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Effect of Neoadjuvant Chemotherapy in the Management of Locally Advanced Breast Cancer (LABC) In a Tertiary Care Center

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Abstract

Background: Locally advanced breast cancer (LABC) encompass a heterogeneous group of patient that includes those with a neglected slow growing tumour as well as those with aggressive disease. LABC is relatively uncommon presentation in developed world accounting for only 5 to 20%. But in the developing world like India it constitutes about 50% of the cases.

Methods: This study was conducted in the various wards of Department of General Surgery, of Mahatma Gandhi and Mathura Das Mathur hospitals attached to Dr. S. N. Medical College, Jodhpur during the period of January 2019 to October 2019. The women of any age group who attended surgical OPD and presented with a lump in breast were screened for Carcinoma of the breast by subjecting them to FNAC or Trucut biopsy, of the lump. After confirming the diagnosis the patients with locally advanced breast cancer were included in the study group.

Results: The clinical response of 30 patients was observed and recorded. Out of the 30 patients the overall objective clinical response of 63.3% was observed. Complete clinical response of 10% (3 Patients) was noted. Partial clinical response was noted in 16 among 30 patients (53.3%). No response (<50% response) was observed in 8 patient (26.7%). However 3 patients (10%) showed progressive disease. In these 2 patients developed vertebral metastasis.

Conclusion: Patients who did not respond to NACT or who showed disease progression during NACT were predicted to have poor prognosis compared to those who had shown objective response to NACT.

Keywords: Locally advanced breast cancer (LABC), Neo adjuvant chemotherapy (NACT),Response.

Introduction

Breast is an apocrine gland- a modified sweat gland derived from ectoderm, act as secondary sexual organ in females. It is rudimentary in males. It acts as mammary glands in females which produce and secrete milk to feed infants. Breast cancer is a devastating illness both physically and emotionally for tens of thousands of women around the world. Breast

carcinoma is the most common malignant tumour and the leading cause of cancer death in women, with more than one million cases occurring worldwide every year and represents over 20% of all malignancies among females[1].

Locally advanced breast cancer (LABC) encompass a heterogeneous group of patient that includes those with a neglected slow growing tumour as well as those with aggressive disease. LABC is relatively uncommon presentation in developed world accounting for only 5 to 20%. But in the developing world like India it constitutes about 50% of the cases.

Neo adjuvant chemotherapy (NACT) is the primary chemotherapy given to patient prior to surgery or radiotherapy. This has been used for treatment of LABC. With development and testing of increasingly effective agents particularly anthracyclines, dramatic responses had been seen in significant proportion of patients[2,3].

Thus leading to interest in breast conservation treatment in larger tumours and to the use of NACT less advanced operable breast cancer [4,5]

NACT is said to have a number of theoretical and practical advantages in treatment of LABC probably including:-

- Early treatment of Micro-metastasis
- Limiting the rapid growth of metastatic foci after removal of primary tumour
- Decreased emergence of chemo resistant clones
- Extension of BCT to more patients with larger tumours[2-5].

Perhaps greatest potential advantage of the approach is opportunity to observe clinical responses to treatment and to assess the effect by pathological examination of surgical specimen. Further more if clinical/pathological response of primary tumour to NACT correlates with or predicts the response of metastasis and the prognosis of the patient such as overall survival, it could greatly accelerate progress in designing newer treatment[3].

Though NACT in the treatment of LABC had been used in clinical trials for the past two decades in the developing countries, not many studies have been conducted in developing countries like ours, where LABC constitutes about 50% of cases. Hence this study was planned to evaluate the clinical/pathological response to NACT in the treatment of LABC.

Materials and Methods

Source of data: This study was conducted in the various wards of Department of General Surgery, of Mahatma Gandhi and Mathura Das Mathur hospitals attached to Dr. S. N. Medical College, Jodhpur during the period of January 2019 to October 2019.

The women of any age group who attended surgical OPD and presented with a lump in breast were screened for Carcinoma of the breast by subjecting them to FNAC or Trucut biopsy, of the lump. After confirming the diagnosis the patients with locally advanced breast cancer were included in the study group.

Inclusion Criteria

1. All admitted female patients more >14 years diagnosed as having locally advanced breast carcinoma according to AJCC staging and who give consent for the study.
2. Patients with ipsilateral breast tumour of any size with skin fixity were included in the study.

Exclusion Criteria

1. Stage IV breast cancer with distant metastasis.
2. patients with severe co-morbid conditions like Tuberculosis, HIV, Uncontrolled diabetes mellitus, chronic liver disease, coronary artery disease, chronic kidney disease or any other factors which adversely affects the outcome.

By above mentioned inclusion and exclusion criteria 30 [Thirty] patients had been enrolled for the study. All the women enrolled in the study were subjected to the following protocol. They had been explained about the chemotherapy regimen and insisted to attend chemotherapy regime regularly. They had been told about surgical and radiation therapy following the NACT.

Before giving Chemotherapy the size of the tumour and the lymph node were measured manually and using ultra sonogram. In both the methods the greatest perpendicular diameters of the lump were measured and the product obtained as the baseline value for the further follow up[69,70].

The patients were subjected to investigations like: Routine:-

1. Blood Hemoglobin, Total count, Differential count
2. Blood sugar, Blood Urea, serum creatinine
3. Liver function tests.
4. X-ray chest PA view
5. Echocardiogram
6. Ultrasonogram
7. FNAC

Some special ER/PR status and bone scan could not be done due to unavailability of facilities in our institution.

After the investigations the patients were given the Neo Adjuvant Chemotherapy.

