SURGICAL ONCOLOGY

Myelo-Suppressive Effects of Breast Cancer Chemotherapy in Nigerian Patients

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ABSTRACT

Breast cancer has become a major surgical burden in Nigeria as in other developing countries. Unlike in `Western societies where the tendency is towards earlier discovery when there are higher chances of cure, the disease still presents late in many African countries. In the absence of regular access to radiotherapy, chemotherapy is the major adjuvant treatment for pre-menopausal lesions in the third world. A prospective study of the myelo-suppresive effects of chemotherapy was undertaken in two hospitals by a single surgical practice between 1994 and 1997. Of the 64 patients treated within the period, 42 were evaluable as they completed the treatment and did not take concurrent native medication or radiotherapy. There was a depression of the blood indices with haematocrit being the least affected. Depression in neutrophil count though significant did not reach neutropaenic levels. Platelet depression was more marked towards the end of treatment. Twenty-five percent of the patients had dose-deferment of less than 2 weeks due to low haemoglobin or platelet count. It is concluded that with adequate monitoring cancer chemotherapy at recommended doses is feasible as outpatient treatment in third world countries ***(Nig J Surg Res 2000; 2:81-87)***

KEY WORDS: Breast cancer, Chemotherapy, Myelo-suppression

Introduction

Breast cancer has been recognized as a major public health hazard in recent years. With an estimated incidence of some one million new cases a year worldwide [1,2] and an increasing incidence in hitherto low incidence areas, [3,4] breast cancer is expected to constitute an increasing burden on already inadequate healthcare facilities. Survival from breast cancer has improved over the years notably from earlier diagnosis [5,6] and consequent stage-shifting [7], and from adjuvant treatment of early breast cancer. [8-10] For metastatic breast cancer, whereas addition of chemotherapy has resulted in improved palliation and a longer disease-free interval, overall survival has not significantly improved.

Myelo-suppression is the commonest life-

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threatening complication of cytotoxic chemotherapy. Neutropaenia is indeed the commonest dose-limiting toxicity with use of chemotherapy.[11] In advanced communities attempts to avoid this complication has necessitated the recommendation of regional chemotherapy.[12] Treatment of myelo-suppression including that resulting from escalated drug doses have included autologous blood stem cell transplantation[13] and agents such as recombinant human erythropoeitin [14] or colony-stimulating factors.[15] In the third world, however, the magnitude of the marrow depression at recommended doses has not been adequately addressed but fear of its possible effects and the absence of rescue facilities has led some to recommend the use of sub-optimal drug doses.[16] We decided to review the haematologic effects in patients receiving chemotherapy for breast cancer in order to determine the safety or otherwise of this treatment modality.

Patients and Methods

Pre-menopausal female patients with a histologic diagnosis of breast cancer undergoing chemotherapy treatment at Nnamdi Azikiwe University Hospital, Nnewi and Ace Specialist Hospital, Onitsha both in Anambra State of Nigeria between January 1994 and June 1997 were recruited into a prospective study.

Chemotherapy was used as adjuvant treatment for Stage I and II lesions and palliative treatment for Stage III and IV lesions in pre-menopausal patients. All the patients had mastectomy (either simple, modified radical or toilet) with wound healing before the commencement of chemotherapy. Investigations performed before starting chemotherapy included haematocrit, white cell count, platelet count and packed cell volume. These were performed weekly in a single laboratory according to standard methods.

Standard chemotherapy doses were given with:

Oral cyclophosphamide 50mg thrice a day from Day 1 to Day 14

Intravenous methotrexate 50mg on Day 1 and Day 8

Intravenous 5-fluorouracil 500mg on Day 1 and Day 8.

