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Original Research

Assessment of Liver Enzymes and Lipid Profile in Male Albino Rate which Treated with Non-Steroidal Antiestrogen Anti-Cancer Drug Tamoxifen

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Abstract:

The second most common cancer-related cause of death, particularly for women, is breast cancer, which is a serious global health issue. A non-steroidal antiestrogen known as tamoxifen (TAM) is utilized as a chemotherapeutic and chemopreventive medication for breast cancer. This study's objective was to look into how tamoxifen may affect the GOT and GPT liver enzymes., and assessment the related tamoxifen with lipid profile .

Materials and methods: For this experiment, fifty male albino rats were employed. Three equal groups of fifty albino rats were created: group I (control), group II (treated), and group III (treated). tow groups given the drug tamoxifen , it was orally administered in dose of 20 and 40 mg /day /day through or gastric tube for 28 days .

Result : The liver enzyme assessment showed significant increased ($p>0.05$) in both enzyme GOT and GPT in group two which treated with 20 mg /kg / day and group three which treated with 40 mg/kg/day of tamoxifen drug compared with control group which treated with distil water only.in other hand the lipid profile assessment appeared significant decrease ($p\leq0.05$) of serum triglyceride and cholesterol in both treatment groups compare to control group.

Keywords: Lipid profile, Non-steroidal antiestrogen , Anti-cancer drug tamoxifen

Introduction:

Breast cancer continues to be the cancer that affects women most frequently worldwide. When estrogen levels are higher, breast cancer seems to be more prone to occur (1). Tamoxifen (TAM), a drug, has been used as an adjuvant and metastatic treatment for anti-estrogen receptor (ER) positive breast cancer cases all over the world for the past 30 years. (2,3).

This information is provided by Breastcancer.org. Make a donation to support free programs and services for breast cancer survivors. In both pre- and postmenopausal women as well as males, tamoxifen is used to treat hormone receptor positive, early-stage or advanced-stage breast cancer. Tamoxifen is frequently prescribed to women with hormone receptor-positive DCIS following surgery to lessen their chance of developing invasive breast cancer. Tamoxifen is also used to lower breast cancer risk in women who have not yet been diagnosed but have a greater than usual risk of the illness (4,5)

In 1998, work began on what would become known as the National Surgical Adjuvant Breast and Bowel Project. (NSABP) due to the fact that therapy with Nolvadex reduced the prevalence of both invasive and non-invasive breast cancer in individuals who were at high risk for the disease (6). Because of its extensive application, tamoxifen has been the subject of research into its potentially harmful effects, including its toxicity to a variety of organs (7). There is evidence that more than thirty percent of breast cancer patients who received adjuvant tamoxifen treatment developed nonalcoholic steatohepatitis with cirrhosis in tamoxifen-induced fatty liver (8). These patients were treated with tamoxifen. It has also been documented in the past that TAM can generate hepatorenal toxicity (9). According to recent findings (10, 11), the damage to organs induced by TAM may be caused in part by both the formation of reactive oxygen species (ROS) and oxidative stress. In addition, adjuvant medicines such as TAM or antineoplastic medications have been indicated as a direct cause of renal function impairment (12).

Due to the risk of fetal malformations, tamoxifen medication was not advised during pregnancy (13).For instance, animal studies have demonstrated a connection between maternal tamoxifen exposure during pregnancy and abnormalities in the offspring's reproductive systems (31); some of these abnormalities were unique to tamoxifen while others were caused by fetal exposure to the synthetic estrogen diethylstilbestrol.Daughters' risk of breast cancer is affected by estrogen manipulations made by expectant mothers during the fetal stage.

Without any established risk factors for steatosis, such as diabetes mellitus (DM), obesity, or hyperlipidemia, non-alcoholic fatty liver disease (NAFLD) is a chronic illness that ranges from simply hepatic steatosis (HS) to non-alcoholic steatohepatitis (NASH) and cirrhosis [15]. NAFLD can arise from illnesses or treatments like chemotherapy and endocrine therapy for cancer patients. The most often prescribed medications that result in HS are 5-Flourouracil (5-FU), methotrexate (MTX), bleomycin (B), and L-asparaginase (LA) (16). The severity of fatty liver disease and liver fibrosis are dramatically increased by TAM treatment (17].The occurrence of HS has been reported in 30–38% of breast cancer patients using TMX, despite insufficient research on the subject. [3, 4].

