International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319 – 6505, Impact Factor: SJIF: 5.438
Available Online at www.journalijcar.org
Volume 6; Issue 2; February 2017; Page No. 2176-2182

Research Article

INTERMEDIATE BREAST CANCER TWO DIFFERENT TREATMENT APPROACHES

Anil Kumar B[1]., Rehman M.M[2] and Kalyan, K.A.S.S.N[3]

[1,2,3]General Surgery, Dr.Pinnamaneni Siddhartha Institute Of Medical Sciences & Research Foundation, Chinaoutapalli, Krishna Dist, Andhra Pradesh, India

A R T I C L E I N F O

Article History:

Received 20th November, 2016
Received in revised form 7thDecember, 2016
Accepted 24th January, 2017
Published online 28th February, 2017

Key words:

Adjuvant, Breast cancer, Chemotherapy, Radiotherapy

A B S T R A C T

Introduction: Breast cancer is one of the commonest malignancies affecting female population all over the world hence standard and universally acceptable treatment strategies are necessary for management

Objectives:

1. To study the impact of neo-adjuvant chemotherapy on local and regional control as well as the disease free and overall survival in T 3 breast cancer.
2. To compare the impact of two different modalities of management, namely pre-operative (neo adjuvant) and postoperative (after primary surgery) adjuvant chemotherapy on outcomes in this intermediate group of breast cancers.

Methodology: Cohort study in a Department of general surgery, Tertiary care teaching Hospital

Sample selection: All cancers of the breast belonging to T3N1M0 and T3N0M0 were grouped together into a category named Intermediate breast cancers. All untreated intermediate breast cancer patients reporting to Dept. of Surgery, Tertiary Care Teaching Hospital between 18 and 85 years of age and willing to provide a written informed consent were recruited into the study. All terminally ill patients, patients who have previously received any form of definitive treatment (surgery/ chemotherapy/ radiotherapy), patients with co-morbidities and patients with poor cardiac function were excluded from the study.

Patients receiving neo adjuvant chemotherapy followed by Surgery formed the exposed group and patients undergoing primary Surgery followed by complete course of chemotherapy formed the unexposed group. Data collection and analysis was done using a specially designed detailed individual case record. The data were entered in Microsoft Excel 2007 and analysed using SPSS 17.0.

Results: Participants ranged from 25 to 85 years age. Early menarche was seen in 14.1 percent of women and late menarche in 9.4 percent. Of the 128 women who participated in the study, 25 percent belonged to the T3N0M0 category and the rest to the T3N1M0 category. Majority of participants were found to have Grade I or Il disease. Immunohistochemistry analysis showed that 39.1 percent cases were negative for all three receptors. The impact of neo adjuvant chemotherapy was assessed after three courses uniformly in all cases. Clinical response was defined using the criteria laid down by the World Health Organisation. Analysis showed that neo adjuvant chemotherapy had a significant positive impact on the clinical as well as pathological response. This positive impact persisted even after adjusting for possible confounders such as age, menopausal status, TNM staging and grading of the tumours as well as the time difference in initiating definitive treatment. Assessment of pathological response after surgery conclusively showed that there was a significant reduction in tumour size in patients who underwent neo adjuvant chemotherapy. The follow up period of six months was too short to study disease free survival as well as overall survival rates.

Conclusion: This cohort study showed that neo adjuvant chemotherapy had a significant positive impact on local control of breast cancers. This should result in modification of treatment protocols with an aim of promoting breast conservation surgery to a greater extent. Conservation of breast can have a highly positive impact on the morale of the women undergoing treatment. There is a need to develop a well defined protocol for deciding between NAC and primary surgery in case of Intermediate breast cancers (T3N0M0 and T3N1M0) and the group needs to be followed up for longer period to obtain clear evidence of benefits of neo adjuvant chemotherapy in long term and disease free survival.

