A Prospective Study on Analysis of Ca15-3 in Breast Cancer Patient as a Prognostic Marker

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Abstract

Objective: To evaluate the role of cancer antigen CA15-3 as prognostic marker in breast cancer patient.

Methods: The prospective study was done from November 2013 to October 2014 at Department of surgery, MGM Medical college and M.Y. Hospital group, Indore. This was a prospective study done on 31 patients with breast cancer. Blood samples were collected from all the patients and from the other patient also. Another samples of blood were collected from all these patients of breast cancer after two to three months to evaluate the rate of disease recurrence after surgery with high level of CA15-3.

Results: Raised value of tumor marker CA15-3 is seen with advanced stage of breast cancer i.e., our data shows mean level of CA15-3 in stage I is 2 U/ml, stage II is 14.92 U/ml, stage III is 34 U/ml and stage IV is 59.6 U/ml. Initial value of CA15-3 significantly predict the response to treatment (i.e. primary/neoadjuvant chemotherapy/surgery). Response to PC with high value of CA15-3 in stage III is 1/5 i.e. 20% & in stage IV is 0/5 i.e 0% and with low value of CA15-3 in stage III is 6/7 i.e.85.7% & in stage IV is 0%. 28 out of 31 patients operated rest 3 cases are inoperable, 24 pt. showed fair response (i.e. no recurrence no progression of disease) and four pt. had disease recurrence after surgery with high level of CA15-3.

Conclusion: As the raised value of CA15-3 is also found in other conditions other than Ca breast, as proven by other study so it could not be used as screening tool but as far as prognosis concern it can used as prognostic marker on serial intervals in advanced stage of breast cancer.

I. Introduction

Breast cancer typically produces no symptoms when the tumor is small and most treatable. Therefore, it is very important for women to follow recommended screening guidelines for detecting breast cancer at an early stage, before symptoms develop. When breast cancer has grown to a size that can be felt, the most common physical sign is a painless lump. Sometimes breast cancer can spread to underarm lymph nodes and cause a lump or swelling, even before the original breast tumor is large enough to be felt. Less common signs and symptoms include breast pain or heaviness; persistent changes to the breast, such as swelling, thickening, or redness of the breast's skin; and nipple abnormalities such as spontaneous discharge (especially if bloody), erosion, inversion, or tenderness. It is important to note that pain (or lack thereof) does not indicate the presence or the absence of breast cancer. Any persistent abnormality in the breast should be evaluated by a physician as soon as possible.

MUC1 (CA 15-3) are the most widely used and investigated in the breast cancer follow-up. Initial studies indicate that CA 15-3 is abnormal in the majority of patients with metastatic breast cancer and that antigen levels are correlated with changes in the clinical status of breast cancer patients1,2. However, CA 15-3 is not recommended as screening tool in early detection for breast cancer, even though it remains an important asset to monitor the efficacy of medical therapies after surgery.

CA 15-3 Tumor marker levels must be used in conjunction with the history, physical examination, and diagnostic imaging. A decrease in marker levels during treatment can indicate tumor response, whereas stable or increasing levels despite adequate treatment can indicate that the tumor is not responding to treatment or that the tumor is recurring.

II. Materials and methods

Ethics Statement: The study including the consent process was approved by the ethics committee of M.G.M. Medical College and M.Y. Group of Hospitals, Indore (M.P.), India. Written informed consent was taken from each subject.

Study Population: The present study consisted of 31 histopathologically confirmed breast cancer patients from Indore region, Patients were enrolled from the outpatient department (OPD) of Dept.Gen.Surgery and Radiotherapy, MGM & MYH, INDORE.

Subject selection criteria and methods: This study included 31 newly diagnosed cases of breast cancer undergoing treatment for ca breasts. Blood samples was collected from all the patients before the treatments and after the treatment at a regular interval of 2 to 3 months to find out level of CA15-3. Data collected will
include patients age, life style, demographical, clinical and pathological investigations. Staging of cancer was documented according to the AJCC-TNM classification system. Relation between Ca breast and CA 15.3 tumor marker level were determined.

**Observations**

**Table 1. CA 15.3 value wise distribution.**

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Value of CA15.3</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>High (&gt; = 30 U/ml)</td>
<td>10</td>
<td>32.25%</td>
</tr>
<tr>
<td>2.</td>
<td>Low (&lt; 30 U/ml)</td>
<td>21</td>
<td>67.74%</td>
</tr>
</tbody>
</table>

**Table 2. Relation of CA 15.3 and staging.**

In this study we also correlate the CA 15.3 with disease (breast cancer) at different stage (TNM -AJCC) and data’s show significant correlation with advance stage of disease.

