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Original Research Article

Evaluation of Epirubicin, Cyclophosphamide and Paclitaxel-based Chemotherapy Response for Treatment of Breast Cancer Patients as Neo-Adjuvant: A Case-Series in a Tertiary Care Hospital in Bangladesh

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Abstract: ***Background*:** Breast cancer is the most common cancer among women across the world. Various treatment modalities in terms of radiotherapy, chemotherapy or surgery along with several neoadjuvant or adjuvant therapies are already established for the better survival of the patients. New modalities are still under research every other day for improvement of quality of life of cancer victims. ***Objective***: This case series was conducted to assess the efficacy and safety profile of primary breast cancer patients by adding Paclitaxel to the established regimen of Epirubicin and Cyclophosphamide. ***Methods*:** This was performed during January 2019 to January 2021 with 9 cases of clinically diagnosed breast cancer patients at Combined Military Hospital, Dhaka. Patients included in our study received Epirubicin in the dose of 75-100 mg/m^2 dl, Cyclophosphamide 600 mg/m^2 dl, every 3 weeks for a total of 4 cycles followed by Paclitaxel at a dose of 175 mg/m^2, every 3 weeks for a sum of 4 cycles. After every cycle of neoadjuvant chemotherapy and at the end of it, response was assessed by ultrasound. ***Results*:** The findings revealed 6 out of 9 patients showed pathological complete response at the end of this neoadjuvant regimen. The remaining 3 cases showed partial response. Toxicity was minimal and well-managed. 5 patients developed leukopenia in terms of haematological events, whereas for other effects, nausea and fatigue was commonly encountered. ***Conclusion*:** Overall, this treatment modality turned out to be feasible and a good option for neoadjuvant therapy in terms of efficacy and safety profile for the breast cancer patients.

Keywords: Breast cancer, Epirubicin, Cyclophosphamide, Paclitaxel, Neoadjuvant, Chemotherapy.

INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy in women and the main cause of cancer deaths, accounting for 25% of all cancer diagnoses (1.68 million) and 15% of all cancer deaths (520,000) worldwide [1]. Bangladesh is the world's ninth most populous country with 172 million inhabitants. In Bangladesh, there are 1.3 to 1.5 million cancer patients with roughly 0.2 million new cancer patients diagnosed each year [2, 3]. Breast cancer is estimated to affect 22.5 per 100000 females in Bangladesh; among Bangladeshi women aged 15 to 44 years, breast cancer has the greatest frequency of 19.3 per 100000, compared to any other type of cancer. Substantial efforts have been undertaken to increase overall survival in patients with breast cancer and disease management approaches towards breast cancer are changing from traditional mortality reduction to complete therapy which allow curation or recurrence reduction. The disease is localized to the breast at

presentation in 61% of cases, regionally advanced in 32% and lastly metastatic in 7% [3].

Neoadjuvant chemotherapy can be regarded as an effective therapeutic option for breast cancer patients. Improvement of operability and breast-conserving surgery rate are observed. In addition, various trials contribute to the fact that, neoadjuvant and adjuvant chemotherapy result in better progression-free and overall survival [4].

Taxanes when administered concurrently with anthracyclines have demonstrated major improvements in disease-free as well as overall survival in breast cancer patients. A previous randomized trial in 2002 in China has shown a remarkable survival for the patients, who were lymph node positive breast cancer cases [5]. Treating metastatic breast cancer with paclitaxel demonstrated a major overall response rate in terms of efficacy when compared to the conventional EC regimen. In addition, it was well-tolerated as well [4].

Epirubicin is found to be less cardiotoxic as well as less myelosuppressive than paclitaxel, however, there is no difference in anti-tumor effectiveness and efficacy [5].

Along with suggestive evidences of enhanced effectiveness, safety profile and reduced toxicities in this treatment protocol and lack of similar study in our national context, this case series aims to elaborate the findings of such cases where EC regimen along with paclitaxel was administered.

MATERIALS AND METHODS

We took data for this case series from the cancer center of a tertiary care hospital situated in Dhaka named Combined Military Hospital. Patients with clinically diagnosed early or locally advanced breast cancer by physical examination and imaging tests were our cases. The presenting cases were included after confirmed diagnosis by core biopsy. This study was conducted during the period January 2019 to January 2021. A total of 9 patients were enrolled in this series. All the patients included in our study received epirubicin in the dose of 75-100 mg/m^2 dl, cyclophosphamide 600 mg/m^2 dl, every 3 weeks for a total of 4 cycles followed by paclitaxel at a dose of 175 mg/m^2, every 3 weeks for a sum of 4 cycles. After every cycle of neoadjuvant chemotherapy and at the end of it, response was assessed by ultrasound. Response was defined as pCR if no residual tumor cells were found in the breast as well as the axillary lymph nodes.

We included those patients who underwent subsequent surgery after chemotherapy and got a post-operative pathological diagnosis. The patients had normal cardiac function with left ventricular ejection fraction ≥50% by Echocardiography before treatment. We excluded those patients who previously took other anti-cancer drugs or suffered from other serious conditions which would affect the treatment outcomes, for instance pulmonary heart disease, severe renal insufficiency, any other malignancy and so on. The main aim was to assess the overall efficacy, safety profile and toxicity levels among these patients. Clinicopathological characteristics collected were age, TNM staging at baseline and post-surgery, baseline immunohistochemistry and overall response. The haematological findings and cardiac examinations were recorded after completion of chemotherapy for toxicity assessment. All of them gave their written informed consent regarding chemotherapy with epirubicin and cyclophosphamide regimen followed by paclitaxel and documentation of their data.

