Tamoxifen Effects on the lipid profile in premenopausal women with Breast cancer: A follow up study

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Abstract:

**Background:** Breast cancer composed of several biologic subtypes that have response to hormonal therapy. Tamoxifen is hormonal therapy with tissue-specific antagonistic or agonist effects, the latter being responsible for multiple effects on lipid metabolism in women.

**Objective:** This study was designed to determine the impact of Tamoxifen on the serum lipid profile in breast cancer women.

**Patients and methods:** Prospective observation cohort study conducted at Oncology Teaching Hospital, Medical city complex, starting from October 2015 to October 2016. A total number of 40 premenopausal women with breast cancer were enrolled in this study according to inclusion criteria. Patients were followed for three months by the measurements TC, TG, HDL – cholesterol and BMI.

**Results:** At the end of three months of hormonal therapy, Tamoxifen showed a significant decrease in TG, VLDL (p < 0.001 for both). On the other side HDL and BMI showed significant increase over three months duration, (p = 0.001 and 0.006, respectively).

**Conclusion:** Beneficial alterations of lipid profiles were seen in pre-menopausal breast cancer patients treated with Tamoxifen.

**Keywords:** Breast cancer, Tamoxifen, the lipid profile, premenopausal women.

Introduction:

Practically two-thirds of females with breast cancer have overexpression of estrogen (ER) and/or progesterone receptors, and will get advantage from anti-estrogen remedy (1, 2). Tamoxifen is a selective estrogen receptor modulator (SERM). Tamoxifen works by blocking estrogen from binding to the estrogen receptor. It does not change estrogen production. (3) It has strongly anti-estrogenic on mammary epithelium, hence use in the treatment of breast cancer, it is pro-estrogenic on uterine epithelium and increased occurrence of endometrial carcinoma. (4) Like definite estrogens, tamoxifen lowers total serum cholesterol, low-density-lipoprotein cholesterol due to estrogenic effect, and potentially reducing the risk of myocardial infarction. It is therefore inappropriate to refer to tamoxifen simply as an anti-estrogen. The term selective estrogen receptor modulator is more appropriate (5).

This study targets to determine the change in serum lipid profile in women treated with Tamoxifen for hormonal positive breast cancer.

**Patients and methods:**

**Study design:** A Prospective, observation cohort study, conducted at Oncology Teaching Hospital, Medical city complex in Baghdad. Starting from October 2015 to October 2016.

**Definition of the case and inclusion criteria:** Breast cancer women on adjuvant hormonal therapy with tamoxifen (in a dose 20 mg once daily), who start on tamoxifen with the start of the study were the target of this study. It included premenopausal women without metastasis disease.

**Exclusion criteria:** Patients with cholesterol reduction formula, with diabetes mellitus, thyroid dysfunction, hepatic or renal impairment, smoker patients, pregnant patients, and hypertensive patients on treatment which have effect lipid profile like beta-blocker and thiazide were excluded. For this long exclusion criteria the sample size is small, and bigger sample needs to be studied in the future.

**Sampling:** This study enrolled all patients who have followed for three months by the measurements of lipid profile (Total cholesterol, Triglyceride, HDL – cholesterol). And calculated: LDL, VLDL and BMI by following formulas:
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Table 1: Baseline characteristics of studied groups (N=40).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base Line</th>
<th>After three month</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>29.71(26-30)</td>
<td>29.71(26-34)</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>120.8(98-153)</td>
<td>119.7(88-135)</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>95.5(67-137)</td>
<td>91.1(37-137)</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>45(37-50)</td>
<td>49.5(43-59)</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>120.14(106-140)</td>
<td>119.7(88-135)</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td>24.16(19-30)</td>
<td>19.1(13-27)</td>
</tr>
<tr>
<td>Type of surgery</td>
<td>Lumpectomy</td>
<td>Mastectomy</td>
</tr>
</tbody>
</table>

Table 2: Statistical characteristics of all studied patients (N=40).

<table>
<thead>
<tr>
<th>Properties</th>
<th>Mean(Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(year)</td>
<td>39.32(26-47)</td>
</tr>
<tr>
<td>Weight(Kg)</td>
<td>81.35(58-138)</td>
</tr>
<tr>
<td>Length(M)</td>
<td>1.61(1.45-1.75)</td>
</tr>
<tr>
<td>BMI(kg/m2)</td>
<td>29.71(26-34)</td>
</tr>
</tbody>
</table>

Table 3: Change in lipid parameters and body mass index (BMI) after 3 months of adjuvant tamoxifen remedy in premenopausal breast cancer patients (N=40).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Median(IQR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>95.5(67-137)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>190(152-212)</td>
<td>0.150</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>49.5(43-59)</td>
<td>0.001*</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>119.7(88-135)</td>
<td>0.067</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td>19.1(13-27)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (Kg/m2)</td>
<td>30.51(25-35)</td>
<td>0.006*</td>
</tr>
</tbody>
</table>

Discussion:

