IJBPAS, October, 2017, 6(10): 1848-1952

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

SURVEY ON ADRS ASSOCIATED WITH GIT DUE TO 5-FLOUROURACIL, DOXORUBICIN AND CYCLOPHOSPHAMIDE (FAC) COMBINATION CHEMOTHERAPY FOR BREAST CANCER

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Received 28th Dec. 2016; Revised 2nd March 2017; Accepted 30th April 2017; Available online 1st Oct. 2017

ABSTRACT

Gastrointestinal disturbances (GI) are of global concern affecting the population health including developed countries. Anticancer drugs are potent in nature having capability to affect various system of body especially those with rapidly dividing cells such as gastrointestinal system and can lead to various adverse drug reactions (ADRs) etc. The objectives of this study are to assess ADRs of FAC anticancer treatment associated with gastrointestinal tract as reported by patients. A descriptive observational study was conducted by collecting patient's feedback on predesigned questionnaire and verified through British National formulary, Lexi comp and Hart wig & Siegel scale. Data included 80 Female Patients aged above 18 years receiving FAC (600/60/600/m^2) treatment via purposive sampling in 2015 at Cancer Hospital Jamshoro. The Gastrointestinal disturbances reported were Nausea 71(88.75%), vomiting 68(85%), Acidity 57(71.25), Anorexia 56 (70%), Indigestion 62(77.5%), and Abdominal pain 36 (45%), Diarrhoea 38 (47.5%), Oral mucositis 23(28.75%) constipation 4 (5%). The survey shows that anticancer combination therapy is associated with variety of ADRs associated with gastrointestinal tract which occur with varied frequency and are potentially severe that can affect not only health of the patient but can also affects the overall efficacy of the therapy by leading patients into malnutrition state.

Keywords: GI disturbances, anticancer drugs, FAC, ADRs

INTRODUCTION

Digestive system/gastrointestinal system plays a key in the maintenance of the health of the individual as it is involve in the processing of the nutrients. Any disturbance in the processing will ultimately affect the overall health system [1]. Gastrointestinal disturbances such as nausea, vomiting, acidity, constipation diarrhoea etc are common in developed countries also .The factors that are responsible for causing these disturbances include: High food intake especially with low fibre and necessary

nutrients, stress, inadequate exercise, travelling, drug etc. Drugs used to treat different diseases are one of the most important factors responsible for causing different gastrointestinal disturbances especially drugs which are administered orally and those which are used to treat disorders of gastrointestinal tract such as antacids, laxativesetc. others include nutritional supplements, antidepressants, narcotics cytotoxic drugs(Anticancer therapy) [1-3].

Anticancer therapy is one of the critical treatments available as these are cytotoxic in nature affects the normal cells along with the abnormal hence associated with different adverse drug reactions (ADRs). Drugs used to treat cancer are very strong in their action and hence capable of affecting the various systems of the body specially the cells having capability to divide rapidly such as gastrointestinal system [4-7]. Their combinations even prove to be more dangerous as result of synergistic effect upon both normal as well as cancer cell cells. Doxorubicin, 5-flourouracil and cyclophosphamide are the one of the effective drugs used in the treatment of variety of cancers as individually as well as in combination. Breast cancer is one of the most frequently occurring cancer its treatment include different chemotherapeutic agents such as doxorubicin, cyclophosphamide, 5-Flourouracil, taxens (paclitaxel, docetaxel) etc these agents are used as individual agents as well as in different combination depending upon the severity of disease in which doxorubicin, cyclophosphamide and 5-Flourouracil combination proves to be one of most effective treatment protocol for treatment of advanced disease. These all have different as well as similar adverse effects upon the gastrointestinal system of the patients such as Doxorubicin adverse effects include: nausea, vomiting, Cyclophosphamide cause nausea vomiting, and 5-florouracil cause nausea ,vomiting, mucositis ,diarrhoea etc. are the common adverse effects produced by these [8-10].

METHODOLOGY

A descriptive observational study was conducted by taking feedback on predesigned questionnaire in Cancer Hospital Jamshoro 80 female patients receiving FAC (600/60/600/m^2) treatment for breast cancer were included in the survey via purposive sampling in 2015.Results obtained were evaluated by comparing data against British national Formulary(2012), Lexi comp (2013) and Hartwig and Siegel scale.

Patient Selection Criteria

- All Female patients receiving anticancer combination therapy for breast cancer aged above 18 years.
- Patients who are unconscious, bed ridden mentally disturbed unable to respond, patients with other severe diseases such as tuberculosis, hepatitis and AIDs were excluded from the study.

Table 1: Frequency of various Age Groups

S. No	Age Group of Patients	No of Patients	Frequency (%)
1	18-40	25	31.25
2	41-60	50	62.5
3	61 and above	5	6.25
	Total	80	100

Table 2: Frequency of Types of Tumor

Tumor type	No of Patients	Frequency (%)
Localised tumor	19	23.75
Infilterating tumor	61	76.25
Total	80	100

Table 3: Frequency of Gastrointestinal Disturbances Associated with FAC (600/60/600/m^2)Therapy

Sr.no	ADRs	No of Patients	Frequency (%)
1	Nausea	71	88.75
2	Vomiting	68	85
3	Indigestion	62	77.5
4	Acidity	57	71.25
5	Anorexia	56	70
6	Diarrhoea	38	47.5
7	Abdominal pain	36	45
8	Oral mucositis	23	28.75
9	Constipation	4	5

