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Original Research Article

A Prospective Observational Study of Response to Neoadjuvant Chemotherapy in Locally Advanced Breast Cancer in Tertiary Centre

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Abstract

Introduction: Carcinoma of the breast from the very beginning has been a feared disease.' Till today, there is an aura of fear that surrounds the mention of this name 'breast cancer'. Neoadjuvant chemotherapy (NAC) is increasingly used to treat patients with locally advanced breast cancer (LABC). Such regimens can increase rates of breast-conservingtherapy (BCT) compared with post-operative chemotherapy and may minimize the need foraggressive nodal surgery with axillary lymph node dissection.

Aims: To assess the change of clinical staging after Neoadjuvant Chemotherapy, Assessment of Lymph node status after neoadjuvant Chemotherapy and type of surgery suitable after neoadjuvant Chemotherapy.

Materials and Method: The present study was a hospital based observational study. The study conducted in Nil Ratan Sircar Medical College & Hospital. The study duration was One year (June 2021 to May 2022). 50 patients were included in this study.

Result: In our study, all patients [50 (100.0%)] had Lymph node involvement. We showed that, most of the patients had Stage IIIA [25 (50.0%)]. However, Stage IIIB [15 (32.0%)] followed by Stage IIIC [10 (20.0%)] which was statistically significant (p=.00168). It was found that, all patients [50 (100.0%)] had Anterior Chemotherapy. Our study showed that, most of the patients had Stage IIB after chemotherapy [22 (44.0%)] and it was statistically not significant (p< .14706) (z=1.4499). Inour study, higher number of patients had Down stage Result [35 (70.0%)] followed by SameResult [15 (30.0%)] but this was statistically significant (p=.00006) (z=4). We showed that,the mean Tumor size of patients was [7.2880± 1.4822 (cm)] and mean % of size reduction ofpatients was [58.0000± 15.0509].

Conclusion: We conclude that, the change of clinical staging after Neoadjuvant Chemotherapy, Lymph node status after neoadjuvant Chemotherapy.

Keywords: Neoadjuvant chemotherapy (NAC), Lymph node status and Breast Cancer.

Introduction

Carcinoma of the breast from the very beginning has been a feared disease. Till today, thereis an aura of fear that surrounds the mention of this name 'breast cancer'. Medical research and efforts by various groups and individuals has given number of modalities of treatment of breast cancer, each of which are incomplete in themselves, and have to be supplemented byanother.

Among all modalities of treatment, surgery has come to be accepted as the 'golden standard', to which all other modalities of treatment have to be compared. Halsted's radical mastectomy has been accepted as the main factor for comparison of results of anyform of treatment, thatis, the results of treatment of breast cancer by any modality or a combination of modalities have to be compared to results obtained by lasted with his radical mastectomy.

Other modalities of treatment such as chemotherapy and radiotherapy are considered as adjuvant to surgery and are incomplete by themselves. Chemotherapy in the treatment of breast cancer has assumed a greater significance ever since researchers have given breast cancer the status of a systemic disease. Surgery as such can eradicate only the local disease, and eradication of the systemic component involves the use of chemotherapeutic agents.

Chemotherapy may be given as an adjuvant postoperatively, or as neo-adjuvant chemotherapy where two to three doses are given prior to surgery, followed by the remaining cycles post-operatively. Occasionally in very advanced cases, chemotherapy alone may be given as a palliative measure, when any form of surgery is likely to result in extensive deformity that will compromise on quality of life without a significant increase in life span. With the suggestion that the behaviour of a breast cancer is often the expression of systemic disease present at the time of diagnosis, surgical management of local disease has become more conservative.

This dissertation deals with the administration of Neo-adjuvant chemotherapy in patients who have been worked up for surgery. All patients were given four cycles of a chemotherapeutic regimen as per recommended doses, and the effect was studied three weeks after the 4th cycle, just prior to surgery. However, the long term follow up of patients and a formal comparison of the 5 - year survival rates and recurrence/metastasis between Neo-adjuvant and routine post-operative chemotherapy was out of the scope of this dissertation.

Neoadjuvant chemotherapy (NAC) is increasingly used to treat patients with locally advanced breast cancer (LABC) [1-3]. Such regimens can increase rates of breast-conservingtherapy (BCT) compared with post-operative chemotherapy [2] and may minimize the need foraggressive nodal surgery with axillary lymph node dissection [4,5]. Other purported advantagesinclude in vivo tumour response assessment and prognostication based on degree of response. Patients with HER2-receptor positive or triple-negative disease may also benefit from early treatment of distant micrometastases due to increased metastatic potential of these disease types [6,7]. Despite these potential advantages, NAC has not demonstrated improved survival over adjuvant chemotherapy in randomized trials.