Material and Method:

The assessment of liver enzyme is done by Agappe lyner kit product by AGAPPE DIAGNOSTICS LTD company . ‘Agappe Hills’, Dist. Ernakulam, Kerala, India. The lipid profile assessment by Agappe Qualicheck Norm and path (51601001)kit to verify the performance of the assay. Each laboratory has to establish its own internal.

Result:

The result showed happen significance increased ($p>0.05$) of liver enzymes GOT and GPT in

Treatment 1 and Treatment 2 groups compare with control group, in other hand assessment of lipid profile appeared significant decrease ($p \leq 0.05$) of serum triglyceride and cholesterol in both treatment groups compare to control group it showed in (table 1 and 2)

Table 1 explain the levels of GPT and GOT with SD

Groups	GPT	GOT
Control	**34 ± 3.4 A**	**99.6 ±76 a**
Treatment 1	**45.2 ± 2.5 A**	**135.7± 34.6 b**
Treatment 2	**87 ± 6.4 B**	**148± 11.1 b**

There are significant increase in GPT in group 2 compared with control and group 2 in other hand GOT increased significantly in both treatment compared with control the lowercase letter explain the significance between groups.

Table 2 explain the levels of Cholesterol and triglyceride with SD

Groups	Cholesterol	triglyceride
control	93 ± 5.71 a	63.75 ± 9.7 A
Treatment 1	71 ± 5.83 b	84.25 ± 33 B
Treatment 2	77.75 ± 20.69 b	141.75 ± 6.18 C

The data explain significant decreased of Cholesterol and significant increased of triglyceride in both treatment compared with control and in group 2 compared with group one the lowercase letter explain the significance between groups.

Discussion:

One of the most prevalent cancers in women around the world is breast cancer. The leading cause of death for women in America is breast cancer, which claims more than 40,000 lives year (20). Clinically, breast cancer has been divided into four main subtypes based on gene expression profiling for the ER, PR, and HER-2 receptors: luminal A (ER/PR+, HER-2+), luminal B (ER/PR+, HER-2+), HER-2 overexpressing (ER/PR+, HER-2+), and basal-like (ER/PR+, HER-2). (21,22).

liver injury or even hepatocarcinoma is one of the most dangerous adverse effects with TAM when used long-term (23-24). Sick man which treated a hormontherapy are need to follow up its hepatic enzyme each four months to follow its liver toxicity. and some studies have showed the side effect of TAM causes the suppression of β-oxidation of mitochondria and partially cause to macrovacuolar steatosis (25,26). first singe was described of the finding of a unique , big lipid vacuole in the cytoplasm of the liver cells (27).

In other side, Carthew *et al* (28) approved that given dietary TAM to Wistar-AP female rats with to just three months was enough to effect backloges the liver DNA degradation, which lead to cause hepatocarcinoma .

A brief (2 weeks) therapy with a modest dose of TAM (6 mg/kg/day) would result in hepatotoxicity and alter microscopic and ultrastructural morphology.When TAM was employed, did it produce hepatotoxicity at the morphological level, or did it harm liver tissue at low doses.(30)

Cell apoptosis is the main responsible of the caused the hepatotoxicity it has essential effect in the operation of liver cell injury (29).

In this study result showed there is some changes of liver enzyme in animal which treated with

tamoxifen drug compared with control group which given orally distal water in both treatment 20 mg/kg/day and 40 mg/kg/day , the increase of GOT and and GPT in treated groups compare with control groups may be the reason of this change because the tamoxifen drug have side effect on hepatocyte which responsible on production the liver enzyme this lead to changes of them, this result compatible with some study like (Dray et al., 2000) He claimed that due to the drug's extensive use, attention has been drawn to its negative effects, particularly its toxicity to numerous organs, and that the tamoxifen group had greater rates of abnormal AST at follow-up time compared to the control group.

Our study showed increased in cholesterol and TG after treatment with tamoxfin because it have role in lipid profile alterations(33), in addition the Estrogen causes hyperlipidemia by altering the metabolism of lipids in a number of ways, including by increasing the production of TG and VLDL and decreasing the activity of LPL and HTGL (22). TAM has minor estrogenic actions but is primarily antiestrogenic. TAM's complex combination of estrogenic and antiestrogenic activities may be responsible for its effects on lipid metabolism, however alternative mechanisms cannot be completely ruled out.(32)

Conclusion:

In conclusion, the available results demonstrated the significance of doing routine assessments of liver enzymes and the protection at the initial stage of the TAM before unfavorable clinical signs manifest.

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