



ROLE AND OUTCOME OF NEO ADJUVANT CHEMOTHERAPY ADMINISTERED IN LOCALLY ADVANCED BREAST CANCER (LABC)

General Surgery

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ABSTRACT

Neo adjuvant Chemotherapy has changed the way in which locally advanced carcinoma breast is managed. An objective response to neo adjuvant chemotherapy in primary lesion provide important in vitro evidence that this therapy being used has antitumor activity. Tumor at remote sites will be sensitive as well. Various chemotherapy combinations have been described in literature. LABC refers to a diverse and heterogeneous group of people with breast cancer which represents one of the commonest malignancy of female population in our region. Patients with this cancer include those with operability at presentation, and inoperability at presentation. Which include stage IIb, IIIa and IIIb. This study shows that the NACT with FAC regimen effects dramatic regression of the Breast lesion in apparently 70% to 80%. The index lesion and axillary metastasis have disappeared following the 3 cycles of FAC regimen. The study also shows that the tumor shrinkage and disappearance increased the sense of well being among of the patients, their confidence level enhanced: After the NACT Technical operability of the tumor has improved. What seemed: Inoperable become Amenable to modified radical mastectomy in 60 to 70% of patients. Out of sixty patients who had completed the 3 cycles of Neo adjuvant chemotherapy. Six patients (10%) who had complete response underwent modified radical mastectomy. The other forty one patients (68.33%) also underwent modified radical mastectomy totally accounting for 78.33% and remaining 13 patients (21.6%) underwent Toilet mastectomy. Neo adjuvant chemotherapy for locally advanced Breast cancer definitely paves the way for successful surgery in most cases, thereby making patients free from agonizing symptoms, giving satisfactory quality of life without much burden to the individual, family & society.

KEYWORDS

Neoadjuvant chemotherapy , carcinoma breast, mastectomy, surgery ,

1. INTRODUCTION

LABC refers to a diverse and heterogeneous group of people with breast cancer which represents one of the commonest malignancy of female population in our region. Patients with this cancer include those with operability at presentation, and inoperability at presentation. Which include stage IIb, IIIa and IIIb. This study also included supra clavicular node in the locally advanced breast cancers. Over the past few decades, the management of the LABC has considerably evolved from radical mastectomy alone to multidisciplinary modalities involving surgery, chemotherapy and radiotherapy (RT), with the advent of Neo adjuvant Chemotherapy many of the previously inoperable tumours have become amenable to surgery. Preoperative administration of hormonal therapy or systemic chemotherapy can result in considerable fall in tumour size in 50% to 80% of the LABC. Patients living with LABC have poor prognosis when treated with surgery or RT. They include Stage IIb, III A and III B. carcinoma breast according to the American Joint Committee on Cancer (AJCC). As a consequence of these poor outcome neo adjuvant chemotherapy has been introduced. This approach is designed to render patients operable, and to eradicate micro metastases at an early stage, when they are still sensitive to chemotherapy several studies have been performed. In General only 3-4 cycles of conventional dose Neo adjuvant Chemotherapy given prior to surgery. Hekmen et al showed that clinical response rate to Neo adjuvant chemotherapy varies between 80% and 90% and 10-35% of clinical remissions. The Neo adjuvant chemotherapy (NACT) enhanced the quality of life of LABC patients. Reduced the morbidity and improved the overall survival rate and disease free interval.

2. AIM AND OBJECTIVES

To determine the role and outcome of Neo adjuvant chemotherapy administered in Locally Advanced Breast Cancer (LABC) and to determine and study what extent the inoperable LABC become amenable to surgery.

3. MATERIALS AND METHODS

The study was done in the department of Surgery Thanjavur Medical college and Hospital Thanjavur. All the patients with Breast cancer was examined clinically. Patients with LABC was selected for the study. Locally advanced carcinoma breast was defined as per AJCC staging and included stage IIb ($T_3 N_0 M_0$) Stage III A and stage III b tumours. Exclusion criteria included any contraindications for chemotherapy.

INCLUSION CRITERIA

- Stage IIb ($T_3 N_0 M_0$)
- Stage IIIa
- Stage IIIb
- LABC without any co-morbid conditions

EXCLUSION CRITERIA

- All early Breast Recurrence
- LABC with Distant metastasis
- LABC with co morbid conditions
- Any contra indications for surgery

INVESTIGATIONS

- Complete Haemogram
- Renal Function Tests
- Liver Function Tests
- FNAC
- X-Ray Chest
- ECG
- Ultrasonogram Abdomen
- Echocardiogram

FNAC was done to confirm the diagnosis, in all patients. Routine investigations like complete hemogram, renal function tests, and liver function tests were done. Metastatic work up was done, X-Ray chest and ultrasonogram abdomen. Cardiac assessment was done with echocardiogram for adriamycin based chemotherapy.

