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**RESEARCH ARTICLE**

# EFFECT OF TAMOXIFEN ON LIPID PROFILE IN IRAQI BREAST CANCER WOMEN.

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## *Abstract*

**Background:** Tamoxifen-citrate, a non-steroidal anti-estrogen, is one of the most widely used hormonal treatments for patients with breast cancer. It has been suggested that its estrogenic activity is mainly responsible for the observed changes in lipid parameters.

**Objective:** the aim of this study is to explore the effects of tamoxifen on lipid profile in women with breast cancer.

**Patients and Methods:** the present study is a cross-sectional study (2010/2011) done at Al-Yarmouk Teaching Hospital. Includes measurement of LP in sera of postmenopausal women with BC (whether newly diagnosed or on tamoxifen treatment). This measurement was done using colorimetric method. In The results of this study include a total of 200 patients with BC were involved in this study, they were classified as newly diagnosed postmenopausal women with BC G1: (n=100); Postmenopausal women with BC on tamoxifen therapy G2: (n=100).

**Results:** Serum Lipid Profile: Serum LP was significantly improved in BC group who receive treatment with tamoxifen when compared with newly diagnosed BC groups whom receive no therapy : this improvement was in term of significant reduction in TC, TG, LDL and VLDL (despite the reduction was insignificant) accompanied by elevation of HDL although it was insignificant.

**Conclusion:** the level of LP was significantly improved upon tamoxifen treatment.



## Introduction:-

Tamoxifen-citrate, a non-steroidal antiestrogen, is one of the most widely used hormonal treatments for patients with breast cancer. Recent studies in pre- and postmenopausal women have shown that tamoxifen exhibits favorable effects on the lipid and lipoprotein profile by decreasing the total and Low Density Lipoprotein (LDL) cholesterol levels as well as the Lipoprotein a (Lp(a)) levels [1-4]. It has been suggested that its estrogenic activity is mainly responsible for the observed changes in lipid parameters [5, 6]. Consequently, an increased VLDL synthesis leading to increased triglyceride levels is expected after tamoxifen administration [7, 8]; However, long-term data from clinical trials have failed to demonstrate a cardioprotective effect [9,10]. Tamoxifen has its own side-effects as may cause fatty liver , otherwise known as steatorrhoeic hepatosis or steatosis hepatis. Nevertheless, Tamoxifen is currently used for the treatment of both early and advanced ER+ (estrogen receptor positive) breast cancer in pre- and post-menopausal women [11]. However, marked hypertriglyceridemia sometimes associated with life-threatening complications is occasionally reported after tamoxifen administration [12]. TAM has been reported to have beneficial estrogenic agonist effects on lipid profiles [13], leading to fewer cardiac events among breast cancer patients [13, 14].The aim of this study is to explore the effects of tamoxifen on lipid profile in women with breast cancer.

## Subjects & Methods:-

Subjects: the study was a cross-sectional study carried out at Oncology Department at Al-Yarmouk Teaching Hospital, during the period from October, 2010 till the end of September, 2011. The protocol for the study was approved by the Ethical committee of Al-Nahrain Medical College, and informed signed consent was given by each subject. The study was conducted 100 Consecutive patients with histological confirmed hormone receptor–positive early-stage breast cancer. Additional inclusion criteria included: (a) no evidence of recurrent or metastatic disease; (b) postmenopausal women and (c) primary-treating oncologist approval. 100 postmenopausal, age-matched, healthy women were also recruited for comparison purposes.

Blood samples: five milliliters of random venous blood were withdrawn from each patient and control after 12 hours fast. in supine position, without application of tourniquet. The samples were transferred into clean new plane tube, left at room temperature for 15 minutes for clotting, centrifuged at 1800 x g for 10 minutes at 4°C, and the separated serum was transferred into Eppendrof tube and was used for measurement of lipid profile. The tubes were stored at $4^{o}$ C until analysis, which was done within one week after collection. [15].

Methods: measurement of serum LP was done by colorimetric enzymatic method using suitable kits (Biomerieux, France).

Statistical analysis: statistical analysis was done using Excel system version 2003 and includes descriptive statistics (mean and standard deviation) and inferential statistics (t-test) to test the significance of mean difference. When P-value was less than 0.05, the difference is considered statistically significant, and the difference is considered highly significant when P-value was less than 0.001.

## Results:-

Subjects: a total of 100 patients with BC were enrolled in this study who were newly diagnosed to have BC who receives no therapy for cancer (G1).The other 100 patients were women with BC who receive Tamoxifen as hormonal therapy for 6 months duration (G2) as in Table 1. Serum Lipid Profile: Serum LP was significantly improved in BC group who receive treatment with tamoxifen (G2) when compared with newly diagnosed BC groups whom receive no therapy (G1) [$P < 0.001$] : this improvement was in term of significant reduction in TC, TG, LDL and VLDL (despite the reduction was insignificant) accompanied by elevation of HDL although it was insignificant [$P < 0.05$] as in Table 2.

