



Assessment of Patient's Response about Adverse Drug Reactions Receiving AC (Adriamycin, Cyclophosphamide) Therapy: A Survey Research

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Authors' contributions

This work was done in collaboration among all the authors. Author JJ designed the study. Authors AD and NM supervised and performed the analysis. Authors URM and MAK wrote the first draft of the manuscript. Author SM analyzed the data. Authors YQ and TK managed the literature search writing of the final manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Adverse drug reactions (ADRs) are most common among cancer patients receiving treatment. AC therapy which is a combination protocol of Adriamycin (doxorubicin) and Cyclophosphamide are the common therapies used for breast cancer treatment due to their effectiveness and cost of therapy breast cancer. AC combination is administered every 3 weeks, and 4 cycles are given.

Objectives: To assess various ADRs reported by patients on AC combination therapy and their severity to ensure safe and effective treatment.

Design: Prospective observational.

Setting: Cancer hospital Jamshoro Pakistan.

Patients and Methods: A hospital based observational study included 160 female patients suffering from breast cancer and receiving AC combination for treatment by purposive sampling method from June 2015- January 2018 at cancer hospital Jamshoro Pakistan. ADRs reported were compared against international standard references of drug literature such as British National Formulary (BNF) 2017 and ADR severity assessment scale (Modified Hartwig and Siegel scale).

Main Outcome Measures: Frequency and severity of ADRs.

Results: The common ADRs reported were, nausea and vomiting, acidity, fatigue, hair fall as common non-hematologic and leukopenia among hematologic ADRs. Those patients reported high severity ADRs according to severity scale persist for longer duration and required antidote for management with medical intervention.

Conclusion: The present study shows that a patient's response towards AC therapy is critical and therefore each patient must be monitored and those at high risk of developing ADRs from this therapy must be provided additional care.

Keywords: AC therapy; Adriamycin; Cyclophosphamide; ADRs.

1. INTRODUCTION

Breast cancer most frequently arises in females including developed and developing countries and accounts for up to 23% of the malignancies affecting females even in developed countries. Breast cancer is a tumor that occurs in the cells of the breast and usually is malignant in nature means that has the capability to invade surrounding tissues but also to spread into the other body parts or organs. It is a disease of female origin, but male is also at risk of developing such condition. There are many risk factors that lead to the development of breast cancer but their role in development is not fully understood yet. These include age, family history, late menopause, first child at the older age, etc. are common risk factors. Hormones usually seem to play a major role in developing but their mechanism is not clear. Others include diet, alcohol consumption, etc. The symptoms that are helpful in diagnosing breast cancer include a lump formation in the breast is most common type it may be painful or painless, hard in nature with edges or tender, soft or circular form. Others include swellings that may be with or without lump, irritation in the skin, breast pain or in the nipple, nipple retraction, discharge, etc [1,2].

The treatment of breast cancer involves chemotherapy, radiotherapy, and surgery depending upon the type of tumor and stage of the disease. Chemotherapy is a systemic therapy and proved more efficient in the treatment and for the best outcome, a combination is preferred for prescription and therefore it has reduced the recurrence in up to half of the patients received as claimed by the survey reports [3-5].

A variety of chemotherapeutic agents are available for cancer treatment and for breast cancer treatment anthracyclines such as doxorubicin, daunorubicin, epirubicin, etc. Cyclophosphamide, taxes including paclitaxel, docetaxel, etc. 5-fluorouracil, usually a combination of 2 or 3 drugs specified above are given among which AC (Adriamycin/doxorubicin and cyclophosphamide) combination therapy is one of the effective regimen for treatment. Doxorubicin and Cyclophosphamide are used to treat various types of cancer but their combination is preferred for breast cancer. The combination has given cycles which are repeated every 21 days and continued for 4 cycles at the dose of 60/600 mg/m² [1,6,7]. AC abbreviated as Adriamycin/doxorubicin and cyclophosphamide therapy. Doxorubicin is one of the effective anthracycline antibiotics used to treat a variety of cancers. Cyclophosphamide is a nitrogen mustard class of antitumor drugs effective in a variety of types of tumors. A combination of both serves as best as adjuvant therapy to remove traces of cancer cells left behind after surgical intervention. Adverse effects of both drugs include nausea, vomiting, alopecia bone marrow suppression cardiotoxicity especially by doxorubicin which affects the functioning of the heart [8-10]. Both drugs can be successfully given to the patients as it is very effective for solid tumors and for also as palliative therapy can reduce the discomforts associated with cancer in terminally ill patients [11-21].

2. PATIENTS AND METHODS

A hospital-based observational study included 160 female patients suffering from breast cancer. The patient's diagnosis was confirmed via

mammography and biopsy and those receiving AC combination for treatment were selected by purposive sampling method from June 2015-January 2018 at Cancer Hospital Jamshoro Pakistan. The questionnaire was validated in initial 60 patients. ADRs reported were compared against international standard references of drug literature for verification such as the British National Formulary (BNF) 2017 and ADR severity assessment scale (Modified Hartwig and Siegel scale).

2.1 Patient Selection Criteria

Female patients aged 18 or above on AC therapy capable to respond the desired questions of the study.

3. RESULTS

The study included 160 patients on AC therapy, age group between 41-60 appeared common group affected with the breast cancer represented by Table 1, mean age found was 44.41 years. The majority of the patients were with infiltrating cancer with a prevalence of approximately 78.12%.

AC patients responded in a different manner towards the therapy in terms of ADRs and the majority showed multiple ADRs at a different level of severity. The ADRs reported were confirmed through the British National formulary

(2017) and those ADRs which were ranked level 2 and above which require medical intervention for their management on modified Hartwig and Siegel scale were recorded and presented in the study data in Table 2 and Fig. 1.

