VOLUME - 10, ISSUE - 06, JUNE- 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Surgery

RESPONSE OF CAF REGIMEN AS NEO-ADJUVANT CHEMOTHERAPY IN DOWNSTAGING LOCALLY ADVANCED BREAST CARCINOMA

Dr. Himanshi Grover*	PG, Department of General Surgery, SRM Medical college hospital and research center, Tamil Nadu. *Corresponding Author
Dr. N Sivarajan	Professor, Department of General Surgery, SRM Medical college hospital and research center, Tamil Nadu.
Dr. Suganth	PG, Department of General Surgery, SRM Medical college hospital and research center, Tamil Nadu.
Dr. Wasim	PG, Department of General Surgery, SRM Medical college hospital and research center, Tamil Nadu.

ABSTRACT

BACKGROUND: In India, locally advanced breast cancer (LABC) is responsible for 30 - 35% of all breast cancer cases. The purpose of preoperative chemotherapy is that it is capable of shrinking large primary tumors rendering many inoperable patients operable

METHODS: The doses of the drugs used were Cyclophosphamide - 600 mg/m^2 IV infusion, Adriamycin - 50 mg/m^2 IV infusion and 5 fluorouracil (FU) - 600 mg/m^2 IV infusion. Clinical response was noted after 3 weeks of third cycle of NACT which was assessed according to RECIST criteria

RESULTS: 78.1% of our patients responded to NACT (cCR + cPR) with pCR in 17.2% of patients. percentage of complete response was higher for patients in stage IIIA than for the patient in stage IIIB

CONCLUSION: neo-adjuvant chemotherapy integrated into a multi-modality program is the standard management in patients with locally advanced breast carcinoma. The patients with pathological complete response and patients without axillary lymph node were associated with improved outcome after neo adjuvant chemo therapy

KEYWORDS :

INTRODUCTION

In India, breast cancer is the 2nd most common cancer in females with approximately 75,000 new cases diagnosed every year as per the cancer registries in the India.[1] 50-70% of the breast cancer patients in regional cancer centers present with locally advanced stage. [2,3]. Factors like lack of education and poor socio-economic status are possible factors behind LABC in developing countries[4]. LABC includes clinical T3 (>5 cm in size), T4 and N2, or N3 disease , stage IIB and III disease. LABC can be classified into two types, Operable LABC (T2N1M0, T3 N0-1 M0) and Inoperable LABC (Stage IIIA except T3N1M0, Stage IIIB, Stage IIIC. Neo-adjuvant chemotherapy has become an important treatment modality in the multidisciplinary approach of management of LABC [5] where three to four doses are given prior to surgery, followed by the remaining cycles post-operatively. Improves the survival of patients with LABC as part of multimodality therapy, compared to locoregional therapy alone. Reduces the risk of distant disease recurrence. Routinely used regimens are FEC, CMF, CAF. Currently anthracycline based regimens such as CAF are the most widely recommended first line regimens in neoadjuvant therapy.

MATERIAL AND METHODS

All patients diagnosed with LABC admitted from may 2018 to May 2019 in SRM Medical college were included in the study. Patients with bilateral cancers, recurrent cancer, prior breast surgery, metastatic disease, pregnant or lactating women, were excluded from the study. Patients diagnosed with LABC who declined admission and did not give consent were also excluded from the study. Patients were assessed according to Triple Assessment with other routine investigations. Metastatic workup done using skeletal X ray and ultrasound abdomen. Initial staging and evaluation was also done as neoadjuvant chemotherapy will alter the staging later on. This prospective study comprised of effects of three cycles of CAF regime as NACT on LABC in terms of operability, clinical and pathological response. The doses of the drugs used were Cyclophosphamide - 600 mg/m^2 IV infusion, Adriamycin - 50 mg/m^2 IV infusion and 5 fluorouracil - 600 mg/m^2 IV infusion. Clinical response was noted after 3 weeks of third cycle of NACT which was assessed according to RECIST criteria. Statistical analyses were done using SPSS version 21.

OBSERVATIONS AND RESULTS

The mean age group was 46 years (range 25 – 66 years). Maximum patients affected with LABC were found to be in between 41 to 50 years of age.

Table 1 : Age Distribution

Age in years	No of patients (n = 32)	Percentage
21 to 30	1	3.1 %
31 to 40	4	12.5 %
41 to 50	20	62.5 %
50 to 60	4	12.5 %
> 60 years	2	9.38 %

Most of the patients (26 patients) presented to surgeon after 6 months of detecting first symptom. Only 2 patients were found to report within 2 months of detecting the first symptom which emphasis the need of spreading awareness among Indian women about breast cancer.

Table 2 : Duration of symptoms

Duration of symptoms	No of patients (n=32)	Percentage
< 2 months	2	6.25 %
> 2 to 6 months	4	12.5 %
> 6 to 12 months	19	59.37 %
> 12	7	21.88

AGE OF ATTAINING MENARCHE AND MENOPAUSE: Most of the patient attained menarche at 13 years of age. Twenty-two patients (67.8%) were premenopausal and 10 patients (31.2%) were post menopausal.

