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**INVESTIGATING THE INFLUENCE OF ATORVASTATIN ANTIOXIDANTS IN
REDUCTION OF THE CARDIOTOXICITY OF ANTHRACYCLINE MEDICINES IN
TREATING PATIENTS UNDERGOING CHEMOTHERAPY**

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ABSTRACT

The rise and increase in the number of cancers has resulted in the greater use of chemotherapy medicines. Anthracycline is one of the widely used chemotherapeutic medicines. Although this medicine is really effective on cancer cells, it has side effects such as cardiotoxicity. The present research seeks to study the influence of Atorvastatin Antioxidants in reduction of the cardiotoxicity caused by anthracycline among 215 patients who had resorted to Imam Reza Hospital (PBUH). The patients were divided into the case and testifier group. Those in the testifier group received no doze of Atorvastatin, while the case group received 20 mg of this antioxidant every day. In the 0th, 3rd, and 6th months, patients were examined through ECG, Echocardiography, and clinical examinations so as to check the progress of Cardiomyopathy. The causes which contributed to the EF reduction of LV, symptoms of heart failure and development of heart failure were checked among them. After the information about each patient was collected, SPSS was used to analyze the data. 9 cases of cardiomyopathy were recorded. One of these cases was observed in the case group, while 8 were seen among those in the testifier group. This difference was observed significantly in two groups ($p < 0.05$). Considering the results obtained in this research, it was shown that Atorvastatin antioxidant has an effective

influence on the reduction of the cardiotoxicity of anthracycline medicine among those undergoing chemotherapy. Thus, it can be used among this group of patients.

Keywords: Anthracycline, Atorvastatin, Cardiomyopathy, Chemotherapy

INTRODUCTION

The last decades have testified a significant and quick growth in the effectiveness of chemotherapeutic medicines on a large group of cancers. These medicines have a significant influence over the survival rate of the patients, but their negative side effects should not be ignored. One of their most important influences is their cardiotoxicity [1]. The prevalence level of cardiotoxicity side effects includes a large scope of various side effects which affect those patients undergoing chemotherapy [2].

Anthracycline is a kind of antibiotics made of the derivatives of streptomyces peucetius widely used in the treatment of cancers [3]. Based on the definition of cardiotoxicity, the prevalence level of anthracycline cardiotoxicity ranges from 5 to 65 percent. This toxicity has always been recognized as a dose-dependent toxication [4]. Just like other medicines, the coronary side effects of these chemical medicines can have negative effects on the survival rate and life quality of the patients. As the reports indicate, some 10 million of those suffering from cancer have also experienced severe coronary side effects due to the influence of chemotherapy

medicines. As the predictions indicate, the majority of the death cases are due to the induced coronary side effects. Thus, the timely and precise diagnosis and treatment of these side effects can have a great effect on the survival rate of those suffering from cancer.

Several studies have taken into consideration the effect of some cardiac drugs on prevention and treatment of the cardiac side effects caused by the negative influences of chemotherapy. One group of such medicines is statins. It is mostly the role of this medicine in improving the cardiotoxicity of the Anaheim which has been widely studied [5]. As no preventive action is taken for those undergoing chemotherapy and it is only in the case of cardiomyopathy where medical treatments are assigned, this research seeks to study the influence of Atorvastatin antioxidant in reduction of the cardiotoxicity of the anthracycline among those patients who had resorted to Imam Reza Hospital (PBUH) in 2014.

METHODOLOGY

215 patients who had resorted to Imam Reza Hospital (PBUH) for the first time for

chemotherapy with HL, NHL, ALL, AML, Gastric cancer, and Breast cancer were selected and the questionnaires were filled by them. They were then divided into the patient and case groups. Patients suffering from ALL and AML were treated by Daunorubicin, while those suffering from HL, NHL, and Breast cancer were treated using Adriamycin and those suffering from Gastric cancer were treated using Epirubicin which were all members of the anthracycline family. The case group used the Atorvastatin medicine with the daily dose of 20 mg, while the testifier group did not use this medicine. In the 0th, 3rd, and 6th months, the patients were checked by ECG, echocardiography, and clinical testing to see the progress of cardiomyopathy. To reduce the error level,

all echocardiographies were conducted by a single device and a single operator. A single device was also used to prepare ECG and only one single operator conducted all the tests.