Due to cost implications involved in discarding opened vials exact calculations based on body surface area was not used as the same dose was used for all patients. Adjunctive treatment included fluids for adequate urinary output and intravenous metoclopamide for occasional patients with vomiting. The cycle was continued monthly for a period of 6 months. A dose was deferred if the blood indices showed a haemoglobin concentration below 10g/dl; white cell count below 2,500 per cu.mm; or platelet count below 100,000 per cu.mm. Patients who had radiotherapy as part of therapy were excluded. Also excluded from further analysis were those unable to complete the course as prescribed.

Statistical analysis was by the Student's 't' test of the difference between means.

Results

During the period 64 patients with cancer of the breast were treated by surgery and chemotherapy. Of these, 42 patients were studied. The remaining did not complete the therapy because of financial reasons (15 patients), or took concomitant native medication (3 patients) or had incomplete

Figure 1: Mean haemoglobin concentration during treatment (g/dl)

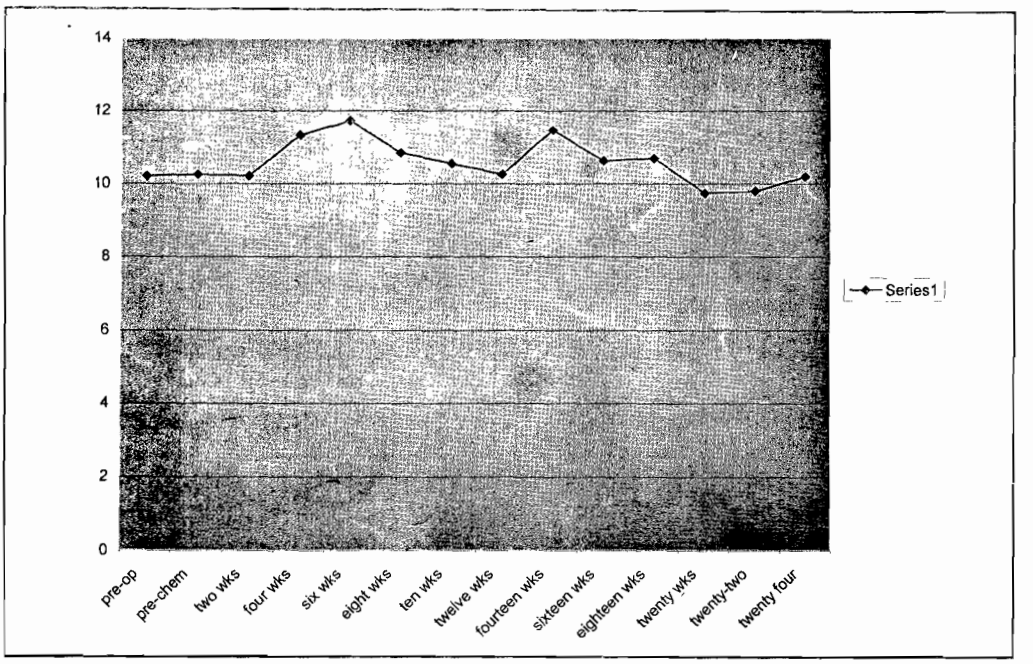


Figure 2: Changes in platelet count

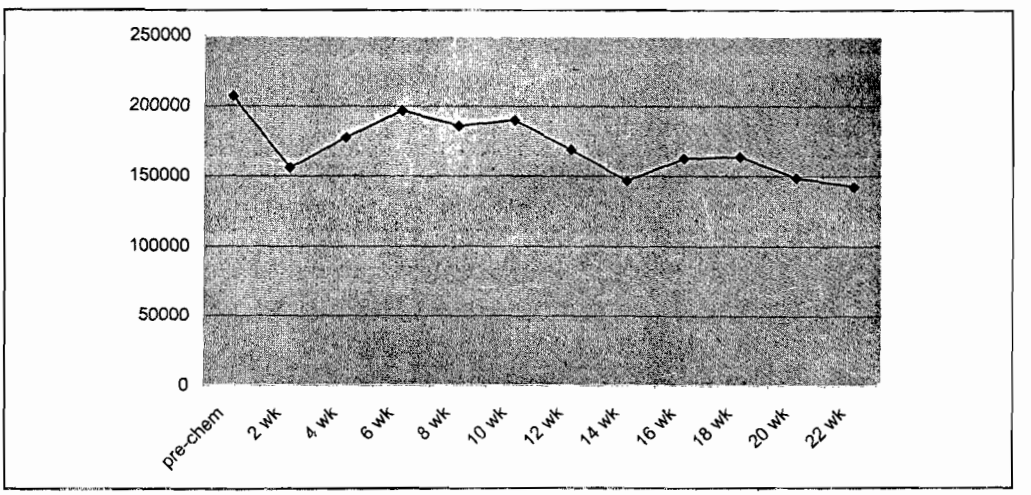
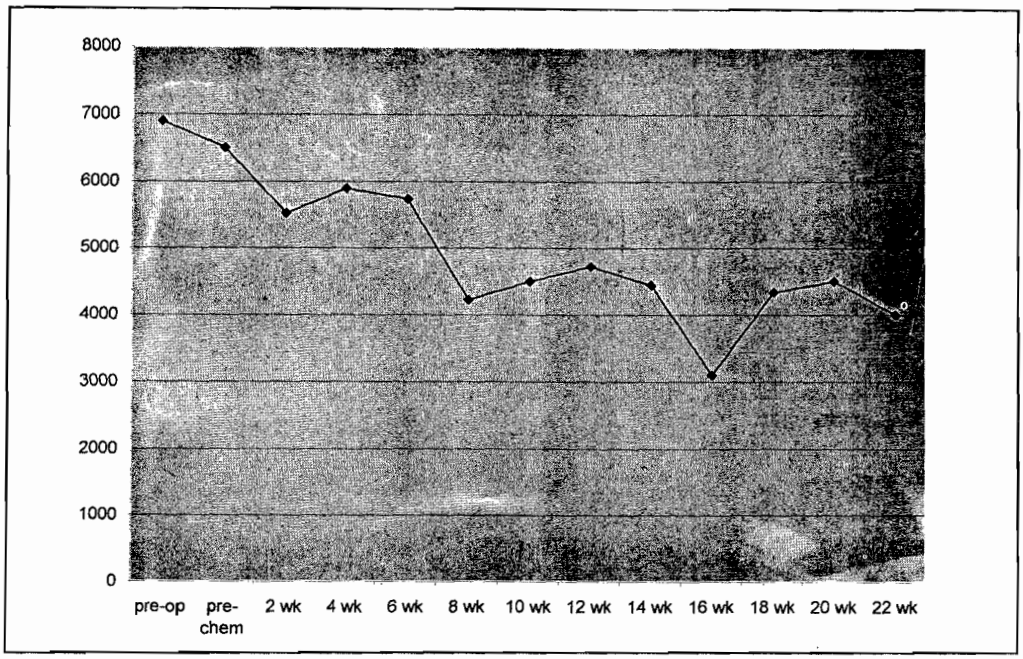


Figure 3: Changes in white blood cell count (/mm^3).



results (4 patients).

There was no death amongst the patients studied. Intercurrent illnesses recorded during treatment were mainly malaria (5 patients; good response to chloroquine).

Of the 42 evaluable patients 18 were Stages I and II, while 24 were in Stages III and IV. The ages ranged from 32 to 51 years with a mean of 45.2 years.

Haemoglobin concentration: The mean pre-operative haemoglobin concentration was 10.21g/dl (Range 9 – 12.5). At the start of chemotherapy the mean haemoglobin concentration was 10.25g/dl. There was a mild increase within the 4-10 week period with a subsequent fall at 20-22 weeks. The changes were not statistically significant ($p>0.05$). Low haemoglobin concentration (<10g/dl) caused a delay in therapy on 6 occasions. The mean haemoglobin concentration is shown in Figure 1. Differential analysis of the data for early and advanced disease did not show any significant difference in depression of haemoglobin.

