Research article

Evaluate the Changes Arise in the Parameters of Liver and Kidney during Adjuvant Chemotherapy in Breast Cancer Patients

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Abstract

To find out the variation in basic parameters of liver and kidney during FAC or CAF adjuvant chemotherapy in breast cancer patients at NIMRA Jamshoro. A follow up study conducted at Nuclear, Institute of Medicine Radiotherapy (NIMRA), Jamshoro, Sindh, Pakistan. Our findings include the variations in the level of Total bilirubin, Alkaline phosphatase and Alanine transaminase as the parameters of liver. The mean ±SD of total bilirubin before FAC (5-Fluorouracil, doxorubicin and cyclophosphamide) or CAF (Cyclophosphamide, doxorubicin and 5-Fluorouracil) Adjuvant Chemotherapy in Breast Cancer Patients was 0.76±0.23 and after it was 1.23±0.16. The mean ±SD of Alkaline phosphatase before FAC or CAF Adjuvant Chemotherapy in Breast Cancer Patients was 96.2±2.89 and after it was 131±14.3 and Alanine transaminase before FAC or CAF Adjuvant Chemotherapy the mean ±SD was 25.5±6.18 and after it becomes 37.7±5.18. We found the variations in the level of urea and creatinine as the parameters of kidney. The mean ±SD of urea and creatinine before FAC or CAF Adjuvant Chemotherapy in Breast Cancer Patients was 15.4±4.98 and 0.85±0.20 and after chemotherapy they were 28.0±1.70 and 1.76±0.09 respectively. The main parameters of liver and kidney were statistical significantly increased after FAC or CAF adjuvant chemotherapy in the woman with breast cancer. These changes will alter the working of these organs by making drastic effects on the normal metabolic and excretory function of liver and kidney.

Keyword: Adjuvant chemotherapy, breast cancer, liver, kidney.

Introduction

Adjuvant systemic therapies such as endocrine therapy, anti HER2 therapy and chemotherapy are very much effective to lower the risk of recurrence both distant and local cancer. Mortality rates of breast cancer are also reduced with the use of adjuvant systemic therapy[1]. 5-fluorouracil has become the backbone drug in the chemotherapy treatment but it is involved in the development of liver injury, certain report showed that steatosis was developed after administration of 5- fluorouracil in the chemotherapy treatment although some reaction may be reversible[2]. The liver toxicity caused by chemotherapeutic agents. They stated that cyclophoshamide, 5-fluorouracil and doxorubicin may cause the liver toxicity at first after administration of these drugs and then come to the normal. Liver has their catabolism mechanism that reduces the toxicity of these drugs in the hepatic cells. Liver toxicity is rarely produced by these drugs observed by King and Perry[3]. Chemotherapeutic drugs also damage the kidney. The functional unit of kidney is nephron and its glomerulus, renal tubules, interstitium badly affected resulting in rise of concentration of serum creatinine. The nephrotoxicity primarily show no sign and symptoms and then goes to serum electrolytes imbalance. Short term side effects were nausea and vomiting as increase in urea and creatinine level in the body[4].

Materials and Methods:

This work was designed as follow up study. We have selected breast cancer patients for research who are seeking treatment at Nuclear, Institute of Medicine Radiotherapy (NIMRA), Jamshoro, Sindh, Pakistan from 1st April 2015 to 30th October 2015.

We observed 131 patients and 105 patients were agreed to participate in our research. 105 chemotherapeutic women with age range between 20 to 60 years, having breast cancer. They underwent surgery and taking adjuvant treatment with FAC or CAF chemotherapy were included. The man having breast cancer, women with age limit Less than 20

or greater than 60 years, who were not willing in participate in research were also excluded. Having any other type of cancer, non-surgical, Radio therapeutic, neoadjuvant chemotherapeutic and other chemo drugs were also excluded. 5 ml human blood sample was collected from the breast cancer women before the administration of FAC/CAF adjuvant chemotherapy and then after each cycle of FAC/CAF adjuvant chemotherapy in neutral jell tubes. The gap between each cycle of FAC/CAF adjuvant chemotherapy was 21 days. After every cycle of FAC/CAF adjuvant chemotherapy blood sample was drawn from each patient by the vacutainer needle for the quantitative analysis of total bilirubin, alkaline phosphates, alanine transaminase as the marker of liver function test and urea and creatinine as the marker of renal function test. The liver function test performed at biochemistry analyzer JH-6020 and the analysis of Urea and Creatinine from serum at Hitachi 902 automated instruments Germany Roche Company at NIMRA hospital Jamshoro. After six plus cycle of FAC/CAF adjuvant chemotherapy the values were calculated to find the mean ±SD of the parameters.