The NSABP B-18 and B-27 trials delivered anthracycline-based NAC (and included taxanes in B-27). Patients who underwent breast conserving surgery (BCS) after NAC received whole breast radiation therapy (RT) alone, while mastectomy patients did

not receive RT. These trials demonstrated locoregional recurrence rates of 12.3% for mastectomy patients and 10.3% for BCS patients [8]; overall survival (OS) rates were 75% at 8 years [6]. Subsequent retrospective studies [9,10] have suggested that adjuvant RT decreases the rate of locoregional recurrence (LRR) and improves survival after NAC and surgery, but this has not been evaluated with randomized trials. Given the absence of level I evidence, routine practice at their centre is to offer radiation therapy after NAC and surgery.

Materials and Methods

Study Area: Department of General Surgery, Nil Ratan Sircar Medical College &Hospital.

Study Population: Patient diagnosed as a case of Carcinoma breast by FNAC/Trucut biopsy.

Study Period: January 2021 to June 2022.

Sample Size: 50(All cases admitted with Locally advanced Carcinoma breast(from I" January 2021 to 31" December 2021 was included in this study. In 2020 a total number of 46 cases were admitted with Locally advanced Carcinoma breast IN General surgery depertment. So, 1 have taken a sample size of 50).

Study Design: Prospective Observational Study.

Material and Method

This dissertation involved the study of 50 patients with locally advanced breast cancer who were admitted at Nil Ratan Sircar Medical College, Dept of surgery.

This is a Prospective Observational study from 1st January 2021 to 31st December 2021 will be included in this study. All patients admitted with breast cancer underwent a detailed assessment. Clinical staging of the disease was done (TNM Staging). (AJCC 8th Edition) Those patients who fall in locally advanced breast carcinoma were considered for study and received 4 cycles Neoadjuvant chemotherapy (AC regimen). Confirmation of diagnosis was done by FNAC/core cut Biopsy of breast lump. Accurate measurement of breast lump was done in each patient, compared before and after neo adjuvant chemotherapy clinically & with Vernier callipers and number and fixity of affected lymph nodes was also recorded before and after chemotherapy. Each patient received 4 cycles of chemotherapy consisting of Cyclophosphamide and Adriamycin, doses calculated according to body surface area, with three weeks interval between each cycle. Patients were evaluated 3 weeks after 4 cycle of chemotherapy. Clinical staging repeated and all factors such as tumour size, lymph node status.& staging after chemotherapy. The data thus collected was then analysed, significance determined and the literature available on the topic was reviewed.

Study Area: Selected from outdoor of Department of General Surgery, diagnosed aslocally advanced carcinoma breast.

Inclusion Criteria: Female breast Cancer Stage IIB(except T2N1M0)- Stage III

Exclusion Criteria:

1. Benign breast lump
2. Male breast carcinoma
3. Female<I8years
4. Metastatic breast carcinoma
5. Patients under other clinical trials
6. Associated co-morbidities that may prevent proper chemotherapy
7. Patients not willing to undergo this study.

Discussion

A Prospective Study was conducted in Department of General Surgery, NRSMC&H. The study period was from

January 2021 to June 2022. 50 patients were included in this study.

Choudhary P *et al* [11] (2020) found that the data regarding incidence, response rates to neoadjuvant chemotherapy (NACT) and factors affecting pathological complete response (pCR) rate in locally advanced breast cancer (LABC) patients are lacking from India. The median age of diagnosis was 46 years (range 24-72years).

Kunnuru SK *et al* [12] (2020) found that to assess the effectiveness of neo-adjuvant chemotherapy and its impact on the clinical and pathological response in locally advanced breast cancer. The median age of the patients at the time of diagnosis was 44 years(range=24– 73).

In our study, out of 50 patients, most of the patients were 51-60 years of age [20 (40.0%)] rest of 15 (30.0%) patients were 41-50 years of age, 10 (20.0%) patients were ≤40 years of age and 5 (10.0%) patients were >61 years of age. Age was statistically significant (p=.00054) (z=3.4641). The mean Age of patients was [49.9600± 9.5404].

In our study, all patients [50 (100.0%)] had Lymph node involvement.

We found that, most of the patients had tumor in size 5-7 cm [30 (60.0%)] followed by Tumor in size 8-10 cm [30 (60.0%)] but this was statistically significant (p=.0455).

Bhattacharyya T *et al* [13] (2014) observed that neoadjuvant chemotherapy (NACT) has dramatically changed the management of locally advanced breast cancer (LABC). A while 28 (18.9%) patients developed distant metastasis.

El-Mahdy MM *et al* [14] (2020) found that presence of TILs in breast cancer indicates better therapeutic responses to neoadjuvant chemotherapy (NAC), increased pCR and improved outcome. Distant metastasis (p = 0.025).