<table>
<thead>
<tr>
<th>Stage</th>
<th>No.(%) of pt.</th>
<th>CA15.3 U/ml mean</th>
<th>No. (%) of pt. with CA 15.3 &gt;30U/ml</th>
<th>CA15.3U/ml Chemo</th>
<th>PostOp/Post Chemo</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1(3.22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>13(41.93)</td>
<td>14.92</td>
<td>14 (92.3%)</td>
<td>8.69</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>12(38.70)</td>
<td>34</td>
<td>20 (90.4)</td>
<td>48.69</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>5(16.12)</td>
<td>59.6</td>
<td>5 (100)</td>
<td>22.75</td>
<td></td>
</tr>
</tbody>
</table>

**Table3. Relation of CA 15.3 with Response to PC(primary chemotherapy):**

Primary chemotherapy given in stage III and stage IV, so response to PC were observed with the help CA 15.3 level.

<table>
<thead>
<tr>
<th>Sr. no</th>
<th>Stage of breast cancer</th>
<th>No of pts</th>
<th>Value of CA 15.3</th>
<th>Response to PC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Stage III</td>
<td>12</td>
<td>High 5</td>
<td>1(20%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low 7</td>
<td>6(85.71%)</td>
</tr>
<tr>
<td>2</td>
<td>Stage IV</td>
<td>5</td>
<td>High 5</td>
<td>0(0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low 0</td>
<td></td>
</tr>
</tbody>
</table>

**Results**

In our study, data of women with breast cancer showed higher incidence[17/31 i.e.54.83%] (the peak age) between 40 and 50 years age group. Most of the patient diagnosed in stage II (13/31 i.e. 41.93%) & stage III (12/31 i.e.38.70%). On the histological basis, most of breast cancers were Ductal filtrating carcinoma (DIC) 25/31 i.e.80.64%

Raised value of tumor marker CA15.3 were seen with advanced stage of breast cancer i.e. our data shows mean level of CA15.3 in stage I is 2 U/ml, stage II is 14.92 U/ml , stage III is 34 U/ml and stage IV is 59.6 U/ml

Our study showed that initial value of CA 15.3 significantly helpful in predicting response to the treatment (i.e. primary/neoadjuvent chemo therapy, radiotherapy, surgery). Response to primary chemotherapy with high value of CA15.3 in stage III is 1/5 i.e.20% & in stage IV is 0/5 i.e 0% and with low value of CA15.3 in stage III is 6/7 i.e. 85.7% & in stage IV is 0% although it is unusual to find low value of CA 15.3 in stage IV. 28 out of 31 pt. operated rest 3 cases are inoperable, 24 pt. shows fair response(i.e. no recurrence no progression of disease) and four pt. has disease recurrence after surgery with high level of CA15.3

**Discussion**

MUC1 (CA 15-3) are the most widely used and investigated in the breast cancer follow-up. Initial studies indicate that CA 15-3 is abnormal in the majority of patients with metastatic breast cancer and that antigen levels are correlated with changes in the clinical status of breast cancer patients. However, CA 15-3 is not recommended as screening tool in early detection for breast cancer, even though it remains an important asset to monitor the efficacy of medical therapies after surgery. In fact, according to the current literature and our study shows that CA 15-3 is not specific or sensitive enough to detect early breast cancer. Elevation of CA15-3 is not a reliable index in the diagnosis of breast cancer since normal serum levels can also be found in women with breast cancer. However, CA15-3 seems to be a reliable prognostic predictor for monitoring disease progression. As in our study, showed that circulating levels of CA 15-3 can be elevated in patients with cancer and that serial determinations of CA 15-3 may be useful in the post-surgical follow-up of breast cancer patients when specific types of benign disease that may cause increase of this antigen are excluded. The main use of CA 15-3 is to monitor the breast cancer patient response to treatment and for early breast cancer recurrence or metastasis.
If CA 15-3 is initially elevated, may be used to monitor treatment and when repeated on a regular basis, to detect early recurrence; CA 15-3 is not useful when breast cancer is detected early by others examinations. In general, higher levels of CA 15-3 are correlated with a larger tumor burden and a more advanced disease. The serum levels of CA 15-3 increase as cancer develops. In metastatic breast cancer, the highest levels of CA 15-3 are often seen when the cancer has spread to the bones and/or to the liver. In fact, Wojtacki and co-workers demonstrated that increased levels of CA 15-3 in patients without clinical evidence of breast cancer recurrence are a strong indicator of the presence of occult metastatic disease. Therefore, an accurate screening for metastatic disease should be the procedure of choice in breast cancer patients with NED (Not Evidence of Disease) and elevated CA 15-3 levels. Accordingly, an initial elevation of CA 15-3 that does not return to the normal range, is an indicator of lack of response to treatment and represents an adverse prognostic factor. Our study show a significant correlation between CA 15-3 and the response to treatment. In fact, we demonstrated a continuous increase of the marker in patients with metastatic disease that had subsequently developed locoregional relapse by analyzing CA 15-3 serum concentrations in breast cancer patients during follow up. Similar observations were reported by different authors. For example, Geraghty and coll, reported that patients with increased levels of CA 15-3 show a significantly shorter latency in developing metastatic disease compared with normal tumor marker levels (20.8+/−3.3 versus 10.3+/−2.7 months, respectively; P<0.03). Moreover, CA 15-3 values at diagnosis were increased in 88% of 115 patients with metastatic disease.

