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Does Adriamycine, Cytoxan with Taxol Treatment Affect FBS and Lipid Profile in Breast Cancer Patients

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Abstract

Introduction: Many breast cancer survivors experience post-treatment metabolic complications based on their regimen. Various results have been reported regarding tamoxifen therapy effects on lipid profile and FBS level. But, no study investigate adriamycine, cytoxan with taxol treatment on them one year after finishing the treatment.

Patients and method: Breast cancer patients under adriamycine, cytoxan with taxol regimen were chosen. FBS and lipid profile items were measured before the treatment and one year after the treatment ended. Patients have been monitored during the year after therapy. These two pairs were compared and Sig<0.05 showed meaningful relation.

Result: A total of 114 breast cancer patients with stage III or IV were participated in this cross-sectional study. Our analysis showed this regimen had no significant impact on FBS and lipid profile items one year after finishing the treatment.

Conclusion: In summery the findings of the current study showed adriamycine, cytoxan with taxol regimen had no meaningful impact of FBS and lipid profile level one year after the treatment. It is advised to monitor breast cancer metabolic items during and after the treatment.

Keywords: Adriamycine; Cytoxan; Taxol; Breast cancer; Lipid profile; FBS

Introduction

Breast cancer is a common worldwide concern which has considerable survivor groups among other malignancies. Breast cancer and lung cancer are the leading causes of mortality in female population. Although breast cancer prevalence has increased recently, mortality rate has dropped to 1.6% yearly [1-3]. Chemotherapy as the main treatment or (neo)adjuvant method has been used for many years. adriamycine, cytoxan with taxol treatment has been used recently [4]. Adriamycine is an antibiotic which is used on malignancies of breast, urine bladder, soft tissue, and leukemia. It has side effects like cardiomyopathy and renal failure [5,6]. Cytoxan (cyclophosphamide) is metabolized into alkalizing agent by liver which plays a role in treating chronic leukemia, lymphoma, and autoimmune diseases. [7,8]. Taxol (Paclitaxel) prevents formation and polymerization of microtubules which is essential during cell mitosis. This new medication treats lung, ovarian, breast, head, and neck cancer; however, it may cause neutropenia and peripheral neuropathy is some cases [9-11].

Not only treatment is crucial in breast cancer patients' prognosis, but also it affects their quality of life after surviving. Breast cancer survivors are posed to various post-treatment challenges such as gaining weight and insufficient physical activity. These complications are correlated with metabolic profile disturbance which may lead to metabolic syndrome. Metabolic syndrome is connected to higher chance of breast cancer mortality and recurrence [3].

No other studies has investigated the effect of adriamycine, cytoxan with taxol on metabolic profile items one year after the treatment. The purpose of this study was to investigate the impact of this treatment on the late stage breast cancer patients' post-treatment FBS and lipid profile.

Patients and Method

Patients

Breast cancer patients between ages 28 to 75 participated in this study. All the patients were chosen from our Oncology clinic at Sayed Al-Shohada Medical Center in Isfahan, Iran. Our inclusion criteria were menopausal status, normal BMI (18.5-24.9), and adriamycine, cytoxan with taxol treatment. If

the patient had a past medical history of previous chemotherapy, radiotherapy, and glucocorticoid or steroid usage, they were excluded from the sample.

Methods

Patients' breast cancer was diagnosed recently based on the histological report and their cancer stages were III or IV. They had not received any kind of treatment previously. They were interviewed before the treatment and the study method was explained to them thoroughly. An informed consent form was fill out by them. Our Ethics Committee approved the study procedure and consent form. Patients could leave the study whenever they wanted, but their information and data was omitted during analysis. During interview, patients were instructed to follow a normal routine diet and acceptable physical activity like jogging for 30 min daily during the program and avoid using fast foods and products containing high amount of starch or sugar. Also, they agreed to regular follow-ups during one year after their treatment. After the interview, they were all referred to our medical lab to measure fasting lipid profile and fasting blood sugar (FBS). Shortly after that adriamycine, cytoxan with taxol treatment was initiated. The treatment took 2.5 months and it was done every 3 weeks. This treatment schedule was similar in all the cases. Also, FBS and lipid profile items were measured one year after finishing the treatment. During this one year follow-up, random FBS or lipid profile was checked for patients presenting diabetes mellitus symptoms such as polyuria and polydipsia. All these tests were done by the same medical lab during the study.

Analysis

All data was inserted into SPSS software V22 and T-Test was used for the evaluation of two pairs. The primary FBS and Lipid Profile of the sample and the follow-up results were compared with each other. A Sig (2-tailed) <0.05 showed a meaningful relation between the pairs and chemotherapy.

Result

This prospective cross-sectional study was conducted between September 2013 and September 2015 at Sayed Al-Shohada Medical Center in Isfahan, Iran.

At first, 156 candidates were chosen for this study. Due to our inclusion and exclusion criteria, 21 patients' data was excluded because they received glucocorticoid for some reason during the study or their past medical history. 12 candidates did not attend their follow-ups and left the study. 9 candidates did not follow our dietary plan and we were forced to remove them from the final analysis.

All in all, 114 patients have participated in this survey till the end. The mean age of them was 47 with the range of 28 to 74 years old. They were all diagnosed by stage III or IV breast cancer and have had a full course of adriamycine, cytoxan with taxol treatment for 2.5 months.

Regarding the primary FBS results, 68 patients (59.6%) had a normal level (FBS ≤ 99 mg/dl). 42 patients (36.8%) were in the prediabetic group. The mean primary FBS was 112.8 mg/dl although 4 patients had 125<FBS<260 who had shown no signs or symptoms of diabetes mellitus. These 4 cases were instructed to follow our diet program and regular exercise.

