Affect of Neo-Adjuvant Chemotherapy in Management of Locally Advanced Breast Carcinoma

Authors
Naveen Konuku, Sahiti Thota, Thatha Rao Vepuri

Abstract

Background: Introduction of neoadjuvant chemotherapy (NACT) has dramatically changed the management of locally advanced breast cancer (LABC). The neo-adjuvant chemotherapy (NACT) has become the initial standard treatment of locally advanced breast carcinoma cases followed by surgery, adjuvant chemotherapy, radiotherapy with or without hormonal therapy. Historically these cases with clinically locally advanced breast carcinoma were treated with radical surgery and/or radiation therapy (RT). However the management of LABC has dramatically transformed over past two decades [Bangladesh journal references 1-4]. Primary chemotherapy (CT) became an integral part of the multidisciplinary management of LABC, probably prolonging the disease free survival and overall survival and making breast conserving, less radical surgeries a possibility for these patients.[Bangladesh journal]

Materials and Methods: All female patients with FNAC or core needle biopsy proven breast carcinoma attending general surgery department and specialty breast clinic at NRI general hospital, chinakakani, Guntur during two years of study.

Sample size of 30 / study period two years.

Results: Assessment of the clinical response was based on RECIST criteria with complete response in (CR) 4 cases (13.33%) partial response in (PR) 25 no (83.32%); minimal response or stable disease in (MR) 1 (3.33%); progressive disease in (PD) zero cases. Complete clinical response by clearance of axillary nodes is seen in 11(64.70%) of cases. No or partial response was seen in 6(35.29%). Assessment of the pathological response from the final surgical specimen showed

Complete response pCR 3 (9.99%)
Partial Response pPR 25(83.32%)
Stable diseases SD 2(6.66%)
Progressive diseases pPd 0 (0%)

Conclusion: Neoadjuvant chemotherapy is a reasonable alternative to upfront surgery in the management of LABC. Clinicopathological variables such as nodal status, response to chemotherapy, pathological tumor size and presence of ECE had significant impact on disease free survival.

Keywords: LABC, NACT, operability.

Introduction
Locally advanced breast cancer (LABC) is defined by presence of a large primary tumor (>5 cm or T3), associated with or without skin or chest-wall involvement (T4) or with fixed (matted) axillary lymph nodes or with disease spread to ipsilateral internal mammary or supraclavicular nodes in the absence of any evidence of distant metastases.\[6\]
LABC accounts for 10-20% in the West,\textsuperscript{[6]} while in India, it accounts for 30-35% of all cases. LABC encompasses a wide spectrum of malignant breast tumors with varying presentation and poses a significant therapeutic challenge. The treatment of LABC has changed dramatically over last few decades. The introduction of neoadjuvant chemotherapy (NACT) in LABC offered us advantages like initiation of early systemic therapy, delivery of drugs through intact vasculature, down-staging of tumors, which makes inoperable tumors operable and renders tumors suitable for breast conserving surgery (BCS).\textsuperscript{[7,8]} It also helps \textit{in vivo} assessment of response. National Surgical Adjuvant Breast and Bowel Project (NSABP) - 18 and Milan trials have shown that there were no difference in disease free survival (DFS) and overall survival between the patients who had received NACT when compared to the patients who had received postoperative adjuvant chemotherapy.\textsuperscript{[8]} This has led NACT to gain a major foothold in the management of LABC.

Materials and Methods
All female patients with FNAC or core needle biopsy proven breast carcinoma attending general surgery department and specialty breast clinic at NRI general hospital, chinakakani, Guntur during two years of study. Sample size of 30 / study period two years.

Results
Majority of the patients were postmenopausal (56.66%). Most of the patients study were in the age group of 50-65 years (46.66 %). Tumor stage was T3 in 63.33% patients. Clinically palpable ipsilateral axillary lymph nodes were present in 56.66% patients.