INTRODUCTION

Background

Breast cancer is the commonest cause of death among women worldwide. Its incidence rate is more than double that of the second ranked cervical cancer, accounting for 23 percent of all newly occurring cancers in women worldwide and 13.7 percent of all cancer deaths(1).

Burden of disease in India

In India, breast cancer is the second most common cancer in women (after cervical cancer) and the second most common cause of deaths from cancer. I Although breast cancer stands second in India, data from the Atlas of cancer in India project, 2008 shows that it is the leading cancer in metropolitan cities, and is predicted to top the list of cancers in India in the coming decade (2).

Epidemiology of breast cancer

Among Indian women, the disease peaks at a younger age (45 to 50 years) than in the western countries and hence, majority of patients in India are in the pre-menopausal age group. Westernization of life style among Indian women, with increasing age at marriage, increasing age at first birth, decreasing period of breast feeding, changes in diet and decreased physical activity(3,4) have contributed to the increasing burden of breast cancer in India. Incidence tends to be higher among the upper socio-economic classes when compared to the low income groups(5). Majority of patients in India receive inadequate or inappropriate treatment due to the poor infrastructure, limited financial resources and a social stigma associated with the disease.(6,7) Majority of women present at a late stage of the disease the early age of occurrence and the late diagnosis resulting in a higher loss of productivity as measured by disability adjusted life years (DALY) due to the disease among the Indian population when compared to the western groups.(8) Majority of patients in India present with locally advanced breast cancer.(9) Table below is a consolidation of multiple studies among different population groups, which clearly points to the fact that the proportion of cases diagnosed in late stages (Stage III) in India is much higher than that in most other populations.

Table Incidence of stage Ill breast cancer among different population groups

Population	Percentage	Study
United states	7.3	Collyar DE 2001(10)
Peru	33	Schwartzman G 2001 (11)
Brazil	53	Schwartzman G 2001 (11)
Western Europe	5-20	Hoffken K 2001(12)
South Africa	41.6	Collyar DE 2001(10),Vorobiof et al 2001(13)
India	50-70	Chopra R 2001(9)

Disease characteristics

Staging of breast cancer

Staging of a cancer is defined as the grouping of patients with the disease based on the apparent extent of the tumour, which is dependent on clinical or pathological findings. The most widely used staging system is that of the American Joint Committee on Cancer (AJCC).

Radiation: The use of high-energy radiation from x-rays, neutrons, and other sources for local control of the tumors. It can be external-beam radiation therapy or internal radiation therapy, implant radiation, interstitial radiation or brachytherapy.

Rationale for the study

All the stages of LABC other than the T3NlMo stage requires initial neo-adjuvant chemotherapy to convert the inoperable state of the disease at presentation to an operable stage prior to surgical removal. However, the LABC in the T3NlM0 stage (the least advanced stage in LABC) can be treated either by neo-adjuvant or by adjuvant chemotherapy. A number of studies have reported the efficacy of neo-adjuvant chemotherapy on the loco-regional control and disease free survival of patients in this group of breast cancers.

Many institutions have developed tailor made protocols to treat this group of patients based on these clinical trials. However, our institution follows either of the two modalities, namely neo-adjuvant chemotherapy followed by surgery or primary surgery followed by adjuvant chemotherapy, for LABC in the T3N1M0 stage. All stages in EBC other than the T3N0M0 stage are treated either by mastectomy or by breast conservation surgery plus radiation, both combined with management of the axillary lymph nodes. In this group of operable tumors when mastectomy is preferred, chemotherapy can be given before or after surgery. But patients with EBC, when administered neo-adjuvant chemotherapy, the tumour can be down staged so that breast conservation becomes possible. The importance of breast conservation lies in the fact that removal of breasts is often associated with a great psychological trauma to the woman and adversely affects her quality of life to a great extent.

