A Drug Utilization Study in Patients Suffering from Breast Cancer at A Tertiary Care Teaching Hospital

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Abstract:

Objective: To evaluate utilization patterns of drugs with their respective regimen in patients suffering from breast cancer at a tertiary care teaching hospital.

Methods: This prospective, observational study was carried out at the Department of Pharmacology and Oncology, GCS Medical College, Hospital and Research Centre, Ahmedabad, to assess the drug utilization pattern in patients of breast cancer. The study was carried out over a period of 19 months from August 2019 to March 2021. A total of 67 patients were enrolled for the study. Patient's demographic, clinical, and therapeutic data were collected from the files and in ward visits and analyzed in Microsoft Excel version 2015.

Results: Diagnosis of breast carcinoma was highest in age bracket of 41–50 years (23 out of 67 patients) for this study. Most frequently prescribed regimen was Doxorubicin and Cyclophosphamide as regimen-1 (initial combination of anti-cancer drugs), commonest prescribed regimen-2 (first change in anticancer drug combination) was Docetaxel while Trastuzumab was commonest prescribed regimen-3 (subsequent change in anticancer drugs combination after initial change). Highest prescribed drugs were Cyclophosphamide (66), Doxorubicin (63) and Docetaxel (32) respectively. All patients were received various pre-chemotherapy and post-chemotherapy drugs to combat various toxicities of anticancer drug.

Conclusion: The study results can help in generating local data regarding drug use pattern of the systemic chemotherapeutic agents in breast cancer patients and promote rational drug use.

Keywords: Carcinoma breast, Drug utilization, Chemotherapy regimen, Rational drug use.

Introduction

By historically, investigator's view on Drug Utilization Research (DRC) importance had been significantly changed in the mid-1960, by the essential work of Arthur Engel in Sweden and Pieter Siderius in Holland. Comparing drug use between different countries and states or even different localised area in the same state can derive important data pertaining to that area.

Neoplasm is the new appearance or development of an abnormal growth. A tumor is an abnormal mass or piece of a tissue whose growth is found to be extreme and unstoppable or uncoordinated and continues or persists even after the cessation of the stimulus which gives rise to the change. Globally noncommunicable diseases (NCDs) accounted for 71% of total deaths and carcinoma is one of the most common causes of morbidity & mortality (Pentareddy MR et al, 2015). In India, NCDs were estimated to account for 63% of all deaths and cancer was one of the leading causes (9%) in previous years. Currently number of patients with cancer in India is 13,92,179 for the year 2020 and the common 5 leading sites are breast, lung, oral cavity, cervix uteri and tongue (Mathur P et al, 2020).

Breast cancers are basically clonal proliferations which can arise from ductal or lobular breast cells with multiple genetic alterations. This process can be influenced by hormonal exposure, inherited susceptibility of genes, and environmental factors or their interplay (Lester SC. et al, 2014). Commonest cancer in India is breast cancer (14% of the total cases) and it is one of the leading causes of cancer deaths (11.1% of the total cases) (Dar M, et al, 2018). The treatment modalities for breast cancer are surgery, radiotherapy, and

chemotherapy: selection of which depends on tumor size, number of lymph node involvement, and overall health of the patient [5].

Drug use is a complex process since optimal benefits of drug therapy in patient care may not be achieved because of under-use, overuse or misuse of drugs. Inappropriate drug use may also lead to increased cost of medical care, resistance, adverse effects and patient mortality. Hence, in recent years drug utilization study (DUS) have become a potential tool to improve the quality, cost effectiveness of drugs used and thereby improve patient care (Sachdeva PD et al, 2010). DUS are defined as the study of marketing, distribution, prescription and use of drugs in a society with special emphasis on medical, social and economic consequences (Truter I. et al, 2008).

Aim:

To evaluate utilization patterns of drugs with their respective regimen in patients suffering from breast cancer at a tertiary care teaching hospital.

Primary Objective:

To evaluate drugs usage patterns in breast cancer patients of different age groups which were admitted to oncology department of GCSMCHRC, in term of different anticancer drugs combinations (also known as regimen)

Secondary Objectives:

- To observe brief epidemiology of different cancers.
- To find out usage patterns of pre-chemotherapy agents, post-chemotherapy agents and supportive drugs.

Material & Method:

Study was carried out at chemotherapy ward (patients were admitted to receive their chemotherapy cycles) with collaboration of department of oncology and department of pharmacology, GCSMCHRC, Ahmedabad from August 2019 to March 2021. It was prospective observational study.