In this research, EF reduction of the LV based on the results of echo, cardiac failure symptoms (edema, exertional dyspnea), symptoms of cardiac failure (S3 Gallup, Tachycardia or both) and a 5% reduction of EF along with the signs or symptoms of cardiac failure or a 10% reduction of EF without any sign or symptom were considered to be the criteria of cardiomyopathy.

Table 1 lists the variables studied, the role of each one and the scales taken into consideration.

Table 1: The variables used, their role, type, scientific definition and the measurement unit of each one

Name of the variable	role of the variable				type of variable / variable scale				scientific-practical definition	measurement unit
					quantitative		qualitative			
	independent	dependent	confounding	background	distance	proportional	nominal	rating		
reduction of EF of LV based on echo										yes / no
signs of cardiac failure (edema, Exertional dyspnea)										yes / no
signs of cardiac failure (S3 Gallup, tachycardia or both)										yes / no
a 5% reduction of EF along with signs of cardiac failure or a 10% reduction of EF without any signs										yes / no
gender									the individual's genotype	female / male
age									how old the individual is	years

Describing and analyzing the data

After the required data was collected, it was analyzed using SPSS software. To study the relationship between the variables, we used correlation, while χ^2 test was used to measure the reduction of the EF of the LV and the prevalence of cardiac failure signs. To compare the data of continuous variables, Mann Withney test was used. To study the role of the variables in occurrence of the outcome, log. Regression was used and $p < 0.05$ was selected as the criterion.

RESULTS

Some 215 patients were studied among whom 119 were male and 9 were female. Figure 1 shows the frequency of each gender in the population studied.

The following diseases were observed among the population: 52 cases of lymphoma, 58 cases of Leukemia, 45 cases of breast cancer, and 60 cases of gastric cancer. Figure 2 represents the frequency of each disease among the population.

In this research, the patients were divided into the testifier and case group among whom, 103 used Atorvastatin every day and 112 as the testifieres did not use that medicine. Figure 3 represents the frequencies of the testifier and case groups.

The average age of the patients was 49.02 with the least and the most ages being 19 and

85 years old respectively. The testifier and case groups were synchronized in terms of their age. The average age of the testifier group was 48.69 ± 15.35 years old, while the average age of the testifier group was 49.32 ± 16.88 years. Figure 4 represents the average age of the testifier and the case group.

The testifier group included 62 male and 50 female patients. The case group was composed of 57 male and 46 female patients. Figure 5 represents the frequency of genders in both male and female groups.

The following diseases were observed among the testifier group: 28 cases of lymphoma, 29 cases of Leukemia, 22 cases of breast cancer, and 33 cases of gastric cancer. The following diseases were observed among the case group: 24 cases of lymphoma, 29 cases of Leukemia, 23 cases of breast cancer, and 27 cases of gastric cancer. Figure 6 represents the frequency of each disease among the case and testifier groups.

9 cases of cardiomyopathy were observed in this study. 1 case was observed in the case group and the other 8 were recorded among the testifiers. This difference was significant ($P < 0.05$). Charts 7 and 8 represent the frequency of cardiomyopathy in the whole population and each one of the groups.