Neo Adjuvant Chemotherapy Regimen

NACT is an accepted treatment for locally advanced and early stage breast cancer as it has shown many advantages. It allows *in vivo* determination of an individual tumour's chemo sensitivity, it reduces micro metastatic disease and it can downstage tumours, allowing for breast conserving surgery in previously ineligible patients for conserving surgery. Randomized studies have reported rates of down staging after NAC between 49%-94% and 20%-40% of patients achieve a complete pathologic response. One of the advantages of NACT treatment in breast cancer is to downstage positive axillary nodes to negative.

Four to six cycles of NAC were administered at 3 weekly intervals.

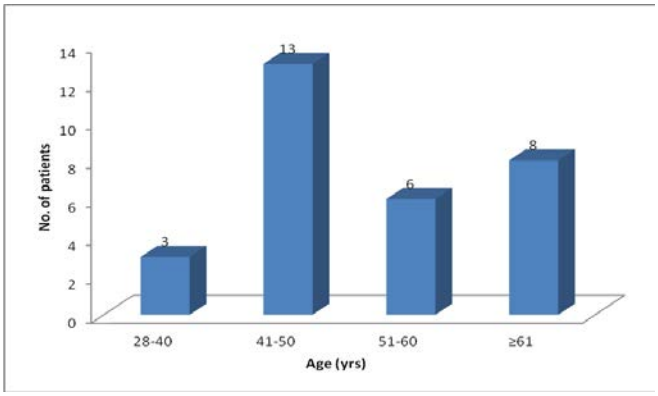
Anthracycline plus taxane-based chemotherapy is the most widely used NACT regimen for all early breast cancer subtypes and is associated with high rates of clinical response (up to 90% in NSABP B-27) [71].

Chemotherapy regimens

- FAC
  - 5 fluorouracil (FU) - 600 mg/m^2 intravenous (iv) day 1
  - Adriamycin - 50 mg/m^2 iv day 1
  - Cyclophosphamide - 600 mg/m^2 iv day 1
- AC → T
  - Adriamycin - 60 mg/m^2 iv day 1
  - Cyclophosphamide - 600 mg/m^2 iv day 1
  - Paclitaxel - 175 mg/m^2 iv day 1
- CMF
  - Cyclophosphamide - 600 mg/m^2 iv day 1
  - Methotrexate - 40 mg/m^2 iv day 1
  - 5 FU - 600 mg/m^2 iv day 1

Patients were subjected to the above mentioned chemotherapy regimen once in 21 days till maximum response was achieved or till response became plateau or if patients were detected to have intolerable toxicity to the drugs given during chemotherapy. Every time before the next cycle of chemotherapy was given, the patient was assessed for response to chemotherapy and toxicity to chemotherapy [72].

Observations and Results



The above fig. summarizes the patient's age distribution. Out of the 30 subjects enrolled, 3 (10%) patients were 28-40 year age group, 13 (43.33%) patients were 41-50 year age group, 6 (20%) patients were 51-60 year age group and 8 patients were aged above 61 years.

Table 1: Stage Wise Distribution

Stage	No. of patients	Percentage
IIIA	16	53.33
IIIB	14	46.67
Total	30	100.00

In the current study, after following the inclusion and exclusion criteria, 30 patients were enrolled, all these patients were having locally advanced breast cancer. Based on the TNM stage grouping, the patients were categorized into 3 groups under stage III. Out of 30 patients 16 patients (53.33%) were categorized under stage IIIA. 14 patients (46.6%) were categorized under stage IIIB, There were no patients under stage IIIC.

Table 2: Clinical Response

Clinical response	No. of patients	Percentage
CCR	3	10.00
CNR	8	26.67
CPR	16	53.33
PD	3	10.00
Total	30	100.00

(CCR-Complete Clinical Response, CNR-Clinical No Response, CPR-Partial Clinical Response, PD-Progressive Disease)

Evaluation of the clinical response of primary tumour and lymph node was one of the primary objective of study. The product of two greatest perpendicular diameter was measured both manually and using ultra sonography before and after every cycle of NACT as defined by criteria.

The clinical response of 30 patients was observed and recorded. Out of the 30 patients the overall objective clinical response of 63.3% was observed. Complete clinical response of 10% (3 Patients) was noted. Partial clinical response was noted in 16 among 30 patients (53.3%). No response (<50% response) was observed in 8 patient (26.7%). However 3 patients (10%) showed progressive disease. In these 2 patients developed vertebral metastasis.

In similar studies conducted by maraz B, Boross G, Cyantiet al an overall objective response of 60%, complete clinical response of 4%, partial clinical response of 56% had been reported. In their study there were no progressive disease observed after NACT [6].

Allassas, choq, Burton et al conducted a study at Lousiana state university health science, the complete clinical response, partial response. Minimal residual disease and no change was reported to be 22%, 33%, 29% and 15% respectively [7].

Table 3: Pathological Response

Pathological response	No. of patients	Percentage
PCR	3	10.00
PINV	27	90.00
Total	30	100.00

(PCR-Pathological Complete Response, PINV-Pathological Non Responders)

In our study was to evaluate the pathological response of the primary tumour and lymph node to preoperative chemotherapy. The pathological response was classified into 2 categories, namely pathological complete response and PINV (invasive cells seen). PCR constituted a group of patients who showed no invasive cells detected. Second group consisted of patients who were termed pathological non responders. (PINV), since their mastectomy specimen showed invasive cells on Histo-pathological examination.

In the present study, 3 patients (10%), showed complete pathological response after NACT. Invasive cells were detected in the mastectomy specimen of 27 patients on HPE (90%).

Conclusion

Patients who did not respond to NACT or who showed disease progression during NACT were predicted to have poor prognosis compared to those who had shown objective response to NACT.

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