The evaluation of serum CA 15-3 concentration was involved in 31 patients in this study, the result showed relatively high value of serum CA15-3 levels in stage III, IV and in recurrence cases (or in which the disease has progressed). According to BMC cancer research article ‘CA 15-3 is predictive of response and disease recurrence following treatment in locally advanced breast cancer’11 Fifteen patients (20.5%) developed disease recurrence after surgery during the study period; 5 patients developed loco-regional recurrence and 10 patients developed distant organ metastasis. Six patients of those with disease recurrence had high levels of CA 15-3 before PC (primary chemotherapy/neoadjuvant chemo.) while high post PC levels were found in nine patients.

In this study 4 patients (14.28%) developed disease recurrence after surgery; 2 patients developed loco-regional recurrence and 2 patients developed distant organ metastasis. 4 patients of those with disease recurrence had high levels of CA 15-3 before and after PC.

As per annals of oncology Volume 20/No.5/May2009, doi: 10.1093/annonc/mdp061 Published on 19 March 2009 ‘Value of CA 15-3 determination in the initial management of breast cancer patients’ An initial CA 15-3 concentration of >30 kU/l was associated with a poor prognosis: 75/200 of these patients (37.5%) had metastases at diagnosis versus 46 of the 1836 patients (2.5%) with initial CA 15-3 concentrations <30 kU/l.

In our study initial CA 15.3 conc. of >30U/ml was associated with a poor prognosis: 5/10 of these pt.(50%) had metastases at diagnosis versus 0 of the 21 pt.(0%) with initial CA 15.3 conc. <30U/ml.

In the study of DM O’Hanlon et al12 a total of 500 patients with breast cancer were included; 181 (36.2%) were premenopausal and 319 (63.8%) were post-menopausal. A total of 168 patients presented with stage I disease. 214 with stage II, 56 with stage III and 62 with stage IV disease. At presentation the mean CA 15-3 level increased with advancing stage of disease. The percentage of patients with elevated levels of CA 15-3 also increased significantly with more advanced stage of disease at presentation.

In correlation with above study, we studied total 31 pt. with breast cancer out of which 12(38.70%) were pre-menopausal and 16(51.61%) were post-menopausal. A total of one pt. presented with stage I disease. 13 with stage II, 12 with stage III and 5 with stage IV disease. We also found significant relation between advanced stage of disease and raised level of CA 15.3 i.e. mean value of CA 15.3 in stage 1 is 2U/ml, in stage II is 14.3U/ml, in stage III is 34 U/ml and in stage IV is 59.6. In post-op/post-chemo interval it also shows there is relative fall in CA15.3 level in stage I, II, III but not in stage IV.

V. Conclusion

As the raised value of CA 15.3 is also found in other conditions other than Ca breast, as proven by other study so it could not be used as screening tool but as far as prognosis is concerned it can be used as prognostic marker on serial intervals in advanced stage of breast cancer.
References

[13]. Department of Surgery, 2National Breast Cancer Research Institute and 3Department of Clinical Biochemistry, University College Hospital, Galway, Ireland.