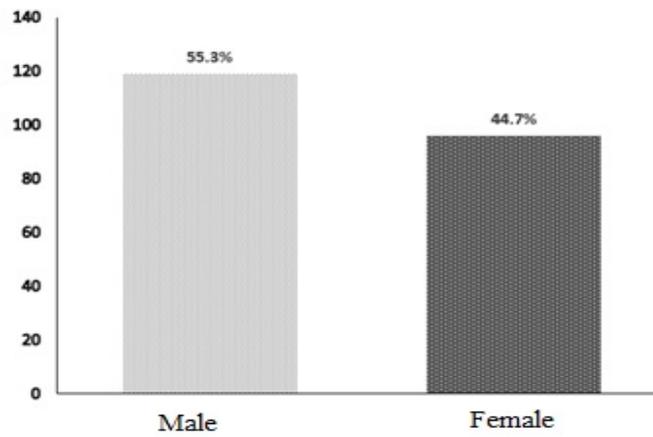


Figure 1: The frequency of gender in the whole population

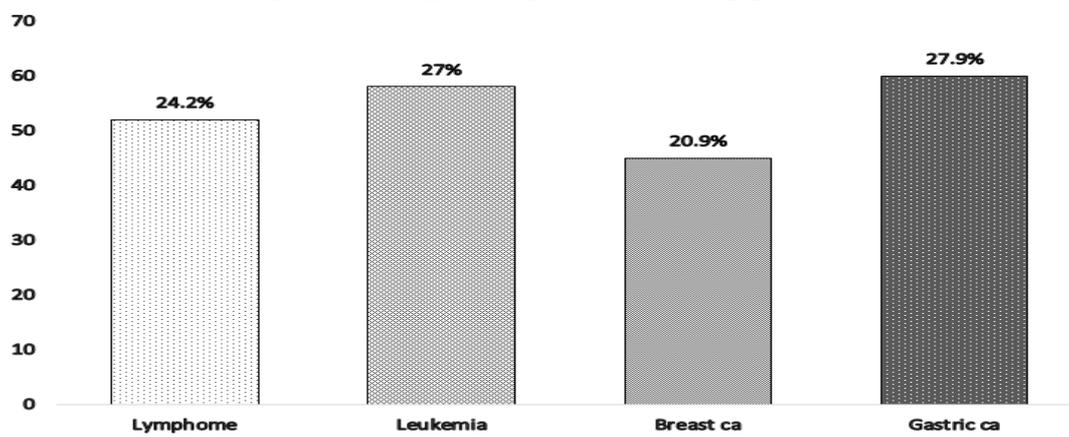


Figure 2: The frequency of diseases

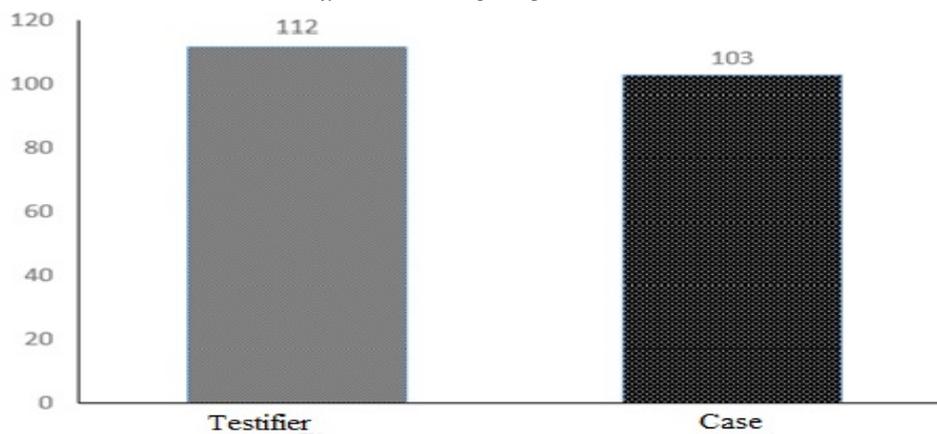


Figure 3: The frequencies of the testifier and case group

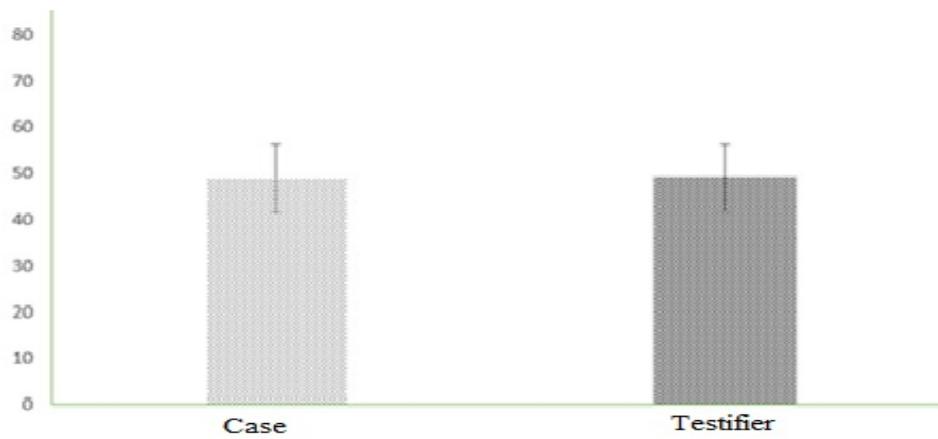


Figure 4: The average age in the testifier and case groups

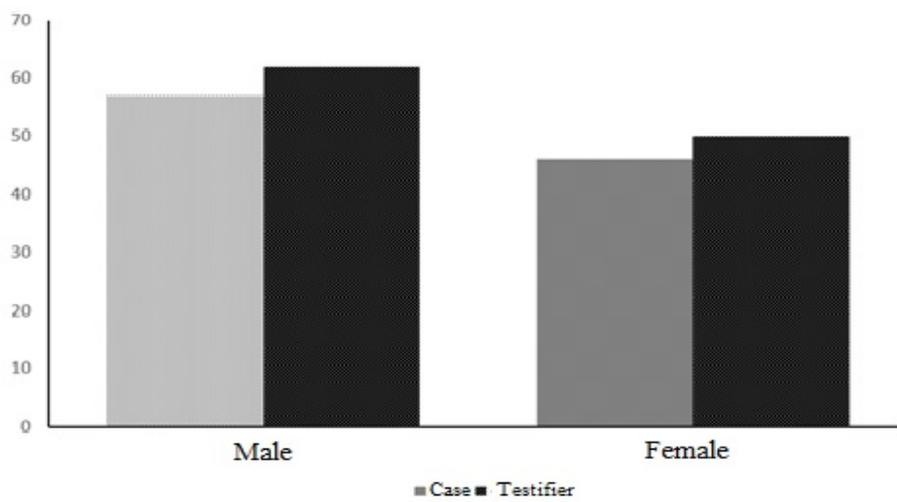


Figure 5: The frequency of genders in the case and testifier groups

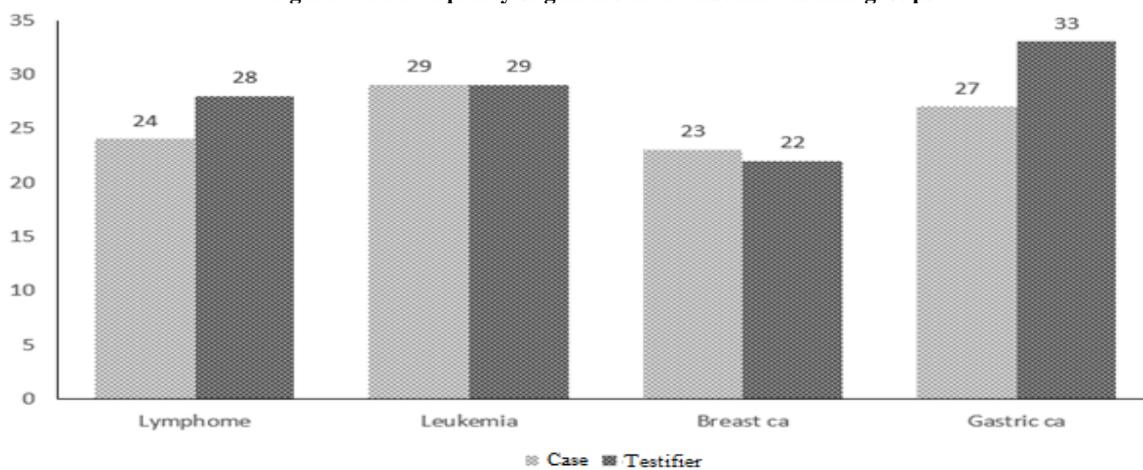


Figure 6: The frequency of diseases in the testifier and case groups

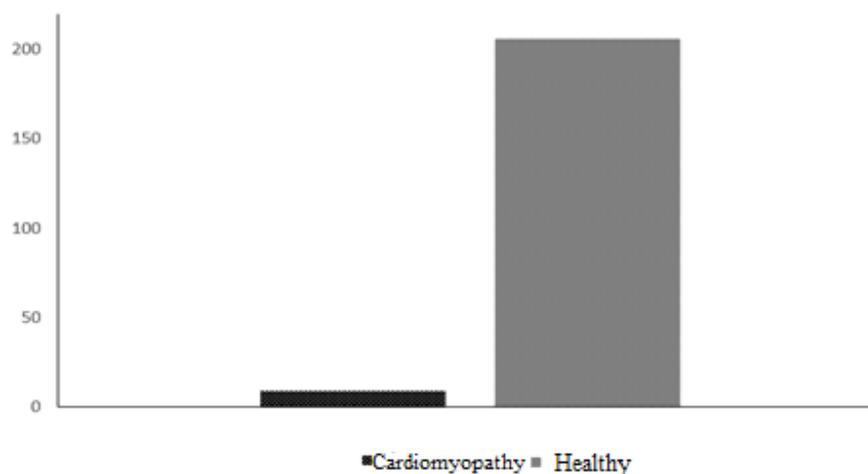


Figure 7: Cardiomyopathy frequency in the whole population

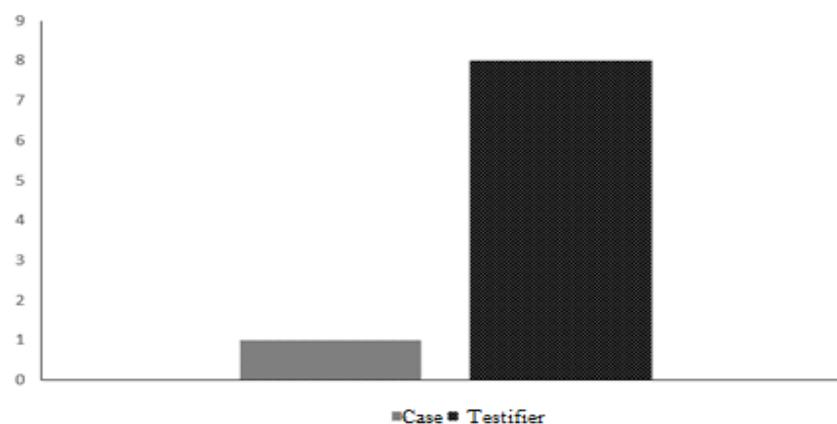


Figure 8: Cardiomyopathy in case and testifier groups

DISCUSSION AND CONCLUSION

The significant and effective growth of chemotherapy medicines has increased the hope for the treatment of many diseases. These medicines have a significant influence on the survival rate of those suffering from cancer. The main goal of chemotherapy is to destroy cancer cells without causing any damage to the surrounding cells. However, those medicines which are used for chemotherapy have side effects [1].

