TO STUDY THE RECEPTOR STATUS BEFORE AND AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CARCINOMA

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ABSTRACT
Breast cancer is a major public health problem for women throughout the world, being the leading cause of cancer death amongst females after carcinoma lung. Treatment of carcinoma breast is multimodal including surgery, radiotherapy, chemotherapy, and the hormonal therapy depending upon the HPE and IHC reports (ER, PR, HER-2-NEU and Ki 67). We conducted an observational study in which the HPE and IHC reports before and after the administration of systemic therapy in the patients with locally advanced breast cancer (LABC) was compared. The preoperative HPE and IHC reports were obtained by the core needle biopsy. Response of the disease so obtained after the NACT was evaluated with RECIST criteria and depending on the type of response (complete and partial), patients were subjected to surgical treatment (Modified radical mastectomy) The final reports of HPE and IHC of MRM specimen thus obtained was compared with preNACT HPE and IHC report. From our study we concluded that NACT brings about a change in the ER, PR, HER-2-NEU and Ki-67 receptor status in carcinoma breast which can change the management of the patient in view of target based therapy and hormonal therapy in the post operative period.

INTRODUCTION
Breast cancer is defined as a group of diseases in which the cells in breast tissue divide uncontrolled, typically resulting in a lump or mass. Breast cancer accounts for major cancer deaths amongst the females after carcinoma lung. There is found to an increase in the incidence of breast cancer by 0.3% per year whereas the breast cancer deaths has shown a decline. Depending on the origin from the tissue the breast cancer are classified as ductal carcinoma (ductal cells), lobular carcinoma (milk secreting glands), sarcomas (Phylloides tumour and angiosarcoma). Carcinoma breast patient presents to us with complaints of a painless breast lump with or without nipple discharge, sometimes an axillary swelling, nipple retraction and edematous or excoriated nipple. Some are incidentalomas found while doing screening sono-mammography. Mammography is the screening investigation of choice for the females above 40yrs of age where the breast tissue is less dense in order to identify the carcinoma breast in a preclinical stage. Ultrasonography is used for same reason in the females below the age of 40 yrs or in the patients with the denser breast tissues. MRI is used when bilateral disease is suspected or large pendulous breasts, recurrences from the previous sites or other investigation modalities fail to characterise the lesion. Histopathological examination is considered the gold standard for the diagnoses of the carcinoma breast. It is done by FNAC, core needle biopsy or if indicated, excisional biopsy can be performed. Core biopsy is the current standard of care for evaluation of masses in breast as it can tell us the histological architecture, invasiveness and the IHC of the specimen. Metastatic workup of the patient is warranted in the cases of LABC and the ones with the symptoms.
Treatment offered to the patient is multimodal including Surgery, Radiotherapy, chemotherapy and the hormonal therapy depending upon the HPE and IHC reports. Surgical treatment includes modified radical mastectomy and sometimes the breast conserving surgery. LABC includes –

1. Large primary tumour with more than 5 cm in size (T3).
2. T4 tumour with chest wall involvement.
3. Peau – d orange appearance or ulceration of skin or inflammatory cancer.

Extensive lymph node involvement is defined by N2 and N3 categories from the AJC cancer TNM classification system. Operable LABC undergo modified radical mastectomy combined with adjuvant chemotherapy and radiotherapy followed by hormone therapy depending upon hormone receptor status on HPR.

Now NACT is the standard care for treatment of LABC. Downstaging by NACT allows breast surgery to be undertaken in most patients considered inoperable prior to treatment and even permits breast conservation surgery in some.

Outcome of the NACT is assessed by the RECIST criteria which is as follows:

- **Clinical complete response (cCR)**: complete disappearance of all target lesions. Any pathological lymphnodes must have reduction in short axis < 10mm.
- **Clinical partial response (cPR)**: 30% decrease in the tumour size, in its maximum dimension.
- **Stable disease (SD)**: Neither sufficient shrinkage to be called as PR nor increase in size to be qualified as PD.
- **Progressive disease**: 20% or more increase in tumour size or appearance of new metastasis.