Tumour size is a well known prognostic factor in the management of breast cancers and so larger tumour should be considered for primary systemic chemotherapy before surgery to reduce the tumour size and hence improve prognosis. Development of an optimal treatment protocol for these two stages of breast cancers can have a very drastic impact on the overall disease free survival of the patient as well as prevent psychological trauma by enabling breast conservation. No comparative study has been done in the population attending our institution, in either of these two stages of breast cancer. The purpose of this study is to compare the clinical outcomes of the above two approaches and to develop an optimal treatment protocol specific for this population, in order to reduce loco-regional recurrence and improve disease free survival.

METHODOLOGY

Objectives of the study

1. To study the impact of neo-adjuvant chemotherapy on local and regional control as well as the disease free and overall survival in T3 breast cancer.
2. To compare the impact of two different modalities of management, namely pre-operative (neo adjuvant) and postoperative (after primary surgery) adjuvant chemotherapy on outcomes in this intermediate group of breast cancers

Study Methodology

a. Study type: Cohort study

b. Study setting: Dept of General Surgery Tertiary Care Hospital
c. Sample size: The intended sample size of 160 was achieved by recruiting the participants from among the candidates eligible as per the inclusion and exclusion criteria on a first come basis. Of the 160 participants, 32 were lost to follow up. Hence, Thirty two of the last recruited participants were omitted from the analysis so as to make the exposed and unexposed groups equal in number. Hence the final sample size for analysis was 128 (64 each in the exposed and unexposed groups), thus giving a total non-response rate of 20 percent. Thus in all 128 cases of intermediate breast cancer were studied of which 32 were from the category T3N0M0 and 96 were from the T3NlM0.
d. Sample selection procedures: All untreated intermediate breast cancer (IBC) patients reporting to Dept. of Surgery, Tertiary Care Hospital , between 18 and 85 years of age and willing to participate in the study and provide a written informed consent were recruited into the study. All terminally ill patients, patients who have previously received any form of definitive treatment (surgery/ chemotherapy/ radiotherapy), patients with co-morbidities which are likely to affect their life expectancy and patients with poor cardiac function (in whom anthracyclines are contraindicated) were excluded from the study.
e. Operational definitions:

Intermediate Breast Cancer (IBC)*:* All cancers of the breast belonging to T3NlM0 (Stage3a) presently classified as a subtype of Locally Advanced Breast Cancer (LABC) and T3N0M0 (Stage 2b) presently classified under Early Breast Cancer (EBC) were grouped together into a category named Intermediate breast cancers.

Effective Neo Adjuvant Chemotherapy*:* After three courses of Neo Adjuvant Chemotherapy (NAC), the tumour size is assessed. If the tumour size has not reduced, then the regime of chemotherapy is changed and further two courses of the new regime are administered. Effective NAC is defined as any reduction in tumour volume on clinical assessment by the surgeon at the end of the above course of chemotherapy.

Exposed group*:* Since the exposure of interest is neo adjuvant chemotherapy, patients with Intermediate Breast Cancer (IBC) receiving NAC followed by Surgery and then completion of chemotherapy and radiation belonged to the exposed group

Unexposed group*:* This group consisted of patients with Intermediate Breast Cancer (IBC) undergoing primary Surgery followed by complete course of chemotherapy and local radiation.

