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NEOADJUVANT CHEMOTHERAPY FOR LOCALLY ADVANCED PRE-MENOPAUSAL BREAST CANCER IN NIGERIAN WOMEN: EARLY EXPERIENCE

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ABSTRACT

Background: Breast cancer, the commonest female malignancy in Nigeria presents late, with bulky loco-regional masses and predominantly in a pre and peri-menopausal setting. Treatment when feasible has been with mutilative surgery with a poor patient acceptance rate. Chemotherapy which is widely used in adjuvant and metastatic settings has recently been indicated in the neo-adjuvant setting.

Methods: Locally-advanced female breast cancer patients [AJCC Stages IIIA, IIIB, IIIC], seen in the breast clinic from July, 2006 to March 2007 were recruited into the study after informed consent. Patients received doxorubicin, 5-fluoro-uracil and cyclophsphamide by intravenous bolus or infusional injection on a three weekly regimen as day cases. The dominant lesion was assessed by calipers at each visit. Therapeutic clinical responses were assessed as none; partial, complete.

Results: During the period 32 women (33 breast cancers) were seen and recruited. The numbers steadily declined over time and only 28 completed the treatment modality. Mean pre-chemotherapy tumour size was 13.5cm which declined to 7 cm at the 5th. One patient (3.6%) exhibited complete clinical response, 25 (89%), partial response and 2 had no response. No serious toxicities were noted.

Conclusion: Neo-adjuvant chemotherapy using anthracycline based regimens is efficacious and safe in reducing tumour bulk in locally advanced breast cancers. The use should be encouraged to make bulky tumours operable.

Key Words: Neoadjuvant, chemotherapy, advanced, premenopausal breast cancer, Nigeria
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INTRODUCTION

Breast cancer is the commonest female malignancy in parts of Nigeria[1] as it is in most other parts of world[2]. Breast cancer in Nigeria presents late, with bulky loco-regional masses and predominantly in a pre and peri-menopausal setting[3]. Treatment when feasible has been with mutilative surgery [total mastectomy, toilet mastectomy]. Whereas an increasingly higher proportion of patients in the developed world now receive conservative surgery due to earlier presentation and patient education the number of patients receiving such treatment in Nigeria is negligible. The use of neo-adjuvant therapy [hormonal in postmenopausal patients and cancer chemotherapeutic agents in pre-menopausal patients] have achieved significant down-staging in reported series in developed societies leading to more conservative surgery[4,5].

Because of the relative younger age of our patients, hormonal manipulation may not be feasible in the majority.

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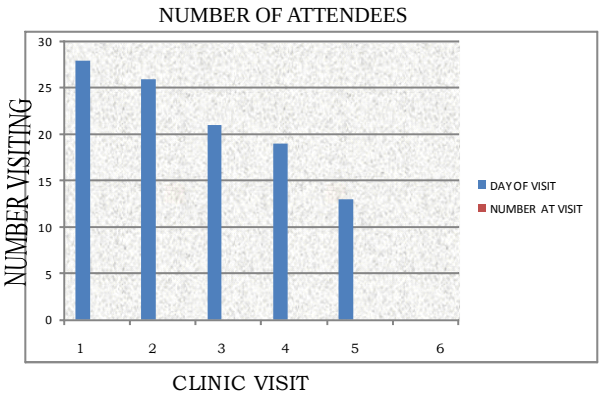
Our previous experiences with cancer chemotherapy in the adjuvant and palliative settings have attested to its acceptability and low rate of side effects[6]. We decided to initiate a study of neo-adjuvant chemotherapy in our pre-menopausal patients with locally advanced breast cancer to see whether significant down-staging will occur.

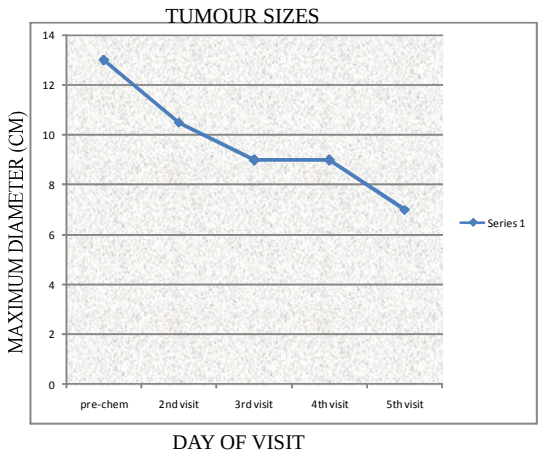
PATIENTS AND METHODS: Locally-advanced female breast cancer patients [AJCC Stages IIIA, IIIB, IIIC] attending the Breast oncology clinics of Nnamdi Azikiwe University Teaching Hospital, Nnewi from July, 2006 to March 2007 were recruited into the study after informed consent. Patients' bio-data, height, weight, menopausal status and blood indices were collected. Primary cancer sites in the breast were measured with calipers at presentation and on subsequent visits. After histological confirmation of invasive ductal breast cancer from corecut biopsies patients were given doxorubicin [50mg/m^2], 5-fluoro-uracil [500mg/m^2] and cyclophsphamide [600mg/m^2] by intravenous bolus or infusional injection on a three weekly regimen as

