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Physiological study of liver and kidney of female patient with breast cancer which treated with different doses of Chemotherapy

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Abstract:- Following the evaluation of tumor histology, organ function is a crucial element to consider when selecting a chemotherapy regimen. Patients undergoing chemotherapy require a comprehensive evaluation of their liver function prior to treatment to determine which medications may not be acceptable and which drug doses should be adjusted. The common protocol in treatment of breast cancer is given mix anticancer drug cyclophosphamide and Adriamycin. It is crucial to understand that anomalies in liver function tests after therapy could be caused by the medication rather than the advancing illness. This page discusses the hepatic toxicity of chemotherapy drugs and offers dose adjustments in response to abnormalities in liver function. The focus is on substances that are recognized to be hepatotoxic, as well as those that have hepatic metabolism and renal failure . In this study taking 150 female patient with breast cancer and 30 healthy women. the 150 female patient divided in to three group depend on the number of chemotherapy dose taking during the treatment and making the following : first taking from one dose to four dose of chemotherapy , second taking from five dose to eight dose of chemotherapy , third taking from nine dose to above dose of chemotherapy may be reach twenty four dose . the result showed significant difference in liver enzyme AST,ALP and ALT . AST , ALT and ALP assessment showed significant decreased in all groups when compared with control group and showed significant increased of urea and creatinine when compared with control group. The different number of chemotherapy dose lead to disturbance of liver enzyme , urea and creatinine , and the side effect increased with increased number of dose .

Keyword:- breast cancer , Adriamycin, cyclophosphamide , liver enzyme ,urea, creatinine .

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material,which is available to autho-rized users.

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Introduction

There are trillions of cells in the human body, and cancer occurs when a small percentage of those cells proliferate uncontrollably and metastasize to other organs. Any part of the body might become a cancerous tumour. The normal process of cell division in humans allows the body to continually replenish its cell supply. When cells die off or get damaged, new ones grow to take their place. When this controlled mechanism fails, abnormal or damaged cells could divide and grow uncontrollably. Masses of tissue known as tumours can form when these cells proliferate. There are two main types of tumours: benign and malignant (1). Tumours that are cancerous can spread to other parts of the body, a process known as metastasis. Because of this mechanism, tumours are able to metastasize, or spread to other parts of the body. Another name for tumours that are cancerous is malignant tumours. Blood cancers, such as leukaemia, usually do not progress to solid tumours, while many other types of cancer do. Noncancerous tumours do not metastasize, meaning they do not invade other tissues (2). In terms of incidence, the first type of cancer (23%) Currently living women make up 7.8 million diagnosed in the last five years, making it the most prevalent kind of cancer worldwide. Cancers arise in women who are not at a heightened risk of breast cancer. Risk factors include aging, obesity, heavy alcohol consumption, and familial history. History, radiation exposure history, and reproductive history (the age at which the first pregnancy occurred and the onset of menstruation), as well as tobacco usage and postmenopausal hormone therapy (10) S100 proteins constitute the largest calcium-binding subfamily EF-hand type protein. These are low molecular weight acidic proteins They play cross- Functional roles as they have been reported to mediate extensively Cancer starts when cells start to proliferate uncontrollably. Men can get breast cancer, but women are nearly always affected.mammary cancer Extremely It's critical to realize that the majority of breast tumors are benign rather than malignant (cancerous). Although they are abnormal growths, non-cancerous breast tumors do not spread outside of the breast. Although rarely fatal, certain forms of benign breasts A woman's risk of breast cancer may increase if she has lumps. Any breast enlargement or alteration A medical expert must examine it to determine whether it is benign or malignant (cancer), and whether it will have an impact on the likelihood of getting cancer later on. (11). Breast cancer can metastasize, or spread, to other parts of the body when cancer cells get into the blood or lymphatic system. The lymphatic system is an element of your body's immune system. Lymph nodes are tiny glands the size of beans that are part of a network of organs and tubes that work together to collect and transfer clear lymph fluid from the tissues of the body into the circulation. The transparent lymph fluid that saturates the lymphatic passages contains cells of the immune system and waste products from tissues. The lymph vessels drain the breast of excess lymph fluid. Lymph veins can facilitate cell entry and proliferation in lymph nodes, which can lead to breast cancer (12).

Adriamycin

The second Adriamycin is his name. This medication is classified as an anti-metabolic, or anti-tumor, class of medication that inhibits the growth of tumor cells through disruption of the DNA of the cell. A new antineoplastic drug produces objective tumour responses in both blood cancers (acute leukaemia and malignant lymphomas) and solid tumours (breast cancer, sarcomas, neuroblastoma, and adenocarcinoma of the breast). (28), Along with studying the responses in specific tumour forms, this study compares the relative clinical efficacy of adriamycin to other anticancer medications. Adriamycin can cause a variety of side effects, including hematologic and cardiac toxicity, stomatitis, nausea, vomiting, and alopecia. Fortunately, most of these toxicities are usually manageable and

predictable. Adriamycin is a novel anticancer medication with notable , Adriamycin is a novel anticancer medication that has shown promising clinical results. Internal Medicine Annals. (29)

Cyclophosphamide

His second name is cetophosphan, It is an anti-cancer drug used in the treatment of cancerous tumors and autoimmune disorders, and is part of the chemotherapy drugs for cancer remains one of the most successful and widely utilized ($C_7H_{15}C_{l2}N_2O_2P_2$). It was unknown how hepatic metastases affected the metabolism of cyclophosphamide. One patient experienced moderate renal failure. In cases of extreme toxicity and protracted alkylating substance retention in plasma Despite the fact that individuals who have previously taken medications that induce microsomal enzymes The total concentration × time product remained relatively constant for a given dose of cyclophosphamide, despite demonstrated marked variation in plasma half-life and peak alkylating levels. This suggests that changes in the rate of cyclophosphamide metabolism by drugs or liver metastases in the absence of renal failure will not affect toxicity or therapeutic effect.