a. Data collection tools: A specially designed detailed individual case record was used for following up the patients over the course of the study. A structured interview schedule was used at baseline for collecting socio-demographic particulars of the patients.
b. Data collection procedure: All patients who met the selection criteria were invited by the principal investigator to participate in the study. Only if willingness to participate in the study was expressed and written informed consent was given were they recruited for the study. Baseline data was collected using the structured interview schedule administered to the patients. The participants were then divided into the exposed and non-exposed groups based on the treatment schedule they were put on. Recruitment to the groups were based on a first come basis and when the requisite number was reached, recruitment to that particular group was discontinued. Each patient's details were recorded in a detailed follow up module specially designed for the study. The patients were advised to return for follow up bimonthly to the Surgery OPD till 6 months after completion of definitive treatment. Details were recorded at each follow up.
c. Data analysis: The baseline and follow-up data for all participants along with the variables collected to elicit socio-demographic particulars were entered in Microsoft Excel 2007 and analysed using SPSS 17.0. Sample characteristics were described by looking at the frequency distribution of all the determinants. Univariate, bivariate and multivariate analysis were done using SPSS version 17.0. Stratification was done for T3N1M0 and T3N0M0 cases. Clinical response to NAC, pathological response to NAC and evidence of recurrence (local and nodal recurrance, distant metastases) were the outcomes studied. The outcomes were compared between the two (exposed and unexposed) groups. The outcomes were also analysed through stratification based on stage at diagnosis and the receptor status. The change in tumour size before and after NAC was analysed to determine the impact of NAC and to check if the difference between the intervention and control arm were statistically significant.
d. Data storage: The filled up interview schedules and follow up cards without any personal identifiers are stored under the safe custody of the principal investigator and shall be destroyed three years after completion of the study.
e. Ethical considerations: Ethical clearance was obtained from Institutional Ethics Committee (IEC), Written informed consent in the local language was obtained from individuals found to be eligible and willing to participate in the study. Respondents were given the option of refusing to take part or opting out of the study at any stage. It was explained clearly that refusing to take part would in no way jeopardise the services they are eligible to receive from the government or any other agency. Participant confidentiality has been respected in all cases. No personal identifiers have been used while reporting the findings.

RESULTS

This presents the analysis of the baseline and follow-up data of 128 women who formed a cohort of intermediate breast cancer patients under study, while being treated at the Dept. Of General Surgery in a tertiary care teaching Hospital during the period from 01 Jan 2011 to 31 Dec 2016. A total of 128 women with intermediate breast cancer were studied of which 32 were in the T3N0M0 stage and 96 were in T3NlM0 stage

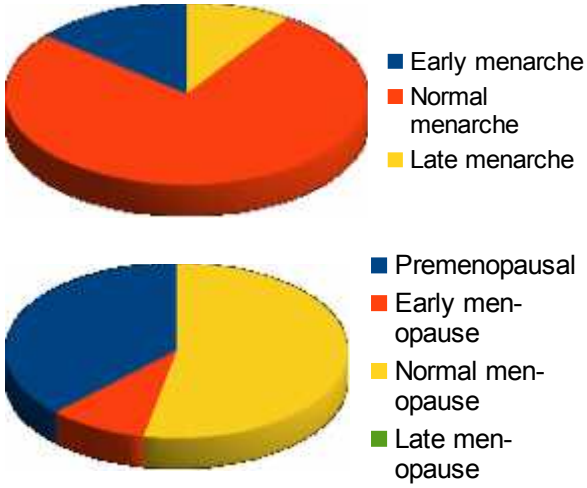
Demographic characteristics

The age of the participants ranged from 25 to 85 years with a mean of 52.11 years. The age distribution of the participants is given below

Table 1 Age distribution of participants in the study

Age Group	Number
20-40	26
40-60	70
60-80	30
>80	2

The age at menarche ranged from 11 to 19 years with an average age of 14.42 years at menarche. Early menarche (before 12 years) was seen in 14.1 percent of women with IBC and late menarche (17 years and above) in 9.4 percent women. The distribution of age at menarche is given in Fig. below. There were 48 women in the pre-menopausal age group, while the remaining 80 had attained menopause at a mean age of48.15 years. Earliest age at menopause was 35 years and the latest was at 53 years. The distribution of age at menopause among study participants is shown in Fig.1 below



Sixteen of the women were nulliparous, while the highest parity of eight was seen in 2 women.

