An Indication of Carcino Embriogenic Antigen in Colorectal Cancer in Iraq


ABSTRACT

Carcino Embrionic Antigen (CEA) is a glycoprotein involved in cell adhesion, which is present in normal mucosal cell. The antigen was present in both fetal and colon adenocarcinoma but that appeared to be absent from healthy adult colon. And is one of the most widely used tumor markers worldwide. This study aims to detect the relationship between (CEA) and colorectal cancer (CRC) in patients of Iraq. Carcinoembryonic antigen was tested by ELISA technique in (79) serum of patients diagnosed with (CRC) aged (7-80 yrs) male & female were collected from a group of Teaching Hospitals in Baghdad /Iraq. And these samples compared with (10) healthy subjects. The results of this study show there was a correlation between patients with adenocarcinoma and healthy group with high significant differences (HS), (P<0.01) (p= 0.001), and non significance between patients genders clear with (p=0.05), (p=0.16) respectively. And non significance differences between others. Conclusion: Our results suggest that Carcino Embriogenic Antigen is an indicator in patients with colorectal cancer, and may play a role with a probability in detection of colorectal carcinogenesis.

INTRODUCTION

Carcinoembryonic antigen (CEA):

Is a glycoprotein involved in cell adhesion, which is present in normal mucosal cells (Thompson et al. 1991) (Perkins et al. 2003). That described by Gold and Freedman in 1965 (Gold & Freedman ).

The antigen was present in both fetal and colon adenocarcinoma but that appeared to be absent from healthy adult colon. However, the serum levels are raised in some types of cancer, which means that it can be used as a tumor marker in clinical tests. (Duffy et al. 1990).

Individuals with colorectal carcinoma often has higher levels of CEA than healthy individuals (above approximately 2.5 ng/mL) (6). CEA measurement is mainly used as a tumor marker to monitor colorectal carcinoma treatment, to identify recurrences after surgical resection, for staging or to localize cancer spread through measurement of biological fluids. (American Association for Clinical Chemistry).

The CEA values are surely increased in approximately half of patients with lymph node disease. Values are elevated in more than eighty percent of patients with distant metastasis (Perkins et al. 2003), probably and also be raised in gastric carcinoma, pancreatic carcinoma, lung carcinoma, breast carcinoma, and medullary thyroid carcinoma, as well as some non-neoplastic conditions like ulcerative colitis, pancreatitis, cirrhosis ( Maestranzi et al.1998) & ( Stanford Cancer Center)

Because CEA can be increased in >75% of patients with distant metastasis it is a potential marker for monitoring response to chemotherapy. Conversely, increases in CEA while receiving chemotherapy generally predict progressive disease ( Begent, 1984; Sugarbaker, 1976).

So as the monitoring of CEA after curative resection of colorectal cancer is to detect recurrent disease at an early and treatable stage (Fletcher, 1986; Berman et al. 2000). As with most tumor markers, both the concentration and proportion of patients with increased values tend to increase with increasing disease stage (Wanebo et al. 1978) . Therefore several studies have shown that well-differentiated colorectal cancers produce more CEA than poorly differentiated specimens (Bhatnagar et al. 1999).
CEA may also provide prognostic data in patients who develop liver metastasis following curative resection for colorectal cancer. The liver is the main site for metastatic disease from colorectal cancer, with more than sixty percent of patients developing metastasis in this organ. Patients who die from colorectal cancer, the liver appears to be the only site of metastatic disease (Wagner et al. 1984).

MATERIAL AND METHOD

For direct antigen ELISA test by HUMAN Gesellschaft Germany for biochmica and diagnostic for the Quantitative determination of CEA in Human. The Human CEA ELISA is intended for professional use as follow procedure leaflet kit:
- Reagents and specimens should be at room temperature before use.
- CAL A-F; in duplicate by adding 25 ML.
- Specimens, controls; in duplicate by adding 25ML.
- Adding of Conjugate 100ML to the calibrators and specimens.
- Rok gently and cover microplate with adhesive strip.
- Incubation for 60 min at 20-25c.
- Washing 3 times by washing buffer by adding 300 ML for the two of specimens and calibrators.
- Adding 100 substrate for the two of specimens and calibrators with no shaking.
- Incubation for 15min at 20-25c.
- Adding 50MLof stop solution with mix.
- Measure the absorbance at 450 nm as soon as possible or withen 30min.

The cut-off for this > 5ng/ml in non smokers and < 10 ng /ml in smokers.

RESULTS AND DISCUSSION:

Carcino embryonic antigen test can detect the amount of this glycoprotein that may appear in the blood of some people who have certain kinds of progressive cancers, especially cancer of the large intestine (CRC). And so as it may be present in these types of cancers like breast cancer (Duffy, 2006) lung cancer and pneumonia (Molina et al. 2008) liver cancer and cirrhosis (Tsukushi et al. 2006), pancreatic cancer (Dragovich et al. 2011), atherosclerosis cancer (Ishizaka et al. 2008).

In order to determine the role of tumor marker CEA in human CRC in the Iraqis population, we investigated the presence of CEA in a cohort of CRC samples male/female (49/30) by using ELISA analysis, with no significant differences in gender studied groups (P > 0.05) P= 0.861 as mentioned in (Table -1) & (fig. –1).