Clinical Response to NACT: (n=30)
Assessment of the clinical response was based on RECIST criteria with complete response in (CR) 4 cases (13.33%) partial response in (PR) 25 no (83.32%); minimal response or stable disease in (MR) 1 (3.33%); progressive disease in (PD) zero cases.

| RESPONSE     | No. of PTS | Percentage |
|--------------|------------|------------|
| COMPLETE     | 4          | 13.33%     |
| PARTIAL      | 25         | 83.32%     |
| STABLE       | 1          | 3.33%      |
| PROGRESSIVE  | 0          | 0%         |

Clinical Response of Axillary Nodes to NACT: (n=17)
Complete clinical response by clearance of axillary nodes is seen in 11(64.70%) of cases. No or partial response was seen in 6(35.29%).

| CLEARANCE     | No. of PTS | Percentage |
|---------------|------------|------------|
| COMPLETE      | 11         | 64.70%     |
| NO OR PARTIAL | 6          | 35.29%     |

Pathological Response to NACT: (n=30)
Assessment of the pathological response from the final surgical specimen showed
Complete response pCR 3 (9.99%)
Partial Response pPR 25(83.32%)
Stable diseases SD 2(6.66%)
Progressive diseases pPd 0 (0%)

| PATHOLOGICAL RESPONSE | No. of PTS | Percentage |
|-----------------------|------------|------------|
| COMPLETE              | 3          | 9.99%      |
| PARTIAL               | 25         | 83.32%     |
| STABLE                | 2          | 6.66%      |
| PROGRESSIVE           | 0          | 0%         |

Applying Student t test for the Measurements of Tumour

| SEX/SEX SIZE IN CMS | MEAN | T-VALUE | P-VALUE |
|---------------------|------|---------|---------|
| PRE-CHEMOTHERAPY    | 6.65±2.2 | 6.33 | <0.00001 |
| POST CHEMOTHERAPY   | 2.89±1.9  |      |         |

Surgery
All 30 patients underwent MRM with level I and level II lymph nodal dissection. And were followed for an average of 10 months.

Discussion
In the present study the initial systemic treatment in the form of neo-adjuvant chemotherapy in locally advanced breast carcinoma patients successfully down staged the tumour in majority
of cases with significant down staging seen in 80% of cases studied and at the molecular level in the cases with complete clinical response\(^4\), complete pathological response with no residual disease burden was achieved in 75%\(^3\) cases. This response to NACT provides scope for extending breast conserving surgeries to the cases with clinically favourable characteristics couples with postoperative radiotherapy and regular follow up.

In the present study these cases with good response clinically were treated surgically by Auchincloss modified radical mastectomy but the study provides the proof and scope for conservative surgeries can be substantiated.

**Conclusion**

Neoadjuvant chemotherapy is a reasonable alternative to upfront surgery in the management of LABC. Clinicopathological variables such as nodal status, response to chemotherapy, pathological tumor size and presence of ECE had significant impact on disease free survival

**References**

1. Rahman MS, Akhter PS, Hasanuzzaman M, Rahman J, Bhattacharjee A, Rassell M et al. Dhaka; Outcome of neoadjuvant chemotherapy in locally advanced breast cancer: A tertiary care center experience. Bangladesh Med J. 2016 Sept; 45(3);
2. Hortobagyi GN, Blumenschein GR, Spanos W. Multimodal treatment of locoregionally advanced breast cancer. 1983; 51: 763-8.
3. Davila E, Vogel CL. Management of locally advanced breast cancer (Stage III); a review. Int Adv Surg Oncol. 1984; 7 : 297-327.
4. Hortobagyi GN, Ames FC, Buzdar AU. Management of stage III primary chemotherapy, surgery and radiation therapy. Cancer. 1988; 62: 2507-16.
5. Hortobagyi GN, Buzdar AU. Localized advanced breast cancer: A review including the MD Anderson experience. In: Ragaz J , Ariel IM, editors. High risk breast cancer therapy. Berlin: Springer-Verlag; 1991.pp. 416-23.
6. Valero VV, Buzdar AU, Hortobagyi GN. Locally Advanced Breast Cancer. Oncologist. 1996;1:8–17. [PubMed]
7. Fisher B, Brown A, Mamounas EL. Effect of preoperative chemotherapy on loco-regional disease in women with operable breast cancer: Findings from national surgical adjuvant breast and bowel project B-18. J Clin Oncol. 1997;15:2483–93. [PubMed]
8. Fisher ER, Wang J, Bryant J, Fisher B, Mamounas E, Wolmark N. Pathobiology of preoperative chemotherapy: Findings from the national surgical adjuvant breast and bowel (NSABP) protocol B-18. Cancer. 2002;95:681–95. [PubMed].