Disease characteristics

Staging of 128 women who participated in the study, 32 (25 percent) belonged to the T3N0M0 category and the remaining 96 to the T3NIMO category. (Details given in Table below)

Table 1 Age distribution of participants in the study

Category	Number	Percent
T3N0M0	32	25
T3N1M0	96	75
Total	128	100

Grading: Majority of participants were found to have Grade I or Il disease. The highest number was from Grade I and the least from Grade III. (Details in Table below)

Table 3 Pathological grading of disease among the study participants

Grade	Number	Percent
I	62	48.4
II	50	39.1
III	16	12.5

Immunohistochemistry

The results of Immunohistochemistry analysis for receptors showed that highest number of cases (39.1 percent) were negative for all three receptors. The number of cases with various combinations of the receptor status is given in Table below.

Table 4 Immunohistochemistry status among the study participants

Receptor status	Number	Percent
ER positive	40	31.3
PR positive	10	7.8
HR positive	2	1.6
ER + PR positive	14	10.9
ER + HR positive	12	9.4
Triple negative	50	39.1
TOTAL	128	100

Outcome measures

The outcomes of interest in the study were:

1. Reduction in tumor size after NAC (Clinical response)
2. Pathological response to NAC and
3. Evidence of recurrence: loco-regional recurrence (local and nodal recurrence) and distant metastasis

The outcome measures were analyzed and compared between the two groups, namely the exposed group (those put on NAC) and the unexposed group (those who underwent primary surgery). The results are detailed below.

Clinical response

Since there was no intervention before surgery in the primary surgery group, as expected the tumour size did not show any reduction in this category. The clinical response in the neo adjuvant chemotherapy group was assessed after three courses of neo adjuvant chemotherapy. Even in cases where the surgery was done after more than three courses of chemotherapy, the clinical assessment was made after the third course of therapy, to maintain uniformity in assessment. Effective Neo Adjuvant Chemotherapy was seen in a total of 60 out of the 64 cases (93.8 percent). The responses to treatment were decided based on the WHO criteria Of these, 22 cases (34.4 percent) showed complete response while 38 cases (59.4 percent) showed partial response. In the primary surgery group, as expected, the tumour either showed no change (93.8 percent) or increased in size in a minority of cases (6.2 percent).

Table 5 Clinical response to neo adjuvant chemotherapy in study participants

Clinical response to NAC*	NAC group		Primary Surgerygroup**	
	Number	%	Number	%
Complete response	22	34.4	0	0
Partial response	38	59.4	0	0
No change	2	3.1	60	93.8
Progressive	2	3.1	4	6.2
TOTAL	64	100	64	100

p- value by Pearson Chi-square test = 0.000
* As per WHO criteria
** The primary surgery group is shown here only for comparison purposes. Since no intervention was made prior to surgery in this group(comparison / unexposed group), no reduction in tumour size was expected

Pathological response

A similar analysis of the pathological response of the tumour after surgery — which was classified into four groups, namely complete / partial pathological response, no response or progression of tumour is shown in Table below.

Table 6 Clinical response to neo adjuvant chemotherapy in study participants

Pathological response	NAC group		Primary Surgerygroup**	
	Number	%	Number	%
Complete	10	15.6	0	0
Partial	54	84.4	0	0
No response	0	0	58	90.6
Progression	0	0	6	9.4
TOTAL	64	100	64	100

p- value by Pearson Chi-square test = 0.000
**The primary surgery group is shown here only for comparison purposes. Since no intervention was made prior to surgery in this group (comparison / unexposed group), no pathological response was expected.

As expected, the primary surgery group in the absence of any intervention did not show any response. In the NAC group, 84.4 percent showed partial response and 15.6 percent showed complete pathological response, thereby showing an overall good pathological response of 100 percent.

Evidence of recurrence

One of the outcome measures of interest was the evidence of recurrence — locoregional (local and nodal) and distant metastasis. Since the follow up was possible only for six months due to time constraints, the results did not show any statistically significant difference in the recurrence among both groups, with neither showing any case of recurrence. The results are tabulated in Table below.

