Evaluation of the Effect of Tamoxifen Therapy on the Endometrium in Premenopausal Breast Cancer Patients

Thesis

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تقييم تأثير العلاج بعقار التاموكسيفين على بطانة الرحم فى السيدات المصابات بسرطان الثدى قبل مرحلة سن انقطاع الطمث

بحث
مقدم توطئة للحصول على درجة الماجستير
فى أمراض النساء و التوليد

مقدم من الطبـيب

إبـــراهيـــم طلعت أبـو الفتـــوح
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Introduction

Tamoxifen citrate is a selective estrogen receptor modulator that is widely used for the treatment of breast cancer ***(Osborne, 1998)***. Recently, it has been found to prevent breast cancer in high-risk woman ***(Fisher et al., 1998).***

Although it acts as an antiestrogen in breast tissue, it has an estrogenic effect in the postmenopausal endometrium and moymetrium.

Long-term tamoxifen therapy is reported to be associated with an increased number of uterine lesions, including endometrial polyps, leiomyomas, endometrial hyperplasia, endometrial carcinoma, and adenomyosis ***(Cohen et al., 1995 and Berliere et al., 1998).*** However, the beneficial effects of tamoxifen in women with breast cancer outweigh the potential endometrial adverse effects of the drug.

National Surgical Adjuvant Breast and Bowel Project (NSABP) ***(Fisher et al., 1994).*** Performed a randomized trial of tamoxifen versus placebo in women with ER-positive beast cancer confined to the breast with

negative axillary nodes. Results from this trial of 4,063 patients revealed a 7.5-fold increase in the risk of developing endometrial cancer in the tamoxifen-treated group. The average annual hazard rate for endometrial cancer was 0.2 per 1.000 women in the placebo group and 1.6 per 1.000 women in the randomized tamoxifen-treated group.

In a case-control study using surveillance, epidemiology, and end-results data ***(Bernstein et al., 1999).*** Confirmed a four-fold increased risk of endometrial cancer in breast cancer patients with more than 5 years of tamoxifen use compared with nonusers. This effect was most pronounced, however, in those with known risk factors for endometrial cancer, including higher body mass index and prior use of estrogen replacement therapy.

The proliferation index in benign endometrial epithelium is higher in tamoxifen users than in non-users, and this might play a role in the reported higher incidence of endometrial cancer in postmenopausal tamoxifen users ***(Mourits et al., 2002).***

Tamoxifen treatment is associated with an increased incidence of proliferative and neoplastic endometrial changes. No obvious correlation was found between the length of tamoxifen exposure time and occurrence of endometrial pathologies. It is mandatory to undertake twice per year gynecological evaluations for patients treated with tamoxifen to promptly identify and correctly manage endometrial changes ***(Colacurci et al., 2000).***

Several techniques such as tritiated thymidine autoradiography, bromodeoxyuridine incorporation, Ki-67 immunohistochemistry, and crypt cell production rate, were used for the evaluation of cell proliferation. Ki-67 immunohistochemistry is one of the most widely available methods for measuring cell proliferation and is also a valuable prognostic indicator in several types of neoplasm. Although Ki-67 immunohistochemistry developed first needed frozen sections, recently developed Ki-67 immunohistochemistry in formalin-fixed and paraffin-embedded tissues can be used as a reliable marker of the cell proliferation activity in both normal and neoplastic epithelium ***(Ikuko Akedo et al., 2001).***

Aim of the Work

The aim of this study is to evaluate the effect of tamoxifen therapy on the endometrium in premenopausal women with cancer breast.

Contents

List of Abbreviations

CT	**:**	Computed Tomography
E	**:**	Eosine
E2	**:**	Estradiol
EIC	**:**	Endometrial intraepithelial carcinoma
ER+	**:**	Estrogen receptor-positive
ESC	**:**	Eosinophilic syncytial change
FCM	**:**	Flow cytometry
FSH	**:**	Follicular stimulating hormone
HBD	**:**	Hormone-binding domain
HR+	**:**	Hormone –receptor-positive
Hx	**:**	Haematoxylin
IUP	**:**	Intra-uterine Pregnancy
LH	**:**	Leutinizing hormone
MR	**:**	Magnetic resonance
NSABP	**:**	The National Surgical Adjuvant Breast and Bowel Project

PCNA	**:**	Proliferating cell nuclear antigen
PgR+	**:**	progesterone-receptor–positive
SERMs	**:**	Selective estrogen receptor modulators
TAM	**:**	Tamoxifen
TGFß-1		transforming growth factor ß-1
TVU	**:**	Transvaginal Ultrasonography
US	**:**	Ultra-Sound

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Table (4): Patients characteristics

	Group(2) :Control Group			
	Mean	**±SD**	**Range**	
Age (years)	36.92	±3.65	35.00	44.00
Parity	3.20	±1.47	0.00	6.00
Weight (kg)	75.04	±10.38	58	90
Duration of Tamoxifen therapy (months)	12.00	±4.96	6.00	25.00

The mean age of patients' age, parity and weight were 36.92, 3.20and 75.04 respectively.