Following patients were included in the study:

- Patients of either gender who were willing to give consent for their participation in study
- Diagnosed patients of breast cancer and confirmed by various investigations (e.g. histopathology reports, biomarkers etc.)

- Patients inclusive of any stage of breast cancer
- Patients requiring to receive anticancer drugs as their treatment plan

Following patients were excluded from the study

- Pregnant females and infants
- Patients having insufficient records
- Patients refused to give consent for their participation
- Anticancer drugs were not part as treatment plan (e.g. curative surgery in some breast cancer patients were available)

Patients were explained about the study in their vernacular language and informed consent was obtained from them in form of signature or thumb impression by themselves or their relative in pre-defined informed consent form. Approval for study was obtained from Institutional Ethics Committee before starting the study.

All the necessary details included but not limited to only demographic details, chief complaints, provisional diagnosis/diagnosis, generic name, brand name, dosage form, route of administration, duration etc. recorded in predefined case record form (CRF).

Analysis done for total 43 patient's data e.g., their demographic pattern, diagnosis, comorbidity & drug usage pattern in the form of total drug, average drug, anticancer regimen, pharmacological classes, dosage form etc.

Data management and analysis: Data were recorded & analyzed through using Microsoft excel version 2015

Results

This prospective, observational study was carried out at the Department of Pharmacology and Oncology, GCS Medical College, Hospital and Research Centre, Ahmedabad, to assess the drug utilization pattern in patients of cancer.

The study was carried out over a period of 19 months from August 2019 to March 2021. A total of 67 patients of breast cancer were enrolled for the study. Following are the findings of our study:

Total 67 patients were included in the study and categorized in different age group out of which highest number (23) of the patients were seen in age group B (41-50 years) which indicate higher prevalence of breast cancers after 40 years.
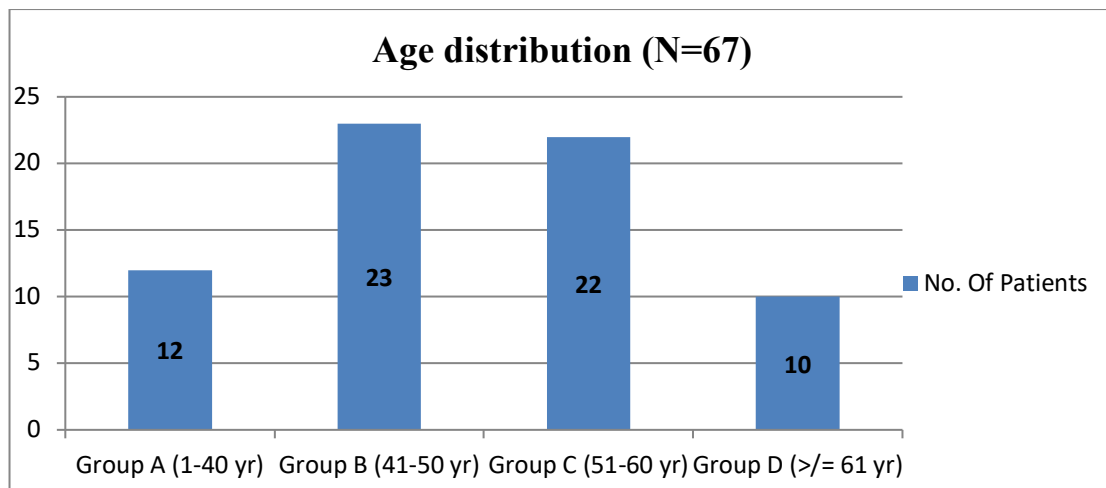
Figure 1: Age distribution (N=67)

Out of total 67 patients, 00 (0%) had history of tobacco consumption while 22 (32.84%) gave positive family history of breast cancer. So, almost 1 out of 3 patients had presence of positive family history of breast cancer. Thus, it is apparent that family history of breast cancer is strongly associated with occurrence of breast cancer in next generation. [Figure 2]
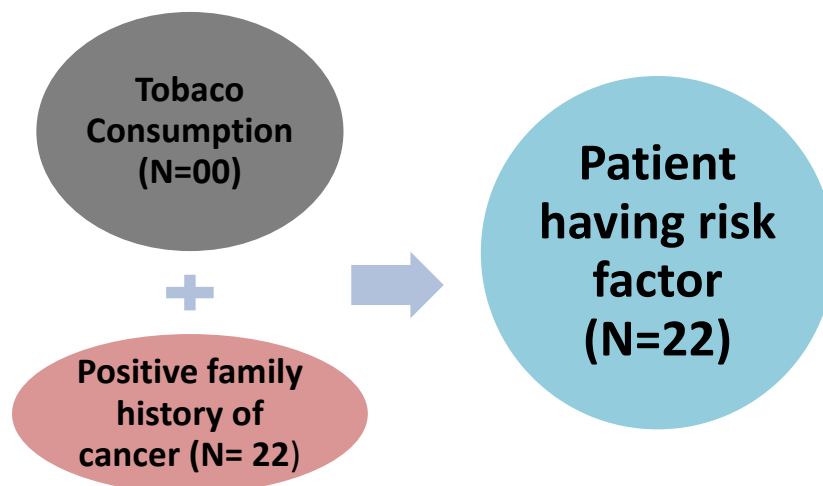