Table 7 Evidence of recurrence on six months follow up among study participants

	NAC group	Primary Surgery group
Local recurrence	0	0
Nodal recurrence	0	0
Distant metastasis	0	0

Six months is considered too little a time for any sort of recurrence whatever may be the treatment modality. For getting clear evidence on any significant difference in recurrence rates with the two modalities of treatment, a follow up of at least two years may be necessary.

Impact of neo adjuvant chemotherapy —stratified analysis to rule out confounding Bivariate analysis states that neo adjuvant chemotherapy had a significant positive impact on the clinical as well as pathological response. But when considering the overall sample characteristics, it could be hypothesized that this difference could be as a result of confounding of the results by the following sample characteristics.

1. Age distribution of the sample
2. Difference in the composition of T3N0M0 and T3N1M0 categories among the two groups
3. Difference in time to start definitive treatment between the two groups.
4. Difference in grading of tumours between the two groups.

In order to rule out the effects of confounding, stratified analysis was carried out for all the above four possible confounders. The results of stratified analysis are detailed below.

Stratification for age

The mean age of the NAC group was 48.66 ± 12.73 years while that of the primary surgery group was 55.56 ± 11.02 years, showing a difference in age structures (p-value = 0.024). It couId be argued that the difference in clinical response could be a result of this difference in age structure. Also, age below 35 is considered to be a risk factor for breast cancer as well as an indicator of poor prognosis with treatment. Hence, to rule out the possibility of confounding due to differing age structures, the study participants were grouped into two based on their age — one group with women up to 35 years age and the second above 35 years. The analysis was repeated after stratification for age using these groups. Results of analysis are given in Table below.

Table 8 Table showing analysis of clinical response after stratification for age

Age group	</= 35years		>35years	
Clinical response	NAC group	Primary Surgery Group	NAC group	Primary Surgery Group
Complete response	4	0	18	0
Partial response	2	0	36	0
No change	0	0	2	60
Progressive	0	0	2	4
TOTAL	6	0	58	64
p-value	0.000		0.000	

It is evident from the above table that there is a significant improved clinical response with NAC even after the effect of confounding by age of the women in the two groups is accounted for.

Again, of the 64 women in the study, 24 were in the pre-menopausal age group while 40 were in post-menopausal stage. To rule out the probability of confounding due to the difference in age structures, the groups were further stratified into pre-menopausal and post- menopausal women and then stratified analysis was carried out. The results of analysis are given in Table below.

Table 9 Table showing analysis of clinical response after stratification for menopausal status

Menopausal status	Pre-menopausal		Post-menopausal	
Clinical response	NAC group	Primary Surgery Group	NAC group	Primary Surgery Group
Complete response	12	0	10	0
Partial response	18	0	20	0
No change	0	16	2	44
Progressive	2	0	0	4
TOTAL	32	16	32	48
p-value	0.000		0.000	

It is evident from the above table that there is a significant improved clinical response with NAC even after the effect of confounding by differing menopausal status of the women in the two groups is accounted for.

Stratification for tumour category

The results of analysis after stratification for the tumour category (T3N0M0 and T3N1M0) are given in Table below.

Table 10 showing analysis of clinical response after stratification for tumour category

Category	T3N0M0		T3N1M0	
Clinical response	**NAC group**	**Primary Surgery Group**	**NAC group**	**Primary Surgery Group**
Complete response	2	0	20	0
Partial response	12	0	26	0
No change	2	12	0	48
Progressive	2	2	0	2
TOTAL	18	14	46	50
p-value	0.000		0.000	

It is evident from the above table that there is a significant improved clinical response with NAC even after the effect of confounding by differing composition of the tumour categories between the two groups is accounted for.

Stratification for time to start treatment

The mean duration to initiate treatment between the intervention (NAC) group and the control (primary surgery) group among the study participants is detailed in Table below.