**Table (1): Clinical criteria of patients` groups with Breast Cancer (newly diagnosed & Breast Cancer on tamoxifen therapy (presented as range and mean ± SD).**

| Group | No. | Age [range] Mean (SD) in years | Age at Menarche [range],mean (SD) in years | BMI[range],mean(SD) |
|---|---|---|---|---|
| G1 | 100 | [57-69], 62( 7) | [11-13.5], 11.7 (0.6) | [23.5-32-2], 28.1(3.5) |
| G2 | 100 | [46-55], 60(6) | [12.5-14], 13.6 (0.3) | [21.5-33.2],27.1 (6) |

**Table (2): The mean serum Lipid Profile in different groups of women with Breast Cancer (presented as mean ± SEM).**

| Variable | No. | TC(mmol/L)* | TG(mmol/L)* | LDL(mmol/L*) | HDL(mmol/L*) | VLDL(mmol/L) |
|---|---|---|---|---|---|---|
| G1 | 100 | 5.8 ± 1.6 | 2.7 ± 0.2 | 5.8 ± 1.6 | 1.06± 0.63 | 1.23 ± 0.23 |
| G2 | 100 | 5.2 ± 0.4 | 2.6 ± 0.2 | 2.9 ± 0.5 | 1.15± 0.1 | 1.15 ± 0.63 |

(G1): Postmenopausal women with BC: newly diagnosed, on no treatment. (G2): Postmenopausal women with BC: on Tamoxifen * t-test: G1 versus G2, $p < 0.001$

## Discussion:-

This cross-sectional study show the effect of tamoxifin as a hormonal therapy on lipid profile in women with breast cancer, the results demonstrate a favourable effect of tamoxifen supported by statistically significant decreases in serum TG, TC and LDL-C after tamoxifen treatment in breast cancer patients. The results demonstrated that the serum TC levels were reduced by tamoxifen, in agreement with the results of comparable studies [ 1,10,11].

However, the results of this study are in contrast with those of a Japanese study: Hozumi et al. [17] reported that the serum TC levels remained unchanged after tamoxifen treatment. Other study by Kanel [18] reported that tamoxifen increased the TG levels after initiation of the drug but in dyslipidemic patients rather than normolipidic patients this increase was resolved after prolonged therapy that proves tamoxifen has a cardioprotective effect which might be explained on genetic base as single nucleotide polymorphism (SNP)[19] or due to the fact that tamoxifen may interfere with hepatic lipid metabolism [20] . The results of the LDL-C level reduction by tamoxifen are consistent with previous series [20,21]. There are potential limitations to this study. In this study, no data on dietary effects, lifestyle, or cardiac events are available. Furthermore, the tamoxifen lipid profile data were presented only for the first six months. The short follow-up period is indeed a limitation of this study. This study does have several limitations. Two obvious limitation are the relatively small sample size and cross-sectional study design. To adequately investigate the impact of adjuvant breast cancer therapy on cardiovascular health, large prospective studies are required to further investigate these findings. In this study, the small number of patients was another limitation. Other limitation of this study which also represent a study for future work is a molecular study of steroid receptors (whether glucocorticoid or estrogen) as these receptors are involved action of tamoxifen and lipid catabolism [14,21,22 ]. Furthermore, a new class of steroid hormone receptors has recently been elucidated: Along with the well documented intracellular receptors, cell membrane receptors have been shown to exist. Their cellular responses are much quicker than those of the intracellular receptors [19,23,24].

In conclusion, tamoxifen as a hormonal therapy for breast cancer, has a favourable effect on lipid profile in postmenapausal women; this effect might be attributed to antiestrogen action of tamoxifin; although it worsen postmenapausal symptoms, it has a favourable cardioprotective effects, the negative effect on the patients' routine daily life can be minimised and the greatest benefit from endocrine therapy can be obtained. In order to give certain behaviour approaches, we need multi-institutional research projects on large numbers of people with the help of future research.