<table>
<thead>
<tr>
<th>CEA (µg/ml)</th>
<th>Patients</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
<th>Minimum</th>
<th>Maximum</th>
<th>t-test (P-value)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>49</td>
<td>10.28</td>
<td>9.11</td>
<td>1.30</td>
<td>4.30</td>
<td>31.60</td>
<td>0.861</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>30</td>
<td>9.91</td>
<td>8.81</td>
<td>1.61</td>
<td>4.40</td>
<td>32.70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

And a correlation with high significant between studied group and healthy (p< 0.01), P= 0.001, as explained by (Table -2).

<table>
<thead>
<tr>
<th>Studied groups</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
<th>Minimum</th>
<th>Maximum</th>
<th>t-test P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health-y control</td>
<td>10</td>
<td>0.43</td>
<td>0.157</td>
<td>0.05</td>
<td>0.13</td>
<td>0.57</td>
<td>0.001</td>
<td>HS</td>
</tr>
<tr>
<td>Patients</td>
<td>79</td>
<td>10.14</td>
<td>8.94</td>
<td>1.006</td>
<td>4.30</td>
<td>32.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>89</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CEA µg/ml</th>
<th>Studied groups</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
<th>Minimum</th>
<th>Maximum</th>
<th>t-test (Pvalue)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy control</td>
<td>10</td>
<td>0.42</td>
<td>0.16</td>
<td>0.049</td>
<td>0.13</td>
<td>0.57</td>
<td>0.003</td>
<td>HS</td>
<td></td>
</tr>
<tr>
<td>Ca. Colon</td>
<td>48</td>
<td>11.26</td>
<td>9.87</td>
<td>1.42</td>
<td>4.30</td>
<td>32.70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ca. Rectum</td>
<td>26</td>
<td>9.14</td>
<td>7.54</td>
<td>1.48</td>
<td>4.40</td>
<td>30.50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ca. polyps</td>
<td>5</td>
<td>4.54</td>
<td>0.43</td>
<td>0.19</td>
<td>4.30</td>
<td>5.30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>89</td>
<td></td>
<td></td>
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</table>
So as a correlation was found between CEA and tumor locations have been represented with high significant in the colon carcinoma, rectum cancer, so as in polyps cancer estimated with (P<0.01), P=0.003 by using (t-test) as in (Table 3). And with no significant among types of CRC so as with healthy explained farther by (LSD test) and (Fig.-2).

Table 4: Distribution of CEA & CRC cancer location by LSD test.

<table>
<thead>
<tr>
<th>Tests</th>
<th>Studied groups</th>
<th>Type of CA</th>
<th>LSD test (P-value)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA (µg/ml)</td>
<td>Healthy control</td>
<td>Ca. Colon</td>
<td>0.00</td>
<td>HS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ca. Rectum</td>
<td>0.007</td>
<td>HS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ca. polyps</td>
<td>0.374</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Ca. Colon</td>
<td>Ca. Rectum</td>
<td>0.302</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ca. polyps</td>
<td>0.092</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Ca. Rectum</td>
<td>Ca. polyps</td>
<td>0.265</td>
<td>NS</td>
</tr>
</tbody>
</table>

Fig. 1: Distribution of CEA IN patients with CRC according to the Gender.

Fig. 2: Distribution of CEA iN patients with CRC according to the location.

Carcinoembrionic antigen which is present in normal mucosal cells but increased amounts are associated with cancers, especially CRC, therefore has a role as a tumor marker. Levels exceeding 10 µg/L are due to malignant disease. Less than 25% of patients with disease confined to the colon have an elevated CEA level. Sensitivity increases with advancing tumour stage. However, poorly differentiated tumors are less likely to produce CEA. The values of CEA are increased in approximately fifty percent of patients with lymph node disease. Values are elevated in 75% of patients with distant metastasis (Perkins et al., 2003).

Levels of CEA are useful in assessing prognosis with other factors, detecting recurrence especially for disease that cannot be evaluated by other means and monitoring treatment in patients with colorectal cancer.

Carcino embryonic antigen is particularly recommended for postoperative follow-up of patients with stage II and III colorectal cancer if further surgery or chemotherapy is an option (Sturgeon, 2009). Colorectal cancer;
when tumors on the right side of the colon tend to produce higher CEA levels than tumors on the left side (Duffy, 2001).

Studies and researches that deal with colorectal tumors suggest that the CEA level equivalent to 2.5 μg/L or less in normal value and in smokers can be in amount. The level of the CEA advised be ordered only after malignancy has been confirmed. The CEA test has a specificity of between 30-80% and it is not recommended by the National Institute for Health and Clinical Excellence (NICE) for the diagnosis of early colorectal cancer (Service NICE 2004). The CEA test is of much more use in determining prognosis than it is as an early diagnostic test for colon cancer (Perkins et al. 2003; Duffy, 2001).

CEA in combination with other tumour markers (eg. mucin tumour markers CA19-9, CA242) can be used in preoperative staging and thereby assist in the planning of the type of surgery required and future management options (Levy et al. 2008). The major role for CEA levels is in following patients for relapse after intended curative treatment of colorectal cancer. CEA levels typically return to normal within four to six weeks after successful surgical resection. The CEA level can also be used to assess the response to chemotherapy. When patients with a normal preoperative CEA level have cancer recurrence, CEA elevation is a sign in nearly one half of them. However, normal levels do not necessarily indicate that recurrence has not occurred (Hara et al. 2008).

REFERENCES


