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Original Research Paper

Surgery

A STUDY OF ROLE OF NEOADJUVANT CHEMOTHERAPY IN DOWNSTAGING OF LARGE OPERABLE BREAST CANCER IN CENTRAL INDIA

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ABSTRACT

Objective: To study of role of neoadjuvant chemotherapy in downstaging of large operable breast cancer in Central India.

Materials and Methods: This was a hospital based prospective nonrandomised study of 32 patients of large operable breast cancer (lobc) conducted at a tertiary centre for a period of 2 years from January 2015 to December 2017

Results: Maximum patients were in age group of 41-50 with mean age of presentation being 43.73 years and median age of presentation 43.5 years. Most women i.e. 23 (71.88%) were premenopausal. Most patients 24(75%) achieved maximal tumour response after 4 cycles of neoadjuvant chemotherapy. 24 patients (75%) had partical clinical response and 4 had complete clinical response.

Conclusions: Neoadjuvant chemotherapy reduces the size of lump in LOBC.

KEYWORDS : LOBC, Chemotherapy

INTRODUCTION:

Incidence of breast cancer is rising in India. Over 1,00,000 new breast cancer patients are estimated to be diagnosed annually in India [1]. As per ICMR – PBCR data, breast cancer is commonest cancer among women in urban registries of Delhi, Mumbai, Ahmadabad, Calcutta and Trivandrum where it constitutes > 30 % of all cancer in females [2]. It is second most common cancer in women in rural India after uterine cervix [2]. Majority of breast cancer patients in India are Pre-menopausal as compared to western countries where they are post menopausal [1].

Management of breast cancer has changed since ages from radicalism to more of conservative approach. Contemporary breast cancer therapy has evolved to a point at which multidisciplinary approaches are the standard of care for most breast cancer patients, even those with early-stage disease. Neoadjuvant therapy is defined as first systemic treatment a patient receives when nonmetastatic breast cancer is diagnosed. Neoadjuvant treatment has the ability to shrink tumors and was first used in patients with inoperable locally advanced or inflammatory. Data from several retrospective analyses showed that the application of multimodal treatment consisting of neoadjuvant chemotherapy, surgery, radiotherapy and hormonal therapy improved survival for patients with these poor prognosis tumors [3].

Present study aims to evaluate the role of Neoadjuvant Chemotherapy Therapy (NACT) in down staging Large Operable Breast Cancer (LOBC) in Central India.

METHODOLOGY: This was a hospital based prospective nonrandomised study of 32 patients of large operable breast cancer (lobc) conducted at a tertiary centre for a period of 2 years from January 2015 to December 2017. Inclusion criteria meant all consenting patients in all age groups presenting with LOBC ie. Stage IIIA.

Patients were admitted and those fit for therapy were treated with:

1. injection cyclophosphamide 500 mg/sq.m
2. injection adriamycin 50 mg/sq.m
3. injection 5-Flurouracil 500 mg/sq.m

Clinical tumour response was graded accordingt o WHO criteria for clinical tumour response (107)

cCR: COMPLETE CLNICAL RESPONSE
cPR: PARTIAL CLINICAL RESPONSE
cPD: PROGRESSIVE DISEASE
cSD: STABLE DISEASE

RESULTS:

The study was carried out in our institute where a total of 32 patients of Large Operable Breast Cancer (LOBC) were treated with Neoadjuvant Systemic Chemotherapy with CAF (cyclophosphamide, adriamycin, Fluouracil) 3 weekly regimen. Maximum patients were in age group of 41-50 with mean age of presentation being 43.73 years and median age of presentation 43.5 years. Most women i.e. 23 (71.88%) were premenopausal. Breast tumour size between 5-7.5 cm was found in maximum i.e. 27(84.38%) women. Upper outer quadrant (14 i.e. 43.75%) and central quadrant (10 i.e. 31.25%) were mostly involved by tumour mass. Most patients 24(75%) achieved maximal tumour response after 4 cycles of neoadjuvant chemotherapy. 24 patients (75%) had partical clinical response and 4 had complete clinical response. All patients reported of nausea at some point during chemotherapy. Statistical analysis was done by paired t test and it inferred that size of breast lump had decreased significantly after chemotherapy.

DISCUSSION:

Management of breast cancer always poses a challenge from making accurate diagnosis to its optimal treatment. Surgery has been the main stay of the treatment.

We included patients in Large Operable group as this is the common presentation in our set up and the management is still the major area of dispute. Choice of management oscillates between primary surgery with adjuvant chemo-radiotherapy and neoadjuvant therapy followed by surgery.

While the majority of breast cancer patients in western countries are postmenopausal and in their 60s and 70s, the picture is quite different in India with pre-menopausal patients constituting about 50% of all patients [4]. The average age of breast cancer patients, at presentation, has been reported to be 50–53 years in various population-based studies conducted in different parts of the country while a significant proportion of Indian breast cancer patients are younger than 35 years of age [5].