day cases. On each visit the dominant cancer lesion was measured in two planes with a caliper, haematological indices were assessed and evidence of drug toxicity was sought. Therapeutic clinical responses were assessed as none; if the tumour progressed or showed non-significant [less than 20%] reduction in largest diameter at last assessment; partial, if there was significant [greater than 20%] reduction in largest diameter but mass still palpable; and complete, if no residual tumour was palpable. Facilities for estrogen or other receptors and histiochemistry were not available during the study.

RESULTS: During the period 32 women (33 breast cancers) were seen and recruited. Five women were not seen again after the first dose. Of the 28 evaluable breast cancers (27 women) the numbers steadily declined to 13(46%) remaining at the 5th week. Reasons for dropout were mainly financial as the hospital operated a fee for service.



Mean patient age was 42.8 years [Range 30-49]. Twenty-five women were pre-menopausal and 2 within 5 years of menopause. Twenty percent had no formal education, 15% tertiary education while the rest had combination of primary and secondary education. The mean parity was 3.92 [Range 0-8]. Nine cancers (25%) were IIIA; 16 (57%), IIIB and 3 (18%) IIIC. The mean pre-chemotherapy tumour size was 13.5cm [Range 7-35cm]. This declined steadily to mean of 7 cm at the 5th visit. One patient (3.6%) exhibited complete clinical response, 25 (89%), partial response and 2 had no response. Pre-chemotherapy size of tumour was not related to response rates. Haematologic or other toxicities were minimal, 25% had dose deferment of 1-2 weeks due to decline in platelet (<100,000cu.mm) or haematocrit (< 10g/dl).



DISCUSSION

Results from this study support those of other workers that neo-adjuvant chemotherapy is beneficial to patients with locally advanced breast cancer. Overall, the complete clinical response rate is lower than in other published figures probably due to higher volume primary masses, higher nodal status and other unidentified factors which Fernandez-Sanchez and colleagues[7] and Prisack et al[8] have suggested might cause lower responses. In addition to down-staging the lesions for operability other reported benefits include breast conservation[9] and assessment of in vivo response to further drug treatment[5].

Clinical (caliper) measurement of tumour bulk, though acceptable in low technology societies has been supplanted by use of imaging modalities for tumour assessment. These modalities include ultrasongraphy, MRM, PET and mammography[10-12]. Caliper measurement is believed to give false higher figures[11], probably because of inclusion of skin and subcutaneous tissue in the measurement, and also possible inclusion of peri-tumoral fibrosis with induration.

The side-effect profiles in this study and in similar studies are acceptable even in absence of dedicated medical oncologist in most hospitals.

Addition of taxanes to anthracycline containing regimens have been reported to give better results as is the use of targeted immunotherapies like trastuzumab[13,14]. Whereas hormonal manipulations using tamoxifen or aromatase inhibitors in estrogen receptor - positive and estrogen receptor unknown post-menopausal patients have been associated with better response and less toxicity, breast cancer still remains a mainly pre-menopausal disease in many parts of the developing world and the use of hormone therapy in this group is still controversial. Hopefully availability of more radiotherapy services and extension of neo-adjuvant therapy to AJCC stage I and II lesions may lead to wider availability and

acceptance of breast conservation in the 3rd world. This might mark a turning point in the fight against the disease where a vicious cycle of ignorance, high mortality and fear of mutilative surgery have conspired to make patients present late to orthodox practitioners.

CONCLUSION

Neo-adjuvant chemotherapy using anthracycline based regimens is efficacious in reducing tumour bulk in locally advanced breast cancers. Since 3rd world breast cancers still present late addition of neo-adjuvant chemotherapy in the treatment guidelines might improve operability and reduce gloom associated with disease.

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