Figure 2:

Differential diagnosis among 67 patients of breast cancer was:

- Invasive ductal cell carcinoma- 57
- Not specified- 05
- Papillary carcinoma- 03
- Invasive lobular carcinoma- 02

A. Regimen-1 (initial combination of anticancer drugs):

Total 5 different types of anticancer drugs regimens were used as regimen 1 in all patients. Out of which commonest prescribed regimen was combination of Doxorubicin and Cyclophosphamide, which was prescribed in 59 patients. Total 140 anticancer drugs were used in regimen-1 in all patients (N=67). So average anticancer drugs used per patients were 2.09. Total 06 different anticancer drugs were used in patients

in initial cycle i.e. regimen-1. Other prescribed regimen and drugs are shown in table-1 & 2.

B. Regimen-2 (first change in combination of anticancer drugs):

Total 06 different types of anticancer drugs regimens were used as regimen 2 in 35 patients. In 32 patients no data pertaining to regimen 2 was recorded due to loss of follow up (Covid-19 pandemic). Out of which commonest prescribed regimen was Docetaxel, which was prescribed in 29 patients. Total 38 anticancer drugs were used in regimen-2 in 35 patients (N=35). So average anticancer drugs used per patients were 1.09. Total 07 different anticancer drugs were used as first change in combination of anticancer drugs i.e. regimen-2. Other prescribed regimen and drugs are shown in table-1 & 2.

C. Regimen-3 (second subsequent change in combination of anticancer drugs):

Total 03 different types of anticancer drugs regimens were used as regimen 3 in 11 patients.

In 56 patients no data pertaining to regimen 3 was recorded due to loss of follow up (Covid-19 pandemic). Out of which commonest prescribed regimen was Trastuzumab, which was prescribed in 08 patients. Total 11 anticancer drugs were used in regimen-3 in 11 patients (N=11). So average anticancer drugs used per patients were 1.00. Total 03 different anticancer drugs were used as second subsequent change in combination of anticancer drugs i.e. regimen-3. Other prescribed regimen and drugs are shown in table-1 & 2.

Table1: Different types of regimens in patient suffering from breast cancer.

Regimen 1	Total patients	Regimen 2	Total patients	Regimen 3	Total patients
DOC, DOX, CYP	04	CIS	01	DOC	01
DOC, EPI, CYP	01	**DOC**	**29**	PAC	02
DOX, CYP	**59**	DOC, PEM	01	**TRA**	**08**
EPI, CYP	02	DOC, TRA	02		
DOC, CAR, TRA	01	DOX, CYP	01		
		PAC	01		
Not recorded/ Lost to follow up	00	Not recorded/ Lost to follow up	32	Not recorded/ Lost to follow up	56

Full form: DOX: Doxorubicin, CYP: Cyclophosphamide, CAR: Carboplatin, PAC: Paclitaxel, DOC: Docetaxel, CIS: Cisplatin, EPI: Epirubicin, TRA: Trastuzumab

Table 2: Individual drug frequency among all regimens

Individual drug frequecy among regimen 1	Total patients	Individual drug frequecy among regimen 2	Total patients	Individual drug frequecy among regimen 2	Total patients
DOC: Docetaxel	06	CIS: Cisplatin	01	DOC: Docetaxel	01
DOX: Doxorubicin	63	**DOC: Docetaxel**	**32**	PAC: Paclitaxel	02
CYP: Cyclophosphamide	**66**	PEM: Pemetrexed	01	**TRA: Trastuzumab**	**08**
EPI: Epirubicin	03	TRA: Trastuzumab	01		
CAR: Carboplatin	01	DOX: Doxorubicin	01		
TRA: Trastuzumab	01	CYP: Cyclophosphamide	01		
		PAC: Paclitaxel	01		
Total drugs prescribed in regimen 1	**140**	**Total drugs prescribed in regimen 2**	**38**	**Total drugs prescribed in regimen 3**	**11**

All patients were prescribed pre-chemo and post-chemo treatment to counteract the nausea, vomiting, hypersensitivity reaction and other anticancer drug related side effects. Ondansetron, Dexamethasone & metoprolol were commonest prescribed drugs as shown in table 3.

