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EFFECT OF TAMOXIFEN ON SERUM LIPID PROFILE IN FEMALE ALBINO RATS

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ABSTRACT

Tamoxifen is a sold under the brand name Nolvadex among others, is a medicine that is used to inhibit breast cancer in women and treat breast cancer in men and women. It is also being studied for other types of cancer. The study included 36 female albino rats divided to three groups the group A include 12 female albino rats whom treated with 20 mg of Tamoxifen for 60 days, group (B) which include 12 female albino rats weight (180-210) g aged (5-6) month whom treated with 20 mg of Tamoxifen for 90 days and control group (group C) which include 12 female albino rats. The results show that Tamoxifen can effect on lipid metabolism by increase the level of HDL and Reduce the level of total cholesterol and LDL. In ConclusionTamoxifen have cardio-protective effects on lipid metabolism.

INTRODUCTION

Tamoxifen (TMX), sold under the brand name Nolvadex among others, is a medicine that is used to inhibit breast cancer in women and treat breast cancer in men and women. It is also being studied for other types of cancer. It has been used for Albright syndrome. Tamoxifen is classically taken daily by mouth for five years for breast cancer. Serious side effects contain a small increased risk of stroke, uterine cancer, ,pulmonary embolism and vision problems. Common side effects include weight loss, irregular periods, and hot flashes. It might cause damage to the baby if taken during breastfeeding or pregnancy (Jump *et al*., 2006).It is a selective estrogen-receptor modulator that works both by decreasing factors that increase the growth of breast cells and by increasing factors that decrease the growth of breast cells. It is of the triphenylethylene group.Tamoxifen was discovered in 1967 (Jordan, 2006). Tamoxifen is a prodrug, having relatively little affinity for estrogen receptor. It is metabolized in the liver by the cytochrome P450 isoform CYP3A4 andCYP2D6 into active metabolites such as and N-desmethyl-4-hydroxytamoxifen (endoxifen)and 4-hydroxytamoxifen (afimoxifene) (Desta *et al*., 2004) which have 30-100 times further affinity with the estrogen receptor than tamoxifen itself.

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These active metabolites compete with estrogen in the body for binding to the estrogen receptor. In breast tissue, 4-hydroxytamoxifen acts as an estrogen receptor antagonist so that transcription of estrogen-responsive genes is inhibited (Wang *et al*., 2004). 4-hydroxytamoxifen binds to estrogen receptors (ER), the ER/tamoxifen complex recruits other proteins known as co-repressors and then binds to DNA to modulate gene expression. Some of these proteins include SMRT and NCoR (Shang *et al*., 2000). Tamoxifenrole can be controlled by a number of maney variables including growth factors (Massarweh *et al*., 2008). Tamoxifen needs to block growth factor proteins such as ErbB2/HER2.because theelevated levels of ErbB2 shown to occur in tamoxifen resistant cancers. Tamoxifen need a protein PAX2 for its full anticancer activity (Hurtado *et al*., 2008). In the existence of high PAX2 expression, the tamoxifen/estrogen receptor complex is capable to suppress the expression of the pro-proliferative ERBB2 protein. In contrast, when AIB-1 expression is higher than PAX2, tamoxifen/estrogen receptor complex upregulates the expression of ERBB2 causing in stimulation of breast cancer growth (Liu *et al*., 2013). 4-Hydroxytamoxifen binds to estrogen receptors competitively in tumor cells and other tissue targets, producing a nuclear complex that reduce DNA synthesis and inhibits estrogen effects. It is a nonsteroidal agent with potent antiestrogenicproperties, which compete with estrogen for binding sites in breast and other tissues. Tamoxifen causes cells to remain in the G_0 and G_1 phases of the cell cycle.