Random FBS tests were done during their treatment and follow-up. Considering the final FBS results, the mean was 114.3 mg/dl. 60 patients (52.6%) with primary normal FBS had a normal final FBS, too. 8 patients of this group had an FBS between 100 and 124 mg/dl.

Regarding the primary prediabetic group, 3 patients had a normal final FBS (<100 mg/dl). On the other hand, the primary diabetic candidates had FBS lower than 200 mg/dl by the end of the study. According to our analysis, no meaningful correlation was found between changes in FBS tests in each category which demonstrates that adriamycine, cytoxan with taxol treatment had no considerable impact on FBS 1 year after the treatment (Sig=0.688) (**Table 1**).

Table 1 FBS results.

Category	FBS 1 (initial) mg/dl		FBS 2 (final) mg/dl	Pair FBS 1, FBS 2 Sig.(2-tailed)
Normal FBS<100	Count	68 (59.6%)	63 (55.4%)	0.672
	mean	89.1	88.3	
Prediabetic 99<FBS<126	Count	42 (36.8%)	57 (50%)	0.543
	Mean	114.2	113.6	
Diabetic FBS>125	count	4 (3.6%)	4 (3.6%)	0.213
	mean	208.4	189.1	
Mean of the whole sample	112.8		114.3	0.688

On the other hand, **Table 2** shows the pre and post-treatment measurement of lipid profile. The mean total cholesterol level was 191 mgs/dl pre-treatment and 220 mgs/dl post-treatment. Although a slight increase is visible in the mean total cholesterol (TC) and LDL level, both profiles were in the borderline category. HDL level was normal (30-60 mgs/dl) before and after chemotherapy; however, a slight decrease was detected after treatment. Moreover, Triglycerides level was increased from 187 mgs/dl to 210 mgs/dl. Regarding the lipid profile analysis, adriamycine,

cytoxan with taxol treatment did not affect its level although slight changes were recorded in each item (**Table 2**).

Table 2 Lipid profile analysis.

Item	Pre-treatment (mean) mgs/dl	Post-treatment (mean) mgs/dl	Pair/Sig.(2-tailed)
Total Cholesterol	191	220	0.241
Triglycerides	187	210	0.431
HDL (High-density lipoprotein)	55	45	0.332
LDL (Low-density lipoprotein)	105	131	0.743

Discussion

Chemotherapy post-treatment complications in breast cancer patients are caused by metabolic profile abnormality [12]. One study demonstrated that more than 16% of the whole breast cancer patients had Diabetes Mellitus and poorer prognosis in comparison to others [12]. Regarding the result of one cohort study, higher rate of mortality and recurrence was detected in direct relation to increased fasting serum insulin level [13]. Postmenopausal breast cancer patients are at risk of cardiovascular and metabolic diseases [14,15]. Furthermore, studies showed that the rate of higher body mass index (BMI) and cholesterol and Triglycerides level increased in premenopausal breast cancer patients after chemotherapy [16]. Glucocorticoides are administered to lower chemotherapy adverse reactions [17] which cause hyperglycemia by disturbing hypothalamic-pituitary–adrenal axis. It has been shown that hyperglycemia interrupts chemotherapy drugs efficacy [4,18].

Many studies claimed that breast cancer risk was increased in patients with higher insulin like growth factor-1 (IGF-1) and lower insulin growth factor binding protein-3 (IGFBP-3). IGFBP-3 inhibits cell growth and stimulates apoptosis. Hyperinsulinemia and insulin resistance are associated with increased IGF-1 level by stimulating its hepatic synthesis which poses the risk of cancer cell proliferation, survival, and migration [19]. Moreover, insulin and IGF-1 promote cell mitogen rate in cancer cells because of higher insulin receptors (IRs) and its bioactivity [20]. Also, one case-control study used Metformin as adjuvant therapy to control breast cancer cell proliferation and chemotherapy efficacy [21]. Based on what mentioned previously, we decided to monitor FBS as a mean to diagnose and monitor DM. A population-based study claimed that tamoxifen was associated with higher risk of DM after the treatment, but it had no long lasting impact. As a matter of fact, no increased probability of DM was found among previous tamoxifen patients and it had promoted hyperglycemia in their candidates. On the other hand, an Asian cohort study claimed that tamoxifen users were at higher risk of developing diabetes regardless of their age, but they had used non-breast cancer women as their control group [22]. Our analysis showed no meaningful relation was found between adriamycine, cytoxan with taxol and post-treatment FBS level. Furthermore, 4 of our cancer patients had DM at the start of the study and their FBS levels were lower at the end. Although some patients had post-treatment prediabetic state after having normal FBS levels, no new DM incidence was found.

Studies on tamoxifen revealed various contradictory results regarding lipid profile items in breast cancer patients [3,23]. One study on 109 breast cancer patients treated by tamoxifen declared lower LDL and TC level. In contrast, metabolic dysfunction and weight gain has happened 4 months after (neo) adjuvant therapy in more than 70% of cases in one study on tamoxifen in breast cancer patients. Our result showed slight increase in TC, TG, and LDL level; however, no relation was found between our treatment regimen and lipid profile changes.

Conclusion

In summery the findings of the current study showed adriamycine, cytoxan with taxol regimen had no meaningful impact of FBS and lipid profile level one year after the treatment. It is advised to monitor breast cancer metabolic items during and after the treatment.

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