Mean age of the patient in study by N Abdel-Bary et. al. (2009) [12] was 42 years with range of 21- 68 years. Similarly median age of the patients in study by Swain et al (1987) [3] was 42 years. Median age in the study by Cance et. al. (2002) [9] was 44 years. In our study mean age is 43.73 years, median of the age is 43.5 years and age range is from 32 to 63 years.

Our study had complete clinical response (cCR) rate of 12.5% and partial clinical response (cPR) of 75% as per the WHO criteria for clinical assessment of cancer response.

In a study by N Abdel-Bary et. al. (2009) [12] out of 34 patients which included patients with lump size more than 2 cm were treated with neoadjuvant chemotherapy, cCR was seen in 7 (20.6%) patients cPR was 17 (50%) with no change seen in 9 (26.5%) patients and disease progression seen in 1 (2.9%) patients. Our study had no disease progression and 4 patients (12.5%) had static disease. Otherwise results are comparable to our study.

In a study Fukutomi T (2006) [12] treated 296 patients with anthracyclines and taxanes sequentially and examined the clinical and pathological results. A total of 14 % (41/296) of the patients achieved a clinical complete response.

Zhou et. al. (2005) [10] 50% obtained complete clinical response (cCR) and 43% had partial clinical response (cPR)

Our study showed an Objective Response (cCR + cPR) rate of 87.5 %. In the study by N Abdel-Bary et. al. (2009) [11] which included 34 cases of operable breast cancer and received 4 cycles of neoadjuvant chemotherapy with FEC regimen had an objective response of 70.6% which is comparable to our study.

In a study by Zhou B et. al. (2005) [9] breast tumor were treated with neoadjuvant chemotherapy and 28 out of 30 patients had a objective clinical response i.e. 90%.

A study by Vlastos et. al. (2000) [7] at Texas which involved 129 patients from a series of 174 with stage IIA, IIB and IIIA treated with paclitaxel or a combination of fluorouracil, doxorubicin, and cyclophosphamide (FAC). They reported a total objective response of 60%.

Our study showed a complete pathological response (pCR) in 2 out of 32 total patients i.e. 6.25 % pCR. But pCR is 2 out of 4 patients of clinically complete response (cCR) i.e. 50%.

In a study by N Abdel-Bary et. al. (2009) [11] out of 34 patients pCR was seen in 5 (14.7%) patients and pathological partial response was seen in 29 (85.3%) patients.

Fukutomi T et. al. (2006) [12] had a pCR of 9.5% of the treated 296 patients with neoadjuvant chemotherapy.

In a study by Zhou B et. al. (2005) [11] out of 30 patients 7 patients (23%) had a pCR.

In a study by Colleoni et. al. (2003) [8] reported a pCR rate of 33% among the 36 patients treated with both pre and post chemotherapy.

Clinically axillary lymph node were palpable in 23 patients before chemotherapy after chemotherapy nodes were palpable in 4 patients, i.e. 82.6% (19/23) of these pathological complete response was seen in 4 out of those 19 patients i.e. 21.05% .

Vlastos et. al. (2000) [7] reported that among patients clinically classified as N1, 34% became histologically negative and 38% had only 1-3 positive lymph node after chemotherapy.

In NSABP protocol B-18 (1997) trial [6], clinical nodal response occurred in 89% of node positive: 73% had a cCR and 44% of those had a pCR.

Our clinical response is comparable to these studies but pathological response in these studies is higher. Thus neoadjuvant chemotherapy helps in downstaging of large operable breast cancer but we had small sample size hence more studies are needed to validate this findings in general population.

TABLES:

1. Table showing Patient characteristics.

Characteristic	No. of patients	Percentage
Age group	13	40.62
31-40	14	43.75
41-50	3	9.38
51-60	2	6.25
61-70		
Menstrual status	23	71.88
Premenopausal	9	28.12
Post menopausal		
Size of breast lump at presentation	27	84.38
5-7.5cm	4	12.5
7.5-10cm	1	3.12
>10cm		
Predominantly involved quadrant	14	43.75
Upper outer	2	6.25
Upper inner	2	6.25
Lower outer	4	12.5
Lower inner	10	31.25
Central		

2. TABLE showing Chemotherapy characteristics.

	No. of patients	Percentage
No. of Cycles preoperatively	6	18.75
3	24	75
4	2	6.25
5		
Clinical response	4	12.5
cCR	24	75
cPR	4	12.5
cSD	-	-
cPD		
Side effects	32	100
Nausea	14	43.75
Vomiting	12	37.5
Alopecia	0	0
Bone marrow supression		

2. Statistical analysis for decrease in breast lump size.

	Pre chemotherapy	Post chemotherapy
Mean of product of dimensions of lump	36.14	13.77
Median of the product of dimension of lump	24.36	9.9
SD	17.60	10.97
95 % C.I.	29.80 – 42.49	9.81 – 17.72
t-value	6.7690	
p-value	<0.0001, Highly significant	

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