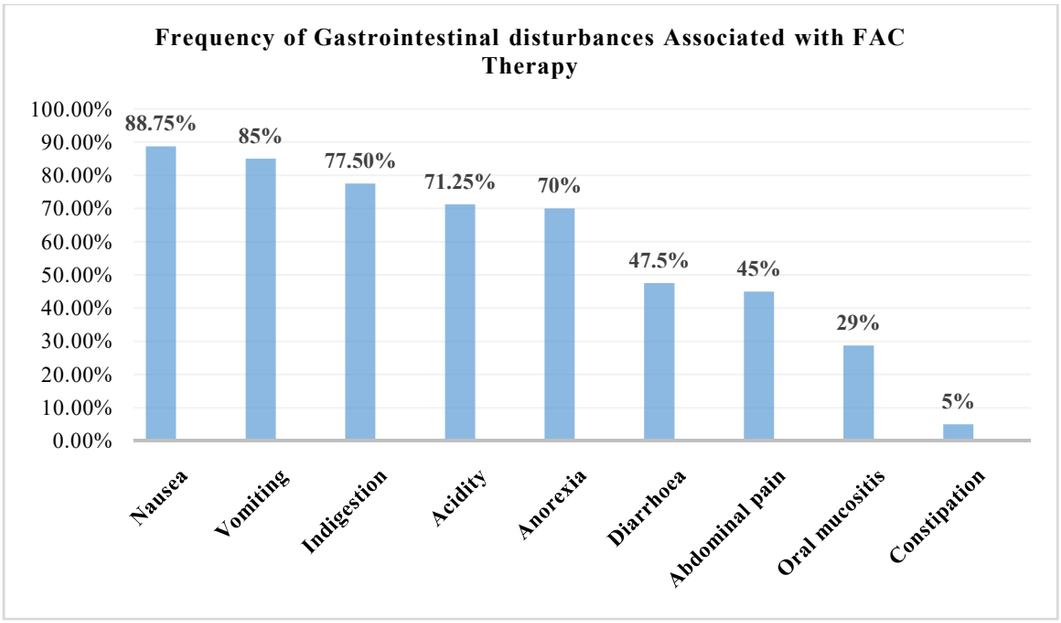

Figure: A

RESULTS

The data of survey included 80 patients who were receiving FAC treatment (600/60/600/m^2) the results are mentioned in the tables. Table no: 1 shows the various age groups of patients suffering from breast cancer. All the patients included in the survey were female suffering from breast cancer and were above the age of 18 with mean age of 44.562 and between 41-60 age group represent the highest percentage of patients suffering from breast cancer that is 62.25% while only 5% patients were above the 60 years. Table no: 2 represent the distribution of disease type among the local population and survey shows that majority of the patients were suffering from the infiltrating tumours and that is 76.25% while only 23.75 % of patients were with localised tumours. Table no: 3 represent the frequency of different gastrointestinal symptoms reported by patients receiving a combination therapy for breast cancer treatment. All the patients included in the survey reported variety of gastrointestinal disturbances which ranked as level 2 or greater in Hartwig and Siegel scale. Majority of patients reported to have more than one gastrointestinal symptoms from which they suffer after having chemotherapy started, among which nausea were the most common symptom reported by the patients which were 71(88.75%) in number and majority of reported that the symptoms persist for more than 48 hours after every cycle of dose. Vomiting was the second most common

gastrointestinal symptom reported by the 68 (85%) patients associated and this symptom also persist for up to or more than 48 hours and put a great impact in patient's life style by limiting the nutritional intake .Indigestion were the next most common problem associated with the therapy and reported by 62(77.5%) patients another problem associated which were acidity reported by in 57(71.25%) which persist for up to or more than 24 hours of therapy. Anorexia another problem reported by 56(70%) patients majority of patients reported that the symptom persist for more than 3 days even up to a week. Diarrhoea was reported by 38(47.5%), and abdominal pain in 36(45%) and these symptoms persist for 24-48 hours. Oral mucositis reported by 23(28.75%) which persist for 3-5 days after each dose. 4(5%) suffered from constipation after starting the therapy and last for 24hour.

DISCUSSIONS

This study identified various gastrointestinal disturbances associated with combination anticancer therapy used to treat breast cancer. All ADRs reported were verified through international standards (British National Formulary (2012) and Lexi comp (2013).The findings of this study are corroborates by the findings of Martin et al' study (2006),which also reported that nausea 38.9% ,vomiting 34.1% and were the most frequent gastrointestinal symptoms associated with the therapy however the occurrence of their frequency were low as compared to the local patients which are 88.75% and 85% respectively. In our study indigestion were reported by 77.5% and were third most frequently occurring gastrointestinal symptoms whereas in Martin's study it was only 2.1%. The other symptoms reported by this study were stomatitis/oral mucositis 24.5% which occur as third most common effect where as in our study it is reported by 28.75%. Anorexia reported by 2.9% where as in our study it was70%, abdominal pain was reported by 3.1% and in our study it was 45%, Diarrhoea occurred in 5.2% in their study while 47% of local patients reported to have diarrhoea. Constipation was the only gastrointestinal symptom reported by least number of patients5% where as in Martin et al'study it was 8.7%.The data comparison shows that local patients are at greater risks towards various gastrointestinal disturbances as compared to the international data available and therefore patient must be monitored during the therapy and special consideration should be given in the nutritional intake as they were ranked as level 2 or greater in ADRs Severity Assessment scale (Hartwig and Siegel scale) and [9].

CONCLUSION

The survey showed that the anticancer therapy (FAC) for breast cancer is associated with variety of different gastrointestinal symptoms which were potentially sever to that can affect patient's health by reducing nutritional intake by patients and lead to more severe state can also affect the overall treatment schedule. The survey will help the prescriber in early diagnosis of these various gastrointestinal disturbances associated with the therapy and minimize them with supportive therapy to avoid main treatment compromises. These studies also help health organisations to make long term strategies to overcome these gastrointestinal symptoms that occur in local patients and improve the therapeutic outcomes of the treatment.

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