Detailed history and clinical examination of the patients were carried out as per the proforma. Tumor size assessed clinically two longest perpendicular diameter and the products of the two perpendicular diameters were calculated. Patient taken CT scan breast before starting Neo adjuvant chemotherapy. After completion of 1st cycle and before starting a next cycle C.T. breast taken to measure the Breast size. After completion of 3 cycles at the end of 3rd week, tumor size measured clinically and C.T. Breast taken regularly. Chemotherapy was administered after admitting the patients after calculating body surface area. Antiemetic pre medications which included ondansetron. 4 mg, Injection dexamethasone 8 mg. and ranitidine 150mg./sq.m. Intravenous infusions of cyclophosphamide 600mg/m² 5 fluorouracil 500mg/m², adriamycin 60mg/m². were given as per FAC regimen. Patients were observed for side effects and discharged on same day with oral ondansetron prescription for 3 days. Chemotherapy was repeated every 21 days after assessing the tumor response clinically for maximum of three cycles. After two weeks of the last preoperative cycle, tumour size was assessed clinically and with a repeat C.T Breast.

RECIST criteria was used to assess the tumor response clinically. Patients with partial response were worked up for modified radical mastectomy. The mastectomy specimens were assessed in patients who showed complete clinical response. All specimen showed tumor free margins. Patients who had complete clinical response according to WHO / RECIST criteria were managed with modified radical mastectomy. Patients who showed no response according to WHO / RECIST criteria were managed with Toilet mastectomy followed with adjuvant chemotherapy and Radiotherapy

4.RESULTS

Seventy two patients who qualified for the inclusion criteria were included in the study. Three patients were excluded as the pre chemotherapy. X-Ray revealed lung metastasis. Four patients lost follow up. Five patients defaulted after 3 cycles of chemotherapy. Hence 9 patients out of 69 did not complete the treatment. 60 patients who were included in the study completed the treatment. Clinical parameters of 72 patients were analysed. The range of patients age was 32 to 72 years and mean age at appearance was 55.45 years. 6.9% patients were in the age group of < 40 years. 16.6% patients fell in the age group of 40-49 years & 50% fell in the age group of 50 to 59 years. 26.5% were above 60 years. Fifty two patients in the study group were post menopausal and 20 patients were pre menopausal. There was a predominance of left sided Breast cancer. Thirty nine (54.2%) patients had cancer of the left Breast where as thirty three patients had right sided Breast cancer (45.8%). Thirty five patients (48.9%) had upper outer quadrant of the Breast. Six patients (13.93%) had tumour in the central quadrant. Thirty four patients (47.22%) had T3 tumor at presentation whereas 38 patients (52.78%) had T4 presentation. Seven (9.72%) patients had stage IIB disease. Whereas 27 patients (37.5%) and III-a, Thirty eight (52.78) patients had III b. The mean size of the tumor in its longest diameter was 7.04 cms. Alopecia and vomiting were the commonest side effects noted in the study. All the patients developed Alopecia of varying intensity. 50 patients had Black discoloration of nails, palms. Five patients developed anemia that was managed with Hematinics and transfusion. 65 patients were finally assessed for study of NACT in locally assessed Breast cancer. Out of sixty five, six patients (9.24%) had complete response. Thirty six patients (55.38%) patients had partial response and 23 patients (35.36) had no response according to RECIST criteria

Table-1 Distribution Of Patients According To TNM

TNM Classification	No. of Cases	Percentage (%)
T ₃ N ₀ M ₀	7	9.72
T ₃ N ₁ M ₀	23	31.94
T ₃ N ₂ M ₀	4	5.55
T _{4b} N ₀ M ₀	5	6.94
T _{4b} N ₁ M ₀	25	34.75
T _{4b} N ₂ M ₀	5	6.94
T _{4b} N ₂ M ₁	3	4.16
Total	72	100

Table-2 Response Rate Of Nact According The Recist Criteria

Response	No. of Cases	Percentage (%)
Complete	6	9.24
Partial	36	55.38
No Response	23	35.38
Total	65	100

Table-3 Type Of Surgery Done

Surgeries	No. of Cases	Percentage (%)
Modified Radical Mastectomy	47	78.33
Toilet Mastectomy	13	21.67
Total	60	100