Table 1. Age groups of the patients

Age group of patients	Frequency (%)
18-40	52 (32.5)
40-60	96 (60.0)
More than 60	12 (7.5)
Total	160 (100)

Table 2. List of ADRs reported at the dose of AC (60/600/mg/m²)

ADRs	Frequency
Nausea & Vomiting	99
Dyspepsia	75
Loss of appetite	69
Acidity	63
Diarrhea	34
Mucositis	38
Tachycardia	29
Fatigue	79
Insomnia	68
Vertigo	60
Numbness	36
Leukopenia	35
Thrombocytopenia	11
Anemia	23
Hair fall	55

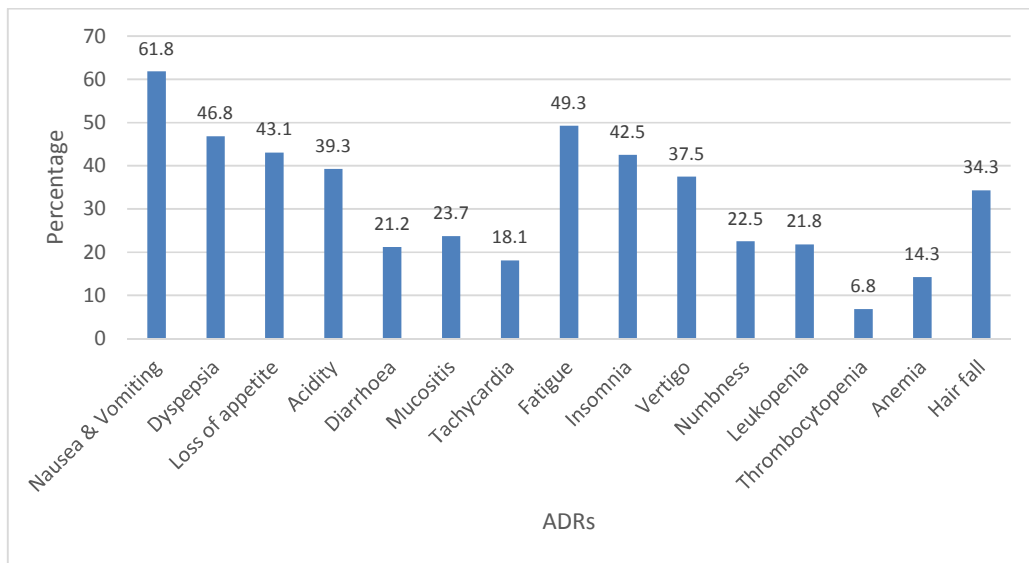


Fig. 1. ADRs with percentages

The majority of the symptoms of the therapy persist for more than 24 hours and up to 72 hours. The cumulative dose range for AC therapy was 60/600-90/900 mg depending upon the body surface area of the patient. High cumulative dose and age above 40 years reported multiple and more severe responses. Nausea and vomiting appeared frequent and most common digestive system problem and most of the patients suffered from the ADR which persisted for more than 1 day after dose administration. Other digestive system problems also appeared as a delayed response. 2nd most common ADR found was fatigue reported by a majority of the patient which persists for at least 1-3 days. ADRs related to blood create problems in a patient's therapy schedule included leukopenia (most common), anemia, and thrombocytopenia. Tachycardia occurs as a result of a cardio toxic symptom of the therapy. Insomnia, vertigo, and numbness are also associated with the therapy and may occur because of neurotoxicity caused by anticancer therapy and the patients suffer from them which persist for 2-3 days after each cycle. In the majority of the patients, these were manageable with supportive therapy.

4. DISCUSSION

The present study identified various ADRs which were severe enough to require medical intervention for management. In a study conducted by Smith and colleagues in 2004 comparing a novel regimen with conventional AC presenting ADRs of grade ≥ 3 as per WHO criteria reported by 215 patients. They found alopecia as the most common non-hematologic ADR with a prevalence of 74%, in this study it was less common among the subjects with a prevalence of 34.37%. Lethargy was reported by only 13% in their study, whereas fatigue was comparatively more common ADR in this study subjects as it was 49.38%. Nausea and vomiting 10%, which in this study subjects was 61.88% and appeared most common ADR. Mucositis 7% which in this study subjects was more common accounts for 23.75%. Diarrhea 2% which in this study subjects was 21.25%. Hematologic toxicities found Leukopenia most common one accounts for 26%, which in this study subjects were 21.875%. Platelet reduction was found in 2%, in this study it was 6.875%.

Moreover, Partridge et al. in 2001 presented data about the risk of ADRs associated with AC therapy. They reported that nausea is the most

common one with a prevalence of 51-95%, this study also found its prevalence around these percentages. Diarrhea presented with a prevalence of 6-20%, which in this study also found it around these but with a very slight difference. Mucositis was reported in their study as compared to this study that is 21-50% versus 23.75% Alopecia they reported with the highest frequency with prevalence percentage of 95% which in this study was comparatively low. Hematologic problems including leukopenia 51-95% and thrombocytopenia 6-20%, in present study these were less frequently reported as compared to these and were approximately 21% and 6%. These comparisons show that patients from different parts of the world can differ in their responses towards therapies followed by reasons that environmental and nutritional and genetic factors can affect positive as well as negative responses [22].

5. CONCLUSION

The present study shows patient's responses towards AC therapy about ADRs. Each patient must be monitored especially those who are at high risk of developing ADRs from this therapy. Appropriate medical intervention can prevent these ADRs and help in maintaining safe therapy.

CONSENT

As per international standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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