In our study, all patients had no distant metastasis [50 (100.0%)].

Klein J *et al* [15] (2019) examined that Neoadjuvant chemotherapy (NAC) is increasingly usedto treat locally advanced breast cancer (LABC). The cohort included 103 patients nearly equally divided between Stage II (n = 53) and Stage III (n = 50). Stage group (p = 0.05).

We showed that, most of the patients had Stage IIIA [25 (50.0%)]. However, Stage IIIB [15(32.0%)] followed by Stage IIIC [10 (20.0%)] which was statistically significant (p=.00168).

It was found that, all patients [50 (100.0%)] had Anterior Chemotherapy.

Tang S *et al* [16] (2020) showed that this retrospective analysis was designed to research whether clinical response partial response (PR)/complete response (CR) and pathological response (PCR) to neoadjuvant chemotherapy can translate into prognosis benefit pathological response in patients with locally advanced breast cancer and whether different chemotherapy regimens will influence the outcomes. Clinical response was strongly correlated with lymph nodes status (P=0.032).

Gogia A *et al* [17] (2014) showed that this study was to assess the response rates (clinical and pathological) with docetaxel and epirubicin combination chemotherapy and its effect on outcome. 90% had clinically palpable lymph nodes at diagnosis.

Our study showed that, Same Lymph node status [27 (54.0%)] was higher than down stage Lymph node status [23 (46.0%)] but this was not statistically significant (p=.42372) (z=8). We found that, more number of patients had Size reduction 25-50% [20 (40.0%)] rest of 50- 75% [15 (30.0%)], >75-99% [10 (20.0%)] and <25% [5 (10.0%)] though it was

statistically significant (p=.00054) (z=3.4641). Our study showed that, most of the patients had Stage IIB after chemotherapy [22 (44.0%)]and it was not statistically significant (p< 0.14706) (z=1.4499).

In our study, higher number of patients had Down stage Result [35 (70.0%)] followed by Same Result [15 (30.0%)] but this was statistically significant (p=.00006) (z=4).

Bharadwaj BS *et al* [18] (2021) examined that breast cancer being a multifactorial disorder outcome depends on various clinicopathological and molecular factors. Four out of 6 pCR cases had preclinical tumor size ≤5 cm.

We showed that, the mean Tumor size of patients was [7.2880± 1.4822 (cm)] and mean % ofsize reduction of patients was [58.0000± 15.0509].

Table 1: Distribution of Tumor insize (CM), Anterior Chemotherapy, Lymph node status, Stage after chemotherapy, Stage and Lymph node involvement

		Number of patients	%
Tumor insize(CM)	5-7	30	60%
	8-10	20	40%
	Total	50	100%
Anterior Chemotherapy	Yes	50	100.0%
	Total	50	100.0%
Lymph node status	Down stage	23	46.0%
	Same	27	54.0%
	Total	50	100.0%
Stage after chemotherapy	IIA	13	26.0%
	IIB	22	44.0%
	Same	15	30.0%
	Total	50	100.0%
Stage	IIIA	25	50.0%
	IIIB	15	30.0%
	IIIC	10	20.0%
	Total	50	100.0%
Lymph node involvement	Yes	50	100.0%
	Total	50	100.0%

Table 2: Distribution of mean Tumor size(CM) and % of size reduction

	Number	Mean	SD	Minimum	Maximum	Median
Tumor size(CM)	50	7.2880	1.4822	5.0000	10.0000	7.0000
% of size reduction	50	58.0000	15.0509	25.0000	80.0000	60.0000

Summary and Conclusion

- In our study, out of 50 patients, most of the patients were 51-60 years of age. Age was statistically significant. The mean Age of patients was [49.9600± 9.5404].
- In our study, all patients had Lymph node involvement and no distant metastasis.
- We found that, most of the patients had tumor in size 5-7 cm followed by Tumor in size 8-10 cm but this was statistically significant.
- We showed that, most of the patients had Stage IIIA. However, Stage IIIB followed by Stage IIIC which was statistically significant.
- It was found that, all patients had

Anterior Chemotherapy.

- Our study showed that, Same Lymph node status was higher than down stage Lymph node status but this was not statistically significant.
- We found that, more number of patients had Size reduction 25-50% rest of 50-75%,
- >75-99% and <25% though it was statistically significant.
- Our study showed that, most of the patients had Stage IIB after chemotherapy and it was not statistically significant.
- In our study, higher number of patients had Down stage Result followed by Same Result but this was statistically significant.
- We showed that, the mean Tumor size of patients was [7.2880± 1.4822 (cm)] andmean % of size reduction of patients was [58.0000± 15.0509].

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