Table-4 Distribution Of Patients According To Size Of Tumour

Mean size of Tumour for

Complete Response	:	5.53
Partial Response	:	6.33
No Response	:	8.83

Mean	:	Before NACT	After NACT
		7.04	3.54

5.DISCUSSION & CONCLUSION

Over the last decades Neo adjuvant Chemotherapy has changed the way in which locally advanced carcinoma breast is managed. An

objective response to neo adjuvant chemotherapy in primary lesion provide important in vitro evidence that this therapy being used has antitumor activity. Tumor at remote sites will be sensitive as well. Various chemotherapy combinations have been described in literature. Over all, clinical response rates vary in different studies between 60% to 90% one most commonly used combination is 5-fluorouracil, adriamycin, cyclophosphamide. In 1978, Bull et al showed a response rate of 82% to FAC regimen when compared with 62% response rate of 5-fluorouracil, methotrexate, cyclophosphamide. In a study of 372 patients who received NACT with 4 cycles of FAC regimen Kuerer showed a complete response in 12%. Boti et al in fifty six patients showed an overall outcome of 82%.

The response rate in European organization for research and treatment of cancer breast cooperative group trial (EORTC) in 1991 using 4 cycles of pre-operative 5 – fluorouracil, epirubicin, cyclophosphamide was only 49%. The recent introduction of chemotherapy regimens using docetaxel have been shown to have significant better response rates. Expecting same line of better results we have followed F.A.C. regimen in our study in TMCH, Thanjavur.

Seventy two patients with LABC breast were included in the study. Three patients have metastasis in the X-Ray chest. Four patients lost follow up. Five patients did not undergo mastectomy. Finally sixty patients completed the treatment protocol. The reasons for this drop out could be the need for multiple hospital visits and side effects of the chemotherapy. Even in western studies like NSABP B – 27 only 80% of the total patients inducted in the study had completed the treatment. The mean age at presentation to hospital 55.45 years with majority in 50-59 years. The mean longest diameter of tumor at presentation in this study was 7.04 and after NACT was 3.54. All patients with LABC received three cycles of FAC regime with cyclophosphamide 600mg/m², 5FU 500mg/m², adriamycin 60mg/m² at intervals of 21 days. In a study on preoperative chemotherapy conducted in patients with operable breast cancer, a response rate of 80% and complete pathologic response in 13% was seen.

After completion of three cycles of NACT the tumor size grave signs like oedema and ulceration decreased in 78% of cases fixity became less. Patients with clinically negative axilla had a significantly better chance of having complete response. Than that in patientst with clinically positive axilla. Out of 48 patients who were node positive 20 patients became clinically negative after completion of 3 cycles of chemotherapy. In the remaining 28 patients size of the node and their number has decreased. Among the specimen of 28 patients, 10 were less than 2 node positive for tumor. 18 were positive for more than 4 nodes. Node positive patients were treated with adjuvant chemotherapy and radiotherapy. Tumors without skin involvement showed a significantly better response to chemotherapy assessed by W.H.O. criteria. The better response shown by tumors with smaller size clinically node negative and no skin involvement suggest that tumor cells may become more resistant as the tumor grows. This is in concordance with the Goldie – cold man Hypothesis that the likelihood that resistant cells are present is a function of tumor size (or) the number of tumor cells and the spontaneous mutation rate of the cells. Histologically all the tumours turned out to be infiltrating ductal carcinoma. This study shows that the NACT with FAC regimen effects dramatic regression of the Breast lesion in apparently 70% to 80%. The index lesion and axillary metastasis have disappeared following the 3 cycles of FAC regimen. The study also shows that the tumor shrinkage and disappearance increased the sense of well being among of the patients, their confidence level enhanced: After the NACT Technical operability of the tumor has improved What seemed:- Inoperable become Amenable to modified radical mastectomy in 60 to 70% of patients. Out of sixty patients who had completed the 3 cycles of Neo adjuvant chemotherapy. Six patients (10%) who had complete response underwent modified radical mastectomy. The other forty one patients (68.33%) also underwent modified radical mastectomy totally accounting for 78.33% and remaining 13 patients (21.6%) underwent Toilet mastectomy.

After establishing the loco regional control by above surgeries, these patients were followed up by adjuvant chemotherapy and adjuvant radiotherapy. The Neo adjuvant chemotherapy for LABC with FAC regimens most of the Inoperable advanced Breast cancer became Technically operable.

Appropriated surgery done with or without post operative events in

78% of patients became symptom free, and their quality of life improved. Survival period is prolonged and their disease free survival also improved. 68.3% patients who partially responded after Neo adjuvant chemotherapy were managed by M.R.M. 10% patients who responded completely also managed with modified radical mastectomy. 21.6% patients who are non responders clinically after Neo – adjuvant chemotherapy are treated with Toilet mastectomy. In a nut shell neo adjuvant chemotherapy for locally advanced Breast cancer definitely paves the way for successful surgery in most cases, there by making patients free from agonizing symptoms, giving satisfactory quality of life without much burden to the individual, family & society.

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