Ethical considerations

The research proposal was approved by research ethics Committee Institute of Biochemistry University of Sindh Jamshoro.

Statistical analysis

All the data was entered and analyzed on Statistical Package for Social Sciences (SPSS) version 16.0 (SPSS Inc., Chicago, Illinois, USA). Mean +SD was calculated for liver function test and renal function test of FAC/CAF adjuvant chemotherapeutic patients.

Results

Our findings include the variations in the level of Total bilirubin, Alkaline phosphatase and Alanine transaminase. The mean ±SD of total bilirubin before FAC (5-Fluorouracil, doxorubicin and cyclophosphamide) or CAF (Cyclophosphamide, doxorubicin and 5-Fluorouracil) Adjuvant Chemotherapy in Breast Cancer Patients was 0.76±0.23 and after it was 1.23±0.16. The mean ±SD of Alkaline phosphatase before FAC or CAF Adjuvant Chemotherapy in Breast Cancer Patients was 96.2±2.89 and after it was 131±14.3 and Alanine transaminase before FAC or CAF Adjuvant Chemotherapy the mean ±SD was 25.5±6.18 and after it becomes 37.7±5.18. we found the variations in the level of urea and creatinine. The mean ±SD of urea and creatinine before FAC or CAF Adjuvant Chemotherapy in Breast Cancer Patients was 15.4±4.98 and 0.85±0.20 and after chemotherapy they were 28.0±1.70 and 1.76±0.09 respectively.

Table 1 Liver Function Test Before and After FAC (5-Fluorouracil, doxorubicin and cyclophosphamide) or CAF (Cyclophosphamide, doxorubicin and 5-Fluorouracil) Adjuvant Chemotherapy in Breast Cancer Patients

Parameters	Before chemotherapy Mean ± SD	After chemotherapy Mean ±SD	Minimum	Maximum	Normal ranges
Total Bilirubin (mg/dl)	0.76±0.23	1.23±0.16	1.11	1.52	0.3-1.3
Alkaline phosphotase (U/L)	96.2±2.89	131±14.3	116	159	40 -150
ALT (U/L)	25.5±6.18	37.7±5.18	31.7	44.2	0-40

Table 2 Renal Function Test Before and After FAC (5-Fluorouracil, doxorubicin and cyclophosphamide) or CAF (Cyclophosphamide, doxorubicin and 5-Fluorouracil) Adjuvant Chemotherapy in Breast Cancer Patients

Parameters	Before chemotherapy Mean ± SD	After chemotherapy Mean ±SD	Minimum	Maximum	Normal ranges
Urea (mg/dl)	15.4±4.98	28.0±1.70	25.8	31.2	6-22

Creatinine (mg/dl)	0.85±0.20	1.76±0.09	1.59	1.89	0.6-1.3

Figure 1 Liver Function Test Before and After FAC (5-Fluorouracil, doxorubicin and cyclophosphamide) or CAF (Cyclophosphamide, doxorubicin and 5-Fluorouracil) Adjuvant Chemotherapy in Breast Cancer Patients