Material and Method

Patients

180 female patient infected with breast cancer was collected from Margan hospital of Babylon and tumor hospital of medical city – Baghdad and 30 healthy women as control group.

Experimental protocol

180 female patient was divided in four groups each group consist of 50 patients according to number of dose from chemotherapy as following:

1-First group breast cancer infected female patient (n=50)and treated with one to four dose of chemotherapy ,one dose each week.

2- Second group breast cancer infected female patient (n=50)and treated with five to eight dose of chemotherapy ,one dose each week.

3-Third group breast cancer infected female patient (n=50)and treated with nine dose and above chemotherapy ,one dose each week.

4-Fourth group healthy women (n=30) as control group don’t use any drug .

Blood preparation:

all blood samples after draw was putting in gel tube and doing centrifuge for samples and isolate serum to assess liver enzyme , urea and creatinine .

Assessment of the biochemical parameters Determination

GOT and GPT measured in serum by The device ABBOTT -C4000/ United States From patients with breast cancer aged 20-50 years.

Urea and creatinine was measured by The Cobas Integra (Roche) completely automated analyzer was used to quantify urea using Urease Berthelot's method [32, 33] and creatinine using the modified Jaffe's approach [31, 32]. These biomarkers' typical ranges were 70–110 mg/dl. serum creatinine for females is 0.5–1.1 mg/dl and serum urea is 15–40 mg/dl..

Statistical analysis

All the results were analyzed by statistical analysis, using statistical package of social science (SPSS) to a significance value of ($P < 0.05$) Duncan test was used to determine the significant differences .

Results:

The result showed significant decrease of liver enzyme AST , ALT and ALP in all three treated groups when compared with control group and the non significant decrease of the third group compared with both first and second group treated group . table 1 explain this result.

The result showed significant inceased of urea and creatinine in all three treated groups compared with control group and the non significant increased of the third group compared with both first and second group treated group table 2 explain it.

Table (2) change in liver enzyme (GOT , GPT and ALP) in female patients with breast cancer treated with different dose of chemotherapy (mean ± SD).

Groups	ALP	AST	ALT
G1	90.144 ± 7.9 a	24± 0.0 a	17.6 ± 0.0 A
G2	90.92 ± 5.81 a	23.4 ±0.0 a	15.4 ±0.7 A
G3	87.2 ±4.2 a	21 ±1.6 a	13.5 ±0.1 A
CONTROL	244.1333 ±13.59 b	35.6 ±1.9 b	33 ±0.4 B

Different litter refer to significant difference ($p < 0.05$)

Similar letters refer to the non-significant difference ($p > 0.05$)

Table (2) : change in urea and creatinine in female breast cancer patients treated with different dose of chemotherapy (mean ± SD).

Groups	Urea	Creatinine
G1	27.7 ± 1.3 a	0.77 ± 0.01 A
G2	31.04 ± 4 a	0.78 ± 0.02 A
G3	33.73 ± 4.4 a	0.9 ± 0.08 A
Control	12.67 ±1 b	0.6 ± 0.035 B

Different litter refer to significant difference ($p < 0.05$)

Similar letters refer to the non-significant difference ($p > 0.05$)

Discussion

The result showed there are significant difference of liver enzyme between the all group which treated with different doses of chemotherapy and control group this refer to the side effect of chemotherapy on liver tissue and it make disturbance of hepatic function. May be this happen because the liver is site of metabolism of drug and chemotherapy drug .

In albino rats, cyclophosphamide caused nephrotoxicity. Changes in body and organ weights are indicators of renal damage induced by cyclophosphamide [20]. Nonetheless, this study's observations of the nephrotoxic effect of chemotherapy did not show any changes in body or kidney weights. Serum creatinine and urea concentrations are measured as part of the assessment of renal function [21]. On the other hand, rats given CP had higher serum levels of uric acid, urea, and creatinine. The observations align with earlier research findings [22]. Rats receiving CP have higher values of these measures, which is indicative of renal impairment. This may be explained by the fact that rats treated with CP had lower glomerular filtration rates, which resulted in decreased excretion of urea and creatinine. [23]] .

It is unknown what causes idiosyncratic hepatotoxicity when using cyclophosphamide. The cyclophosphamide-induced sinusoidal obstruction syndrome is most likely caused by the drug's direct toxic effects on the liver's sinusoidal cells, which lead to their necrosis and release into the sinusoids, obliterating hepatic veins, and creating obstruction. The hepatic cytochrome P450 system extensively metabolizes cyclophosphamide, resulting in the identification of over 150 metabolites. However, the pharmacokinetics and toxicities of these metabolites remain unclear.. this tissue damage lead to disturbance of liver enzyme levels(34).

The observed histological alterations in the liver and kidney tissues in this investigation could potentially be linked to a rise in cellular oxidative stress and a fall in antioxidant agents. Therefore, before administering chemotherapy medications to patients with malignancies, it is crucial to administer hepatoprotective and renoprotective drugs, preferably an antioxidant. Patients undergoing chemotherapeutic regimens should also have their liver and kidney function tests regularly monitored.(35). According to reports, safranal decreased unsaturated membrane lipids and reactive oxygen species, stabilized bio-membranes in biological systems, and improved serum enzyme levels, which prevented intracellular enzyme infiltration.(36This supports the widely held belief that serum transaminase levels revert to normal with hepatic parenchyma repair and hepatocyte regeneration. (37)

Recommendations:

Patient with breast cancer and treated with chemotherapy should be make follow-up to liver function and kidney function.

Results:

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