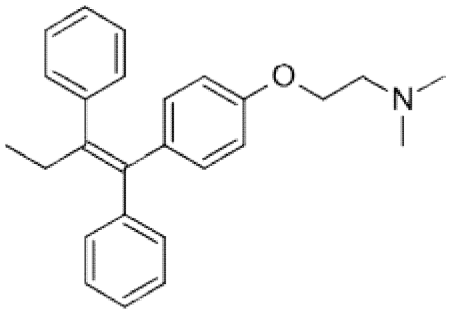

Figure 1. Tamoxifen structure

Because it prevents (pre)cancerous cells from dividing but does not cause cell death, tamoxifen is cytostatic rather than cytocidal (Liu *et al*., 2013).

Subjects and methods

The study was a cross-sectional study carried out Al-Nahrain Medical College, during the period from September, 2014 till the end of January, 2015. The Ethical committee of Al-Nahrain Medical College approved the protocol for the study, and each subject gave informed signed consent. The study included 36 female albino rats divided to three groups the group A include 12 female albino rats weight (180-210)g aged (5-6) month whom treated with 20 mg of Tamoxifen for 60 days, group (B) which include 12 female albino rats whom treated with 20 mg of Tamoxifen for 90 daysand control group(group C) which include 12 female albino rats as in table 1.The measurement of serum Lipid profile done by using kit formRandox, U.K

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

Table 1. The Mean ± SD for the studied groups

Parameters	Group (A) After 60 day	Group (B) After 90 day	Group(C) Control group
Total Cholesterol	70.163±2.731	67.507±16.39	72.254±2.27
Triglycerides	44.198±2.336	42.797±2.212	45.141±4.322
HDL	34.723±1.039	33.210±1.050	35.52±2.046
LDL	39.041±1.617	37.681±1.373	40.15±2.15
VLDL	11.968±2.572	11.496±1.691	12.031±2.79

DISCUSSION

The study revealed that Tamoxifen have cardio-protective effect bydecreasing the levels of total cholesterol and LDL-C while increase level of HDL as shown in table (1). This study agree with Che Lin *et al*., who examined the tamoxifen relation with lipid profiles, and reported a statistically significant decreases in serum TC and LDL-C after tamoxifen treatment in Taiwanese breast cancer patients (Che *et al*., 2014).

Tan *et al*. (2008) revealed that genetic polymorphisms effect the epirubicin metabolism, along with the in vitro activity of tamoxifen. Genetic polymorphisms and epirubicin might effect tamoxifen and the lipid profile in vivo. The cause might be an apolipoprotein E (APOE) polymorphism. Chang *et al*. (2009) reported that the effects of tamoxifen on serum TG levels are controlled by the APOE polymorphism.The estrogen receptor and the glucocorticoid receptor is membrane to a group of type I steroid hormone receptors. Glucocorticoid motivates fat breakdown in adipose tissue.

The fatty acids released by lipolysis used for the creation of energy in tissues like muscle. The released glycerol offers the substrate for gluconeogenes is. Based on these explanations, it looksrational to consider steroid hormone receptors whentalk over tamoxifen, the estrogen receptor, and the lipid profile (Pitroda *et al*., 2009)Additionally, a new class of steroid hormone receptors has recently been explained: Beside with the well-recognized intracellular receptors, cell membrane receptors have been shown to exist. Their cellular responses are much faster than those of the intracellular receptors (Pitroda *et al*., 2009) since estrogen is known to decrease serum LDL-C levels by increasing LDL particle clearance through LDL receptor upregulation (Shojiro Sawada *et al*., 2005). This study reported that Tamoxifen increase the level of HDL and that disagree with study done by Love *et al.,* who reported that Tamoxifen have no significant influence on HDL-C levels, while it surge serum apo-AI levels (Love *et al*., 1994). Estrogen increase hepatic apo-AI expression and henceforth the upregulate in apo-AI mightbe an estrogen agonistic influence onapo-AI expression, so that leading to increased serum apo-AI levels. In this way, tamoxifen is considered to show a strong estrogen agonistic effect on lipoprotein metabolism.

Conclusion

Tamoxifen have cardio-protective effects on lipid metabolism.

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