SIDE AND QUADRANTS OF BREAST INVOLVED: Fifteen patients (46.9%) of the patients had right sided breast carcinoma and 17 patients (53.1%) with left side breast

cancer. Upper outer quadrant (59.4%) was most commonly affected quadrant and lower half part of the breast were least involved.

RESPONSE AFTER NACT

Table 3 : Changes after NACT

Parameters	Before NACT	After NACT
1.Average tumor size	8 cm	4.8 cm
2.Skin changes present	65.7 %	19 %
3.Fixity to chest wall	21.8 %	5 %
4.Clinically palpable lymph nodes	87.5 %	28.8 %
5.Nipple discharge	6 %	0
7.Ulceration	6 %	0
8.Pain	12.5%	0

Table 4 : Clinical response after NACT

Clinical response	No of patients (n=32)	Percentage
Clinical complete response (cCR)	2	6.25 %
Clinical partial response (cPR)	23	71.87 %
Stable disease/ clinical no response (cNR)	3	9.37 %
Progressive disease	3	9.37 %
Overall clinical response (cCR + cPR)	25	78.1%

Table 5 : Stage wise response after NACT

Stage of disease (pre NACT)	No of patients (n=32)	Clinical response			
		cCR	cPR	cNR	PD
IIIA	13	2 (15.4%)	9 (69.2%)	1 (7.7%)	1 (7.7%)
IIIB	19	0	15 (78.9)	2 (10.5%)	2 (10.5%)

Table 6 : Clinical response according to pretreatment hormone receptor status

Hormone receptor status	No. of patients (n=32)	Clinical response			
		cCR	Cpr	cNR	PD
ER+ve/PR +ve	7	0	4(57.1%)	1(14.3)	2 (28.5%)
ER+ve/PR-ve	8	0	6 (75%)	2 (25%)	1 (10%)
ER-ve/PR+ve	10	1 (10%)	8(80%)	1 (10%)	0
ER-ve/PR-ve	7	1(14.3%)	6	0	0

Table 7 : Pathological types

Pathological types	No. of patients	Percentage
Invasive ductal carcinoma (IDC)	29	90.6%
Invasive lobular carcinoma (ILC)	2	6.25 %
Others	1	3.1%

Patients were followed upto 6 months to 2 years. Out of 29 responsive patients, 10 patients lost their follow ups, either they were non compliant or may have died. Patients with CCR were having no loco-regional recurrences or metastasis. Over all 6 patients developed metastasis, out of which 3 patients developed prior to surgery and 3 patients during follow ups.

DISCUSSION

The mean age of presentation in our study is 46 years, 46.9% of the patients had right sided breast carcinoma. This doesn't go with the studies reporting higher incidence of left sided invasive and in situ lesions by Faidah Badru et al (2011).[6] Upper outer quadrant (59.4%) was commonly affected quadrant and lower half part of the breast were least involved. In our study 67.8% of the patients were premenopausal, which is lower than other studies by Chen et al (2004).[11] Out of 32 patients who received neoadjuvant chemotherapy 3 patients (9.37 %) had <30% reduction of size of tumor, 14 patients (43.7%) had 30-50% of size reduction, 4 patients (12.5%) of patients had up to 75% size reduction and 2 patients (6.25%) of patients had up to 99% of size reduction. Two patients (6.25%) had clinically complete resolution (cCR) of tumor and 3 patients (9.37%) had increase in tumor size. Thus 78.1% of our patients responded to NACT (cCR + cPR) with pCR in 17.2% of patients, similar to study done by Ochonma et al (2013)[7] found that complete clinical response occurred in 12.9% patients whereas 61.3% patients responded partially and patients with stable disease were 25.8% of patients .In our study, percentage of complete response was higher for patients in stage IIIA than for the patient in stage IIIB. In this study 15 patients (46.87%) showed estrogen receptor(ER) positivity and 17 patients (53.12 %) showed progesterone receptor(PR) positivity. Out of 32 patients, 7 (21.9%) patients were both ER and PR positive and 7 (21.9%) patients were both ER&PR negative. Similar results werte obtained by D. Gupta et al,[11] . Overall clinical response was better in estrogen receptor negative patients, ie 50% (16 patients). This result is similar to a study by Lippman et al[13], which showed increased response to chemotherapy in patients with low or absent ER values when compared to patients with higher ER values. In our study complete pathological response obtained in 5 patients (17.24%) and invasive disease found in 24 patients (82.75%). Similar study done in 2013 by Trupti et al[15], with 14% patients had complete pathological response,70% patients had partial response and residual disease was found in 8 patients (16%).In our study, invasive ductal carcinoma (IDC) comprised 90.6% patients whereas invasive lobular carcinoma (ILC) with 6.25% patients which is comparable with studies by Ahmet Gökhan et al.(2019) where 89.8% patients had invasive ductal carcinoma, 9.6% patients had invasive lobular carcinoma and one (0.6%) patient had medullary carcinoma.[15] In present study loco-regional recurrence (LRR) was seen in 3 (13.6%). Cance et al.(2002) reported an recurrence rate of 10% among patients with advanced primary tumors treated with BCS after NACT.[16] In this study 3 patient developed findings of fresh metastasis during the course of NACT, and 3 patients developed metastasis during follow up. This study had various limitations like Short follow ups, Small study group, Non compliant patients.