RESULTS

Table 1: Patient and tumor characteristics with clinical outcome (n=9)

Case number	Age (years)	TNM staging at baseline	Baseline immunohistochemistry	TNM staging post-surgery	Response
1	35	T3, N1, M0, G2-3	ER 20%, PRG 20%, HER2+, Ki67 30%	ypT1 mic, pTis (DCIS, 95%), pN0 (0/15), M0, G3, R0.	PR
2	33	T3, N1, M0, G2	PRG 50%, HER2+, Ki67 50%, ER 30%	ypT0, ypN0 (0/20), M0, L0, V0, R0	pCR
3	30	T3, N2, G3	PRG 5%, HER2+, Ki67 60%, ER 5%	ypT0, ypN0 (0/12), M0, V0, L0, R0	pCR
4	48	T3, N2, M0, G3	PRG 0%, HER2-, Ki 67 30%, ER 0%	ypT0, ypN0 (0/13), M0, L0, V0	pCR
5	44	T2, N0, M0, G3	PRG 0%, HER2-, Ki67 30%, ER 0%	ypT0, ypN0 (0/10), M0, L0, V0, R0	pCR
6	32	T2, N0, M0, G3	PRG 0%, HER2-, Ki67 90%, ER 0%	ypT0, ypN0 (0/16), M0, L0, V0	pCR
7	33	T1, N0, M0, G3	ER 90%, PRG 10%, HER2-, Ki67 20%	ypT1a, pN0 (0/2 sn), M0, G2, L0, V0, R0	PR
8	58	T2, N0, M0,	ER 95%, PRG 95%, HER2-,	ypT1a, pN0 (0/11), M0,	PR

		G3	Ki 67 25%	G3, L0, V0, R0	
9	65	T2, N1, M1 (liver), G2-3	ER 5%, PRG 15%, HER2-, Ki 67 40%	ypT0, ypN0 (0/10), M0, L0, V0	pCR

*TNM: Tumor, Lymph Node and Metastasis staging; ER: Estrogen Receptor Expression; PRG: Progesterone Receptor Expression; HER2: Human Epidermal Growth Factor Receptor 2; Ki 67: percentage of positively stained tumour cells among the total number of malignant cells assessed; yp: assesses the pathologic stage for patients who have surgical resection following neo-adjuvant therapy; PR: Partial Response; pCR: Pathological Complete Response.

From the period of January 2019 to January 2021, 9 patients with clinically diagnosed or locally advanced breast cancer who were diagnosed confirmedly by core biopsy were part of this case series. Table 1 illustrates the detailed overview of the patients, tumor characteristics and clinical outcomes. Their mean age was 41.50 (± 12.030) years. Tumor sizes were 1.6 to 10.0 cm in diameter. Among the patients, 3 patients were HER2+ and the rest were HER2-. After completion of neoadjuvant chemotherapy, all patients demonstrated responses. Out of 9 patients, 6 patients responded with pathological complete response and the rest 3 with partial response.

Table 2: Adverse events experienced during neoadjuvant therapy (n=9)

Case number	Adverse event(s)
1	Haematological: leukopenia; Non-haematological: nausea
2	Haematological: none; Non-haematological: mucositis
3	Haematological: anemia; Non-haematological: fatigue, mucositis
4	Haematological: leukopenia; Non-haematological: nausea; fatigue
5	Haematological: anemia; Non-haematological: nausea
6	Haematological: leukopenia; Non-haematological: sensory polyneuropathy; hand-foot syndrome
7	Haematological: leukopenia; Non-haematological: nausea; mucositis
8	Haematological: anemia Non-haematological: nausea; fatigue
9	Haematological: leukopenia Non-haematological: hand-foot syndrome; fatigue

Table 2 above illustrates the adverse events experienced by the patients. In terms of haematological toxicities, 5 patients suffered from leukopenia whereas anemia was found in 3 patients. Only 1 patient was found without any haematological adversities. Regarding non-haematological toxicities, 5 patients had nausea; 4 of them fatigue; 3 patients were found to suffer from mucositis; 2 from hand-foot syndrome and only 1 patient experienced sensory polyneuropathy as a result of neoadjuvant chemotherapy.

DISCUSSION

In this series of 9 cases, neoadjuvant therapy with EC regimen followed by paclitaxel; 4 cycles each for locally advanced breast cancer cases turned out to be a potential therapeutic modality. The results obtained are more or less similar to previous literature, although it is known these data have their own limitations.

We found 6 out of 9 cases to demonstrate pathological complete response. A case series conducted in Germany in 2014 showed pathological complete response in 11 out of 16 patients [4]. A clinical trial conducted from 2010-2016 in China revealed that 5-year disease-free survival (DFS) for breast cancer patients receiving this treatment regimen was 81% and 5-year overall survival (OS) was 95% [6].

Regarding the adverse effects, 5 out of 9 patients had leukopenia, whereas 3 of them were found to have anemia. In addition, 5 patients had nausea, 4 of them developed fatigue and so on. A case series in Germany revealed findings somewhat consistent with our series. They found that, leukopenia was present in 13 out of 16 cases. However, anemia was present in only 4/16 cases. In addition, nausea was a prominent finding (12/16) followed by fatigue (9/16) [4]. Another trial in China showed, leukopenia, anemia, nausea were found more frequent in patients as compared to fatigue which was minimal (14.8% patients) [6].

Previous study conducted in Japan during 2008 demonstrated that this regimen was feasible and without serious complications [7].

Major drawback of this case series was the limitation in the number of patients. If more patients could have been enrolled, then better results could have been obtained.

CONCLUSION

This case series revealed that this Epirubicin and Cyclophosphamide regimen along with Paclitaxel as neoadjuvant chemotherapy for locally advanced breast cancer patients was very effective as well as well-tolerated.

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