Table 3: Pre-chemo and post-chemo drugs

Pre chemo drug	Total patients	Post chemo drug	Total patients
Ondansetron	67	Metoprolol	67
Dexamethasone	67		
Pheniramine malate	06		

In all patients, supportive drugs like prochlorperazine, domperidone, ondansetron, folic acid and rabeprazole had been prescribed after completion of indoor chemotherapy to combat various toxicity like alopecia, constipation, diarrhea, stomatitis etc. (Table 4).

Table 4: Supportive drugs to combat various toxicity

Supportive drugs	Total patients	Supportive drugs	Total patients
Prochlorperazine	67	Riboflavin	24
Domperidone	67	Niacinamide	24
Folic acid	67	Dexamethasone	08
Rabeprazole	67	Aprepitant	01
Ondansetron	67		

Discussion

Breast carcinoma is one of the most common neoplasms in women and is a leading cause of deaths worldwide (Mary Rohini Pentareddy et al, 2015). Various anticancer drugs are classified according to subgroups like Platinum compounds (e.g., Carboplatin, Oxaliplatin, Cisplatin), Anthracyline which also known as anticancer antibiotic group (e.g., Doxorubicin, Epirubicin), Alkylating agents (e.g., Cyclophosphamide, Ifosfamide), Taxane (e.g., Paclitaxel, Docetaxel) which are beneficial in treating breast cancer patients. 5FU, Cyclophosphamide, and Adriamycin (FAC regimen) is now the most commonly used, effective and well tolerated adjuvant treatment regimen for breast cancer patients and has shown survival benefit too. (Amin KA, et al, 2012). In contrast to these findings in our study only Cyclophosphamide and anthracycline (regimen-1) were used for the management of breast carcinoma (61 out of total 67 patients) and in remaining 06 patients (Cyclophosphamide + anthracycline + taxane) combination was used.

Taxanes are the fundamental drugs used in the treatment of breast cancer. Because of convenient pharmacokinetic parameters and consistent positive clinical results docetaxel is the preferred agent in this group. Addition of docetaxel or paclitaxel to the combination of doxorubicin and Cyclophosphamide has been observed with nearly equal in frequency in the present study too.

Out of total 67 patients of breast carcinoma in 35 patients we recorded more than 4 cycles in which docetaxel alone was given in 24 patients and docetaxel with hydrocortisone/ pemetrexed in 08 patients. In 2 patients, cisplatin (01) and paclitaxel (01) given as regimen-2 while in remaining 1 patient doxorubicin and cyclophosphamide continued as regimen-2 according to clinician's judgement. In study of Pentareddy et al, Paclitaxel was more commonly used in taxane group

Nausea and vomiting are serious and directly related side effects of cancer chemotherapy. These adverse effects can cause significant negative impacts on patients' quality of life and on their ability to comply with therapy. Also, nausea and vomiting can result in anorexia, decreased performance status, metabolic imbalance, wound dehiscence, esophageal tears, and nutritional deficiency (Williams & Wilkins; 1983, Fernández-Ortega P et al, 2012). To combat these side effects various anti-emetic drugs commonly used in clinical practice before starting of chemotherapy and after completing it. In our study, in all patient's dexamethasone and ondansetron were used as pre-chemotherapeutic agents while metoprolol used as post-chemotherapeutic agent in all patients.

As, chemotherapeutic agents are highly effective on rapidly multiplying cells, they also exert unwanted side effects towards the cells which have relatively short cell cycle (e.g., Cells of G.I. tract, Hair, Cells of bone marrow etc.) Thus, Various supportive drugs are commonly prescribed after the chemo cycles. In our study, all patients received prochlorperazine, rabeprazole, domperidone and folic acid to neutralize the chemotherapeutics' agents effect on rapidly multiplying normal cells.

Advantage of the study: This study analysed the various chemotherapeutic drugs were used up to 12 chemotherapeutic cycles.

Limitation of the study: Relatively small sample size does not predict prevalence of various cancers accurately.

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