Anthracyclines are a group of antibiotics used in chemotherapy derived from a kind of bacteria. These medicines are widely used to treat cancer due to the positive influence they have in stopping the cancer cells from developing [3]. The most serious side effect of the anthracycline is the cardiotoxicity. The patients who are treated using this method may experience side effects such as reduced ventricular performance, general symptoms of cardiac failure, and cardiac failure symptoms. To prevent and treat these

side effects, various medicines and instructions are available. One such instruction is detailed cardiac examination before the commencement of chemotherapy and the regular follow-up of those undergoing chemotherapy and their careful examination while undergoing chemotherapy. Other medicines such as beta-blockers (Carvedilol) and Angiotensin receptor inhibitor 2 and statins are also used to prevent or treat cardiomyopathy [4].

In the study conducted on mice, the influence of Probucol in preventing cardiomyopathy following the consumption of Adriamycin was investigated. It was proven that the above-said medicine is capable of preventing cardiomyopathy [6].

The influence of consuming Lovastatin in preventing cardiomyopathy due to taking Anthracycline was studied on mice and, as the results indicated, lovastatin was capable of reducing cardiomyopathy [7].

Jevo et al. studied the influence of traditional Chinese medicine in preventing cardiomyopathy and, as their results indicated, the above-said medicine is capable of preventing cardiomyopathy [8].

In a research conducted by Juan et al., the antagonist influence of the receptor of platelet growth factor in preventing cardiomyopathy caused by Anthracycline

was studied and it turned out that the above-said medicine prevents the death of cardiac cells [9].

The study conducted by Sing et al. showed that sulfur as an antioxidant prevents the death of cardiac cells [10].

Another research studied the influence of carvedilol, spironolactone and valsartan separately. It turned out that all these medicines reduce the cardiomyopathy caused by anthracyclines [11-14].

The present research studied 215 patients undergoing chemotherapy in two groups which were synchronized in terms of their age, disease outbreak, gender, etc. The case group took Atorvastatin with a dose of 20 milligrams, while the testifier group did not take this medicine. Patients underwent cardiac examination in the 0th, 3rd, and 6th months of their treatment and their cardiomyopathy criteria was taken into consideration. Finally, it turned out that 8 patients from the testifier group (7.14%) and 1 patient from the case group (0.97%) were afflicted with cardiomyopathy.

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