**The authors declare no conflict of interest**

## References


1. Lin ,C ; Chen, L ; Kuo, S; Chen ,D (2014) Adjuvant Tamoxifen Influences the Lipid Profile in Breast Cancer Patients. Breast Care 2014;9:35–39
2. Tominaga T, Kimijima I , Kimura M , Takatsuka Y , Takashima Sh
3. Nomura Y, Kasumi F, Yamaguchi A, Masuda N, Noguchi S and Eshima N. Effects of Toremifene and Tamoxifen on Lipid Profiles in Post menopausal Patients with Early Breast Cancer: Interim Results from a Japanese Phase III Trial. Clin Oncol 2010;40(7)627–633.
4. Gupta S, Tandon VR , Kapoor B , Gupta A , Gupta GD , Khajuria V. Effects of Tamoxifen Therapy on Plasma Lipid Profile in Patients of Breast Cancer. JAPI . 2006: 54 :183-186.
5. Bruning PF, Bonfrer JM, Hart M et al. Tamoxifen, serum lipoproteins and cardiovascular risk. Br J Cancer 1988; 58: 497-9.
6. Ingram D. Tamoxifen use, oestrogen binding and serum lipids in postmenopausal women with breast cancer. Aust NZ J Surg 1990; 60: 673-5.
7. Powles TJ, Jones AL, Ashley SE et al. The Royal Marsden Hospital pilot tamoxifen chemoprevention trial. Breast Cancer Res Treat 1994; 31: 73-82.
8. Mouridsen H, Keshaviah A, Coates AS, et al. Cardiovascular adverse events during adjuvant endocrine therapy for early breast cancer using letrozole or tamoxifen safety analysis of BIG 1-98 trial. J Clin Oncol 2007;25:5715 – 22.
9. Liu CL, Yang TL: Sequential changes in serum triglyceride levels during adjuvant tamoxifen therapy in breast cancer patients and the effect of dose reduction. Breast Cancer Res Treat 2003;79:11–16.
10. Lewis S: Do endocrine treatments for breast cancer have a negative impact on lipid profiles and cardiovascular risk in postmenopausal women? Am Heart J 2007;153:182–188.
11. Love RR, Newcomb PA, Wiebe DA et al. Effects of tamoxifen therapy on lipid and lipoprotein levels in postmenopausal patients with node-negative breast cancer. J Natl Cancer Inst 1990; 82: 1327-32.
12. Bertelli G, Pronzato P, Amoroso D et al. Adjuvant tamoxifen in primary breast cancer: influence on plasma lipids and antithrombin III levels. Breast Cancer Res Treat 1988; 12: 307-10.
13. Dziewulska-Bokiniec A, Wojtacki J, Skokowski J, Kortas B. The effect of tamoxifen treatment on serum cholesterol fractions in breast cancer women. Neoplasma. 1994; 41(1):13–16.

14. Markopoulos C, Polychronis A, Zobolas V, Xepapadakis G, Papadiamantis J, Koukouras D, Lappas H, Gogas H: The effect of exemestane on the lipidemic profile of postmenopausal early breast cancer patients: preliminary results of the TEAM Greek sub-study. Breast Cancer Res Treat 2005;93:61–66.10.
15. Esteva FJ, Hortobagyi GN: Comparative assessment of lipid effects of endocrine therapy for breast cancer: implications for cardiovascular disease prevention in postmenopausal women. Breast 2006;15:301–312.
16. Rifai-N; Bachorik-PS; Albers-JJ. Lipids, lipoproteins and apolipoproteins,in: Tietz Textbook of Clinical Chemistry. Burtis-CA, and Ashwood-ER. (Eds.), 3rd ed. 1999, Saunders Company, Philadelphia: 837-856.
17. Love RR, Wiebe DA, Feyzi JM, Newcomb PA, Chappell RJ. Effects of tamoxifen on cardiovascular risk factors in postmenopausal women after 5 years of treatment. J Natl Cancer Inst. 1994; 86(20):1534–1539.
18. Hozumi Y, Kawano M, Saito T, Miyata M: Effect of tamoxifen on serum lipid metabolism. J Clin Endocrinol Metab 1998;83:1633–1635.
19. Kanel KT, Wolmark N, Thompson PD. Delayed severe hypertrig lyceri- demia from tamoxifen. N Engl J Med 1997; 337: 281.
20. Almeida S, Franken N, Zandona MR, Osorio-Wender MC, Hutz MH. Estrogen receptor 2 and progesterone receptor gene polymorphisms and lipid levels in women with different hormonal status. Pharmacogenomics J 2005;5:30–34.
21. Holleran AL, Lindenthal B, Aldaghlas TA, Kelleher JK. Effect of tamoxifen on cholesterol synthesis in HepG2 cells and cultured rat hepatocytes. Metabolism 1998;47:1504–1513.
22. Powles TJ, Jones AL, Ashley SE et al. The Royal Marsden Hospital pilot tamoxifen chemoprevention trial. Breast Cancer Res Treat 1994; 31: 73-82.
23. Love RR,Wiebe DA, Newcomb PA et al. Effects of tamoxifen on cardiovascular risk factors in postmenopausal women. Ann Intern Med 1991; 115:860-4.
24. Shewmon DA, Stock JL, Abusamra LCL, Kristan MA, Baker S, Heiniluoma KM Tamoxifen decreases lipoprotein(a) in patients with breast cancer. Metabolism 1994; 43: 531-2.
25. Elisaf M, Bairaktari E, Nicolaides C et al. The beneficial effect of tamoxifen on serum lipoprotein-a levels: An additional antiatherogenic property. Anticancer Res 1996; 16: 2725-8.