
Pancreatitis 33.33% (n=2)
Discussions:

In present study we have reported assessment of CEA in male and female patients suspected off or diagnosed with GIT cancers, especially CRC. It was observed that, CEA is a significant biochemical marker to evaluate and determine GIT cancers, with considerable specificity in CRC and gastric cancers. Substantial elevated values of CEA were noted in all groups of male and female patients diagnosed with malignant diseases of pancreatic, gastric, CRC and hepatic carcinoma.

Commonly considered cut-off point for CEA is 2.5-5.0 ng/ml for distinguishing normal from abnormal level of serum or plasma. Survey conducted with vast population of healthy persons showed that 85% to 87% had serum CEA level less than 2.5 ng/ml, 95% to 98% less than 5.0 ng/ml and none had level greater than 10.0 ng/ml. Moreover, CEA concentration is often found raised in smokers than in non-smokers. Elaborated efforts have also been made in 1970s and 1980s to review the clinical usefulness of CEA through a larger forum of international scientists and researchers. It is concluded that the diagnostic utility of CEA is established in adenocarcinoma of colon, where 80% or more of patients showed increased level of circulating CEA. However, suggestions were made that CEA assay alone should not be used as the sole diagnostic test. As stated earlier, CEA level, greater than the cut-off value of 5.00 ng/ml but less than 10.00 ng/ml, may also detected in non-malignant conditions, such as liver diseases.

This has also been reported that there is a rise in both frequency of positive CEA assay and the plasma CEA level, with increasing tumor burden. Example is the incidence of positive CEA assay in patients with Dukes stages A (20%), to Dukes stages D (90%) colon cancer. Significant CEA elevation ranging from 18% to 79%, was demonstrated in patients with colon cancer of Dukes stage A, B1, B2, C1 and C2. It is argued that serum CEA assay alone, have not been a useful marker in the screening and diagnosis of colon cancer. However, it plays an important role in the clinical management of patients with colorectal adenocarcinoma. In this respect, the application of monoclonal antibody (mAB) technique targeting CEA have shown promising results due to high sensitivity for diagnosing colon adenocarcinoma. Prognostic utility of CEA in patients with CRC and some other cancers have been thoroughly investigated. Pre-operative serum levels are found to be elevated in 40% to 70% patients with CRC. Pre-operative CEA levels are also found to correlate inversely with tumor grade and directly with pathological grade. Therefore, it is documented that CEA is raised in 95% of patients with well-differentiated tumors, where as only 30% in poorly differentiated adenocarcinoma. Several studies have demonstrated that a significant inverse relationship exist between pre-operative plasma CEA levels and patients’ survival, suggesting poor prognosis. CEA is also an important prognostic marker of breast cancer. In most case studies, the pre-operative CEA levels have been found to correlate with poor prognosis. Moreover, pre and post-operative or treatment levels of CEA may also serve as a good prognostic marker in breast, stomach and lung cancers. In conclusion, currently, treatment monitoring is the most significant area of CEA assay. A post-operative raise in CEA level in patients undergone a treatment regime strongly suggest recurrence of tumor. At present, serial CEA-monitoring is considered the best non-invasive technique for detecting recurrent CRC. Numerous studies substantiated that intensive follow-up CEA assays facilitate the identification of treatable recurrence at an early stage. It is also suggested that when CEA increases more rapidly than an average 12.6% per month, recurrence should be strongly suspected. The studies are in progress in our department to correlate pre and post-operative values of CEA with diagnosis and prognosis of CRC and GIT cancers in general.

References:


25. Arnaud JP, Koehl C, Adloff M. Carcinoembryonic antigen (CEA) in diagnosis and prognosis of colorectal carcinoma. Diseases of the Colon &
Rectum, 1980 23(3): 141-144.