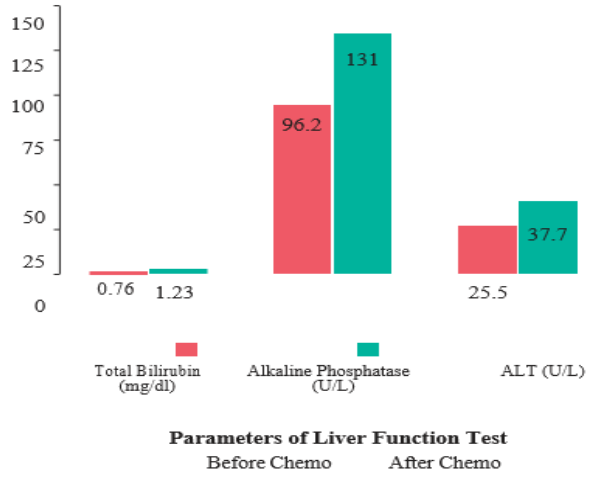
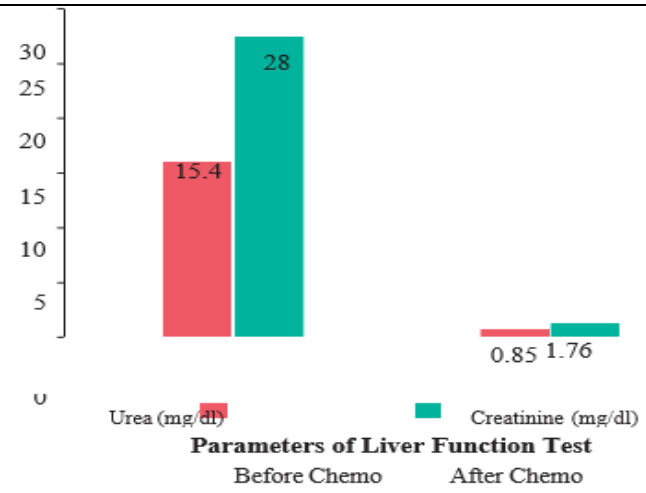


Figure 2 Renal Function Test Before and After FAC (5-Fluorouracil, doxorubicin and cyclophosphamide) or CAF (Cyclophosphamide, doxorubicin and 5-Fluorouracil) Adjuvant Chemotherapy in Breast Cancer Patients



Discussion

Liver is the metabolic center of the body. It plays a major role in detoxication. The metabolites of drugs and toxicities that are produced by the administration of drugs will cause the hepatoxicity. There are statistically significant results reported regarding level of Total Bilirubin, Alkaline phosphatase and Alanine transaminase in liver function test before and after the cycles of CAF or FAC adjuvant chemotherapy as shown in the Table 1. The normal levels of the parameters of liver were increased at the end six plus cycle of FAC/CAF adjuvant chemotherapy. King and Perry 2001 also discussed that the doxorubicin with cyclophosphamide and 5 – flurouracil in adjuvant setting developed liver abnormalities within the first three months and these elevated levels were normalized with the passage of time[3]. Rise in the levels of alkaline phosphatase with alanine transaminases and total bilirubin initially caused the hepatotoxicity but will be normalized after the completion of treatment.

Kidney is the major excretory organ of the body that is chiefly performed the removal of nitrogenous waste from the blood and filter the blood. The elevated level of nitrogenous waste will affect the blood physiology and cause imbalance in the normal plasma concentration of the blood. During the study urea and creatinine levels were increased after CAF or FAC administration and statistically significant before and after the cycles of chemotherapy as appeared in the Table 2. Before administration of FAC/CAF adjuvant chemotherapy the mean ±SD of urea was 15.4 ±4.9 and creatinine was 0.85 ±0.20. After six plus cycles FAC/CAF adjuvant chemotherapy the mean ±SD of urea was 28±1.70 and creatinine was 1.76±0.09. this increased level of urea and creatinine will damage the nephron, glomerulus and put drastic effect of function of kidney. Warmkessel 2011 reported that alkylating agent cyclophosphamide caused nephrotoxicity include increases urea and creatinine level in the blood. Urea and creatinine was metabolic waste product of nausea and vomiting that accumulate in blood[4]. These elevated levels caused the asymptomatic renal disorders[7,8].

Conclusion

The main parameters of liver and kidney were statistically significantly increased after the adjuvant chemotherapy in woman with breast cancer. They may put drastic effects on the normal metabolic and excretory function on both the organs. The patients should be warned regarding the drastic changes and must be known that how to face and recover from the changes occurring during and after FAC/CAF adjuvant chemotherapy.

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