Platelet concentration: The mean pre-chemotherapy count was 207,000/cu.mm. There was a significant immediate fall to 156,000/cu.mm ($p<0.01$) at two weeks followed by recovery to almost normal levels at 6 weeks and a subsequent steady slow decline in count throughout the treatment period as indicated in Figure 2. Falls to below 100,000 occurred in 6 patients at 2 weeks and in 1 patient at 14 weeks necessitating a

weekly delay in each case. At the completion of treatment mean count of 142,000 was significantly less than pre-treatment values ($p<0.01$)]. Platelet count depression affected patients with both advanced and early disease.

White cell count: The mean pre-chemotherapy count was 6,500/cu.mm. At 8 weeks the decline in mean count [4,225/cu.mm] had reached levels of statistical significance ($p<0.01$). This decline continued steadily during the treatment period averaging just 4,000/cu.mm at the end of treatment. The count was below 2,500/cu.mm in 5 patients at 16 weeks necessitating a deferment of therapy for a week in 3 cases and 2 weeks in 2 cases. The decline in white cell count was significantly more ($p<0.05$) in patients of all ages with advanced disease. On the whole there was deferment of therapy in 10 patients (24%) but in all cases a one to two week delay was enough to get the patient fit again.

There were no infective crises and no patient had a bleeding dyscrasia.

Discussion

Breast cancer contributes an increasing load on the practice of surgery in Nigeria. Unlike previous reports indicating that breast cancer is rare in blacks recent findings indicate that the hospital incidence is indeed increasing in Nigeria[17-21] and in other parts of the third world. Indeed at the Nigerian National Cancer Registry based in Ibadan, Nigeria breast cancer has overtaken cancer of the cervix uteri as the commonest cancer in Nigerian females.[22] Unfortunately the disease still presents late with a majority of cases at Stages III and IV when hopes of 'cure' may be unrealistic. In the absence of radiotherapy facilities in most parts of the country and poverty that precludes travel to the few centres, chemotherapy and hormonal manipulation will remain the main non-surgical means of control in the near future.

Whereas genuine fears have been raised about toxicity of chemotherapy on outpatient treatment[16] the results shown in this study show that chemotherapy either as adjuvant in 'early' breast cancer, or as therapy in advanced disease is associated with tolerable haematopoietic side-effects. Depression of white cell count seems to be the most profound effect and this seems to persist during the period of treatment. This depression did not reach neutropenic levels (<1000 per cu. mm) during the study period, like in other reports[12-13] in which neutropenia has been identified as rate-limiting factor in dosage. Patients need to be closely monitored to prevent infective crises.

The haematocrit remained at near baseline values as the treatment progressed. There was a slight increase after 4 weeks presumably as part of recovery from surgery. In a few patients, the persistence of anaemia required the deferment of some doses. Towards the termination of treatment however there was a trend towards a fall which did not reach levels of significance.

The platelet count was adversely affected in the immediate treatment period falling significantly within 2 weeks. There was equally rapid recovery approaching pre-chemotherapy levels at 6 weeks. However thereafter a steady decline ensued throughout the rest of the period but again this did not fall below critical levels (<100,000per cu. mm).

On the whole chemotherapy was well tolerated. Whereas almost 25% of the patients had some dose deferment this was temporary lasting a maximum of 2 weeks. Most

importantly however, there were no life threatening effects as the only major morbidity seen was malaria which is endemic in the community. There were also cases of nausea easily controlled by metoclopramide medication.

Conclusion

Breast cancer advanced at presentation is a common problem in Nigeria. Until facilities including availability of radiotherapy improve the treatment modalities will remain some form of surgery combined with chemotherapy and hormonal manipulation. Cancer chemotherapy is feasible on outpatient basis as side-effects are low and easily controlled. Proper monitoring of the patients will be required of any practitioner involved in this care.

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