Breast carcinoma is the most common malignant tumor and the leading cause of carcinoma death in women.(7) Tamoxifen is the most universally endocrine treatment used in females with hormone-
positive breast cancers, which interfering with estrogen waving by a selective estrogen-receptor modulator, and exerts a beneficial effect on lipid profiles. (8) The main influence of tamoxifen on breast is anti-estrogenic, although several of its further properties, such as those on the lipid metabolism, considered to be estrogen-agonistic. (9)

In the present study, tamoxifen was found to cause significant reduction in TC (P < 0.001) in premenopausal patients, but the outcomes of this study are in contrast to Liberopoulos et al. (10) (2002) who state that tamoxifen increased the TG levels, this difference may be due to difference in diet, duration of follow up and others. Increase in TG is a pharmacological effect resulting from the hepatic first pass effect of estrogens however, tamoxifen does not share this estrogen agonist effect. Also in current study, tamoxifen cause no important decline in TC and LDL which is different from observations have been made on breast cancer women in Gupta et al(11) (2006) but the results of this study are similar to Hozumi et al. (12) (2006) reported that the serum TC levels remained unchanged after tamoxifen treatment.

The estrogen agonist/antagonist properties of SERMs can be partly described through the two activation domains AF1 and AF2 of ER that mediate the transcriptional control of the receptor. Tamoxifen blocks the effect of estrogen by inhibiting AF2 but it does not inhibit AF1. Therefore, tamoxifen has largely antagonistic activity in breast tissue where AF2 is dominant but more agonistic activity in other tissues where AF1 is dominant. Estrogen agonist or antagonist effects are thus dependent on the organ-specific type and amount of ER available for ligand binding. Also the menopausal status modulates the effect of SERMs. Tamoxifen look like more estrogen antagonist than agonist in premenopausal women. (13-14). More ever in this study there is statistically significant increase in HDL (P = 0.001) was detected in premenopausal patients, due to estrogenic outcome of tamoxifen, this result in contrast to Singhai et al. (2011) (15) did not find change in HDL level, but similar to Bruning et al(16). The change in body weight is similar to Hoskin et al(17) (1992), which due to great concentration of estrogen and other gonadotropins (17)

Conclusion:
Beneficial changes of lipid profiles were seen in women treated with Tamoxifen in pre-menopausal breast cancer women. Triglyceride, and very low density lipoprotein, show statistically significant decrease. While there is statistically significant increase high density lipoprotein over time from baseline.

Authors’ contribution:
Zainab A. Mohammed Ali*: Study design, sample collection and manuscripts writing.

Wasan K. Jasim: Selection of sample, collection and analysis of data.

Dilan Z. Hussein: Support in writing the theses and statistical analysis.

Manwar Abdulaleh Alnaqash: Support in writing the theses and sample collection.

References:


تأثير التاموكسفين على مستوى الدهون في النساء ما قبل سن اليأس المصابات بسرطان الثدي

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ام. د. منور عبد الله النقاش

خلاصة البحث

سرطان الثدي هو الورم الخبيث الأكثر شيوعا بين النساء في جميع أنحاء العالم، بل هو أيضا السبب الرئيسي للوفيات المرتبطة بالسرطان في الإناث. عقار التاموكسيفين هو العلاج الهرموني الشائع للمرضى الذين يعانون من سرطان الثدي. حيث يعمل بانتقائية عالية عن طريق منع تأثير هرمون الأستروجين بواسطة منع إصدار الأستروجين للمستقبلات الهرمونية للإصبع في الأجسام، وينقل الوقت يقوم بفعالية الاستروجين في جزء أخرى. لعقار التاموكسيفين تأثير إيجابي على مستوى الدهون في الجسم.

هدف البحث:

تم تصميم هذه الدراسة لتحديد تأثير التاموكسيفين على مستوى الدهون في الدم لمريضات سرطان الثدي وتحديد تأثيرهما على مستويات الكوليسترول في الدم، وما لهوار من تأثير على أمراض القلب والشرايين.

المرضى والطرق:

دراسة مستقبلية، أجريت في المستشفى الأورام التعليمي في المدينة الطبية بدأ من أكتوبر 2015 إلى أكتوبر 2016. شملت (40) مريضة بسرطان الثدي الذين تم تطبيق التاموكسيفين في جرعة 20 ملغم مرة واحدة يوميا مع متابعة المريضات لمدة ثلاث أشهر.

النتائج:

(40) مريضة بسرطان الثدي تم ادراجهن في هذه الدراسة. وقد أظهرت الدراسة انخفاضاً ملحوظاً إحصائياً على مر ثلاثة أشهر في الدهون الثلاثية والدهن المنخفض الكثافة بدءاً من البداية، وعلاوة على ذلك زادت محصلة احصائية في نسبة الدهن العالي الكثافة. ورغم هذه ارتفاع التاليمزية في الوزن، زادت دلالة احصائية عند نهاية الدراسة.

الاستنتاجات:

التعارضات الحادة في مستوى الدهون في المريضات من تأثير عقار التاموكسيفين في مرحلة ما قبل سن اليأس لمريضات سرطان الثدي. لا تغيرات مفيدة وذات دلالة مهمة في نسب الدهون.

مفتاح الكلمات: سرطان الثدي، عقار التاموكسيفين، مستوى الدهون، قبل سن اليأس.