The present study is an effort to study the effect of NACT in patients of breast cancer in terms of changes in ER, PR, Her-2-neu, and Ki-67 receptor status, sensitivity of the chemotherapeutic agents and to see the response as per the RECIST criteria.

**MATERIAL AND METHODS**

The study is a prospective study conducted in the department of General Surgery, Pt. B. D. Sharma PGIMS, Rohtak. All patients of LABC presenting in surgery OPD were included in the study except the patients in whom chemotherapy was contraindicated, the inoperable breast cancers and the metastatic breast carcinoma patients. Each patient’s history was recorded and were subjected to triple assessment which involved local examination of breast and axilla, radiological examination and histopathology at the time of initial diagnoses to assess the state of primary tumour in breast and lymph nodes. Metastatic disease was adequately examined by relevant clinical, radiological and biochemical examination. Core needle biopsy was done to arrive at histopathological diagnosis and IHC for ER, PR, Her-2-neu and Ki-67. Then NACT was offered. After the three cycles of NACT, the patients were reassessed clinically and radiologically, and depending on the response surgery was offered, and the specimen was then sent for HPE and IHC. The relevant data was collected, compared and analysed.

**RESULTS**

After the proper collection of the data for the 30 patients, it was compared. The patients response after receiving the NACT as per RECIST criteria was recorded, of which 3.33% of patients had complete response, 83.33% had partial response, 13.33% had stable disease and none showed progressive disease. The skin changes were markedly reduced by NACT, there was 13.33% decrease in peau-d-orange, 20% decrease in puckering and 20% decrease in dimpling. The mean size of clinically palpable lump decreased from 7 cm pre-NACT to 4.10 cm at post-NACT. And similar results were recorded sono-mammographically. There was decrease in the number and the size of the involved lymph nodes in Post NACT patients. All the patients underwent MRM and not BCS due to non availability of LINAC. After the systemic therapy we observed that number of patients in pre NACT phase with ER and PR negative status were 10 in comparison to 13 patients in the post NACT phase. Number of patients with ER negative were increased from 6.6% to 10%, PR negative increased from 3.3% to 6.6% and Her-2-neu negative were increased from 17 to 19 in post-NACT phase. Also the ki-67 value <20% was increased from 13 in pre NACT phase to 26 in post NACT phase thus depicting a decrease in proliferation rate of the tumour cells.

Thus, the HPE and IHC reports of pre NACT and post NACT phase were compared and the observation and related results were very important for the patient management in post surgery planning of endocrine therapy, target based therapy and assessment of overall prognosis, disease free survival and overall survival.

**DISCUSSION**

NACT has become standard of care, for the patients with LABC and is being increasingly used even in early breast cancer patients. The proposed advantages of NACT include making inoperable breast cancers into operable one, downstaging the tumour size, and increasing breast-conserving surgery rates, in vivo testing of chemosensitivity and treatment of the micrometastasis at the early stage of tumour thus improving the prognosis.

Breast cancer is characterized by its cellular heterogeneity, thus NACT might lead to an in vivo selection of a fraction of the tumour cells with different expression levels of tumour biological markers and a different expression levels of tumour biological markers.
and a different phenotype compared to pre-treatment tumour. Prior to NACT tumour biological factors, such as HER-2-neu, ER and PR status, are routinely performed to decide post operative, adjuvant treatment decisions regarding trastuzumab and endocrine therapy. Patients receiving NACT should be re-assessed thoroughly to make sure that the post surgery treatment is tailored to the residual tumour cells. This study was done to get a better insight into breast cancer response to chemotherapy.

CONCLUSION

From our study we can conclude that NACT brings about a change in the ER, PR, Her-2-neu and Ki-67 receptor status in carcinoma breast which can change the management of the patient with regard to hormonal therapy and target based therapy in the post operative period. These changes also play a role in the prediction of overall prognosis, disease free survival and overall survival of the patient. As our study is a small volume study, it needs a much larger volume of patients to better characterize the effect of NACT with regard to these changes.

REFERENCES