Table 11 showing mean duration to initiate definitive treatment after diagnosis

	NAC group	**Primary Surgery group**
Mean duration (days)	10.84	21.91

It is seen that there is a difference in the mean time to start treatment between the two groups, and hence it could be argued that the results were confounded by this difference. To rule out any effect of confounding due to the delay in initiating treatment, stratified analysis was carried out. The results of analysis after stratification for the time to start definitive treatment are given in Table below.

Table 12 showing analysis of clinical response after stratification for time to start treatment

Time to start treatment	0-14 days		15 or more days	
Clinical response	**NAC group**	**Primary Surgery Group**	**NAC group**	**Primary Surgery Group**
Complete response	22	0	0	0
Partial response	34	0	4	0
No change	2	8	0	52
Progressive	2	0	0	4
TOTAL	60	8	4	56
p-value	0.000		0.000	

It is evident from the above table that there is a significant improved clinical response with NAC even after the effect of confounding by difference in time to start definitive treatment between the two groups is accounted for.

Ruling out confounding by difference in grading grade of the tumour is also a highly relevant prognostic factor, with higher grades showing poor prognosis when compared to lower grade tumours. To rule out any confounding due to the composition of tumour grades within the groups, the frequencies of all three grades of tumours were analysed for any significant difference. The results are shown in Table below.

Table 13 showing distribution of tumour grades between intervention and control groups

Grade of tumour	NAC group	Primary Surgery group
Grade I	36	26
Grade II	24	26
Grade III	4	12
TOTAL	64	64
p-value	0.241	

It evident from the above table that there is no significant in the proportion of participants belonging to different grades of tumour and hence the two groups are comparable and so it is not possible for confounding to occur due to the composition of the tumor grades.

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

This cohort study was undertaken to study the impact of neo-adjuvant chemotherapy on local (clinical and pathological response) and regional control, disease free survival and overall survival in T3N0 and T3N1 breast cancers. It also attempted to compare the impact of two (neo adjuvant) and postoperative chemotherapy (after primary surgery) on prognosis in this intermediate group of Breast cancers.

Impact of neo adjuvant chemotherapy on local control

The impact of neo adjuvant chemotherapy was assessed after three courses uniformly in all cases. World health organization defined complete and partial clinical responses as complete disappearance of the palpable disease and partial response as a decrease of more than 50 percent in total size of the tumour. A significant proportion of cases showed complete or partial response to chemotherapy. This improvement remained significant even after adjusting for possible confounders such as age, menopausal status, TNM staging and grading of the tumours as well as the time difference in initiating definitive treatment. Thus, this study provides clear evidence that neo adjuvant chemotherapy has a positive impact on local control of disease.

The Pathological response was also assessed after surgery, which conclusively showed that there was a significant reduction in tumour size in patients who underwent neo adjuvant chemotherapy. This improved pathological response along with conclusive evidence of tumour size reduction can help guide development of treatment protocols for this intermediate group of breast cancers.

One major impact of this result is that with conclusive evidence of local control of disease in the local population, including reduction in tumour size as well as pathological response, the institution protocols can be modified with an aim of promoting breast conservation surgery to a greater extent. With evidence of reducing tumour size, breast conservation surgery after neo adjuvant chemotherapy can become the standard mode of treatment in majority of cases.

Conservation of breast can have a highly positive impact on the morale of the women undergoing treatment — with marked reduction in the psychological and emotional trauma associated with removal of the breasts, especially in younger age groups, in addition to reducing the long term physical distress associated with mastectomy.

Impact on disease free survival and overall survival

The follow up period was limited to six months due to time constraints. This period proved too short to study disease free survival as well as overall survival rates. Both the neo adjuvant chemotherapy group and the primary surgery group did not show any case of recurrence - either locally or regionally nor did it show any evidence of metastases locally or at distant sites. This highlights the need for following up the same cohort for longer periods preferably two years to look for evidence of recurrence and for a minimum period of five years to look at overall survival rates.