CONCLUSION

Prognosis is not satisfactory in tribal females as compared to other groups because of lack of education, resources and awareness in outreach tribal areas and presenting late to our tertiary center. The patients with pathological complete response and patients without axillary lymph node were associated with improved outcome after neo adjuvant chemo therapy. Patients with hormone receptor negativity had better clinico-pathological response after NACT.

REFERENCES

1. Chopra R. The Indian Scene JCO 2001;19:106S-111S
2. Sandhu DS, Sandhu S, Karwasra RK, Marwah S.Profile of breast cancer patients at a tertiary care hospital in north India. Indian J Cancer 2010;47:1622.
3. Khokhar A. Breast cancer in India: Where do we stand and where do we go? Asian Pac J Cancer Prev 2012;13:4861-6.
4. Desai PB. Breast cancer profile in India: Experiences at the Tata Memorial Hospital, Bombay. In Paterson AHG, Lees AW, editors. Fundamental Problems in breast cancer,Martinus Nijhoff.
5. Kuerer HM, Hunt KK, Newman LA, Ross MI, Ames FC, Singletary SE. Neoadjuvant chemotherapy in women with invasive breast carcinoma: Conceptual basis and fundamental surgical issues. J Am Coll Surg 2000;190:350-63.
6. Faidah Badru et al, Laterality of breast cancer- is it true?, European Journal of Surgical Oncology, November 2011,Volume 37,Issue 11
7. Ochonma Amobi Egwuonwu, Anyanwu SN, Nwofor AM. Efficacy of neoadjuvant chemotherapy in down staging locally advanced pre-menopausal breast cancer in Eastern Nigeria: Is four courses adequate?. Journal of cancer research and therapeutics. 2013 Oct 1;9(4):638.
8. Tapesh Bhattacharyya, Suresh C Sharma, Budhi Singh Yadav, Rajinder Singh, and Gurpreet Singh et al ; Outcome of neoadjuvant chemotherapy in locally advanced breast cancer: A tertiary care centre experience. Indian J Med Paediatr Oncol. 2014 Jul-Sep; 35(3): 215–220.doi: 10.4103/0971-5851.142038.
9. Raina V, Bhutani M, Bedi R, Sharma A, Deo SV, Shukla NK, et al. Clinical features and prognostic factors of early breast cancer at a major cancer center in North India. Indian J Cancer. 2005;42:40–5.

10. Min SY, Lee SJ, Shin KH, Park IH, Jung SY, Lee KS, et al. Locoregional recurrence of breast cancer in patients treated with breast conservation surgery and radiotherapy following neoadjuvant chemotherapy. Int J Radiat Oncol Biol Phys. 2011;81:e697–705
11. Chen AM, Meric-Bernstam F, Hunt KK, Thames HD, Oswald MJ, Outlaw ED, et al. Breast conservation after neoadjuvant chemotherapy: The MD Anderson cancer center experience. J Clin Oncol. 2004;22:2303–12
12. Gupta D, Raina V, Rath GK, Shukla NK, Mohanti BK, Sharma DN: Clinical and pathological response rates of docetaxel-based neoadjuvant chemotherapy in locally advanced breast cancer and comparison with anthracycline-based chemotherapies: eight-year experience from single centre: Indian J Cancer. 2011 Oct-Dec;48(4):410-4.
13. Lippman ME, Allegra JC, Thompson EB, et al: The relation between estrogen receptors and response rate to cytotoxic chemotherapy in metastatic breast cancer. N Engl J Med 298:1223-1228, 1978.
14. Patel T, Gupta A, Shah M. Pathological predictive factors for tumor response in locally advanced breast carcinomas treated with anthracyclin-based neoadjuvant chemotherapy. Journal of cancer research and therapeutics. 2013 Apr 1;9(2):245.
15. Ahmet Gökhan Santaş, Orçun Yalav , Yalçın Kekeç, Gürhan Sakman, Emine Bağır Kılıç, Suzan Zorludemir, Melek Ergin , İsmail Cem Eray, İsmail Oğuz Kara, Semra Paydaş; Effect of neoadjuvant chemotherapy on estrogen receptor, progesterone receptor, C erb-B2, vascular endothelial growth factor and Ki-67 in patients with locally advanced breast cancer; Cukurova Med J 2019;44(1):226-231.
16. Cance WG, Carey LA, Calvo BF, Sartor C, Sawyer L, Moore DT, et al. Long-term outcome of neoadjuvant therapy for locally advanced breast carcinoma: Effective clinical downstaging allows breast. Ann Surg. 2002 Sep;236(3):295-302; discussion302-3.