Limitations of the study

The follow up period of six months was too short to identify differences in overall survival rates and disease free period and hence one of the objectives of the study could be met only partially.

Strengths of the study

1. This is one of the few studies which have looked into the impact of neo adjuvant chemotherapy in the local population catered to by this institution.
2. This study can guide development of treatment protocols specific for the local population.

Recommendations

1. There is a need to develop a well defined protocol for deciding between NAC and primary surgery in case of Intermediate breast cancers (T3N0M0 and T3N1M0)
2. The study group needs to be followed up for longer period to obtain clear evidence of benefits of neo adjuvant chemotherapy in long term survival and disease free interval.

CONCLUSIONS

This study has tried to understand the impact of chemotherapy for breast cancers administered using two different methodologies -- as neo adjuvant chemotherapy and as adjuvant chemotherapy after primary surgery. The most obvious of the results is the need to develop a protocol specific to the local population, which stresses on the usefulness of neo adjuvant chemotherapy and its use to increase breast conservation surgery and replace mastectomy with breast conservation in maximum possible proportion of cases. This could have a tremendous impact on the psychological and emotional well being of women undergoing the trauma of breast surgery.

More importantly, the study needs to be continued for longer follow up to understand the long term impacts of neo adjuvant chemotherapy. We hope that this study marks a beginning of such interventions as well as concomitant research to look into the feasibility of breast conservation in all but the most advanced of breast cancers, thus paving way for mainstreaming a group of women marginalized by the impact of a disease on their body images.

References

1. Ferlay J BF, Pisani P, Parkin DM. GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0. 2001.
2. Programme NCR, Time Trends in Cancer Incidence Rates 1982-2005. Bangalore, India: *Indian Council of Medical Research*; 2009.
3. Dhillon PK, Yeole BB, Dikshit R, Kurkure AP, Bray F. Trends in breast, ovarian and cervical cancer incidence in Mumbai, India over a 30-year period, 1976-2005: an age- period-cohort analysis. *Br J Cancer*; 105:723-30.
4. Dhillon PK, Yeole BB, Dikshit R, Kurkure AP, Bray F. Trends in breast, ovarian and cervical cancer incidence in Mumbai, India over a 30-year period, 1976-2005: an age- period-cohort analysis. *Br J Cancer;* 105:723-30.
5. Yeole BB, Kurkure A, Advani S, Lizzy S. An Assessment of Cancer Incidence Patterns in Parsi and Non Parsi Populations, Greater Mumbai. *Asian Pac J Cancer Prev* 2001; 2:293-8.
6. Agarwal G, Pradeep P V, Aggarwal V, Yip CH, Cheung PS. Spectrum of breast cancer in Asian women. *World J Surg* 2007; 31: 1031-40.
7. Agarwal G, Ramakant P, Forgach ER, et al. Breast cancer care in developing countries. *World J surg* 2009; 33:2069-76.
8. Breast Cancer Factsheet, Preet K Dhillon. South Asia Network for Chronic Disease, Public Health Foundation of India.
9. Chopra R. The Indian Scene. *J Clin Oncol* 2001;19: 106s-l11s.
10. Collyar DE. Breast cancer: a global perspective. *J Clin Oncol*. 2001 Sep 15; 19(18 Suppl): 101s-105s.
11. Schssartsmann G. Breast cancer in South America: challenges to improve early detection and medical management ofa public health problem. *J Clin Oncol*. 2001 sep 15; 19(18 Suppl): 118s-124s.
12. Höffken K. The European experience. *J Clin Oncol*. 2001 Sep 15;19(18 Suppl): 112s-117s.
13. VorobiofDA, Sitas F, VorobiofG. Breast cancer incidence in South Africa. *J Clin Oncol*. 2001 sep 15; 19(18 Suppl): 125s-127s.

****