Canadian Journal of Applied Sciences 3 (4): 100-104; 2014
ISSN 1925-7430; Available online http://www.icdtdi.ca

Original Research Article

RESPONSE EVALUATION OF TAMOXIFEN VS AROMATASE INHIBITORS

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ABSTRACT

Objective: The study was conducted to evaluate the accuracy of use of aromatase inhibitors (AI) and tamoxifen treatment in pre-menopausal and post-menopausal breast cancer patients.

Method: The prescription data of 143 patients was reviewed for evaluation of letrozole, anastrazole and tamoxifen utilization between years 2006-2013 at SKMCH&RC. Use was analyzed against pre-menopausal and post-menopausal status of the patients using hospital information software (HIS) for data collection. NCCN Breast Cancer Guidelines were used as reference.

Results: Tamoxifen upfront use in pre-menopausal women with breast cancer was 93.3%, while that of Aromatase inhibitor was 6.7%. Tamoxifen was used as second line therapy in pre-menopausal women in 6.7% while aromatase inhibitor was used as second line therapy in pre-menopausal women in 93.3%. Tamoxifen upfront in post-menopausal was 18.6%, aromatase inhibitor upfront in post-menopausal was 81.4%.

Conclusion: Tamoxifen is used as first line therapy in majority of pre-menopausal breast cancer patients while aromatase inhibitors are used as second line. In case of post-menopausal breast cancer patients aromatase inhibitors are used as first line in majority of patients while tamoxifen is used as second line.

Keywords: Tamoxifen, aromatase inhibitor, breast cancer

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INTRODUCTION

Despiteprogresses in breast cancer therapy, there is still an increased number of patients with diagnosed metastatic diseases. Early identification and timely treatment of women with breast cancer can surely decrease the mortality associated with the disease(1)**.**Etiology of breast cancer is still unknown but factors responsiblemay include hereditary predisposition, late menarche, early menopause, obesity, late child birth, oral contraceptives use, high fat diet, age, alcohol, smoking, toxins, exposure to radiographs and even high socioeconomic status (1).

Estrogen helps in promoting the growth of normal and cancerous epithelial cells of breast. It does so by activation of estrogen receptors which in turn activate gene promoters. These gene promoters then activate several genes which play role in inhibiting cell death, promoting cell division, formation of new blood vessels and protease activity (3).Aromatase (cytochrome P-450 [CYP] 19) is the enzyme which catalyzes

the rate limiting step (conversion of steroidal C-19 androgens to C-18 estrogens) of estrogen formation. It is the last step in the formation of estrogen and considered important for the inhibition of steroid formation (4)

Letrozole is third generation non-steroidal aromatase inhibitor. It has proven efficacy in hormone sensitive postmenopausal breast cancer (5).Letrozoleacts by hindering the final step of the estrogen biosynthetic pathway. Randomized controlled trials conducted in postmenopausal women showed that Letrozole is more effective than tamoxifen (6).Anastrazole is another third generation non-steroidal aromatase inhibitor and is used in breast cancer patients with positive hormone receptor test (7). Studies have shown thatanastrazole is more effective in postmenopausal women with breast cancer than tamoxifen(8-9).

Tamoxifen is non-steroidal drug having anti-estrogen properties used in cases with positive estrogen receptor (ER) test. It inhibits prostaglandin synthetase and has effects similar to anti-estrogen drugs. Target organs include endometrium, bones and blood lipids. It has very low affinity for androgen receptors (10)**.** National Surgical Adjuvant Breast and Bowel Project (NSABP) did study on 13388 high risk patients who were more than 35 years of age. It was seen that patients who were given tamoxifen had significant less occurrence of breast cancer than the patients who were given placebo (11).Tamoxifen has very good tolerability profile for breast cancer patients and effective both in pre-menopausal and post-menopausal patients. These characteristics make tamoxifenmaintain its position in treatment of estrogen receptor positive breast cancer patients (12).It is one of the most commonly used FDA approved medicine for prevention of breast cancer (13)**.** In clinically high risk patients e.g. patients with two first degree relatives with diagnosed breast cancer, history of atypical hyperplasia or history of in-situ lobular carcinoma, tamoxifen is recommended specially if risk is more than 5% and benefit outweighs harms. Duration of therapy in such patients should be 5 years (14)

Complexity of tamoxifen is also explained in another paper as an anti-estrogen with complex pharmacology encompassing variable species-, tissue-, cell-, gene-, age- and duration of administration-specific effects, from estrogen-like agonist actions to complete blockade of estrogen action. This complexity is consistent with various, and sometimes paradoxical, effects that have been associated with tamoxifen administration in animals and humans (15).

According to ASCO guidelines Update 2014, women diagnosed with ER positive in pre-menopausal and peri-menopausal stage should be treated with Tamoxifen and adjuvant endocrine therapy for 5 years, and after that, any additional therapy can be recommended. In pre-menopausal women Tamoxifen is recommended as a treatment for first 10 years and in post-menopausal women either Tamoxifen or aromatase inhibitor up to 10 years can be given with adjuvant endocrine therapy (16**)**

However, in case of post-menopausal women it is reported that aromatase inhibitors is preferred as first line therapy and Tamoxifen is preferred second line (17, 18**).** Nabholtzet al. concluded that there was lower incidence of vaginal bleeding and thromboembolic events that is the reason why anastrazole is preferred over Tamoxifen in post-menopausal women with breast cancer (19). According to another study aromatase inhibitor use in post-menopausal women reduced the chances of reoccurrence (20)**.**Itexplains why aromatase inhibitors are preferred over anti-estrogen medicine like tamoxifen in post-menopausal breast cancer patients.

Among the treatments given to breast cancer patients, tamoxifen (non-steroidal anti-estrogen) and aromatase inhibitors (letrozole and anastrazole) are widely used. However, tamoxifen is preferred medicine in premenopausal women while aromatase inhibitors are preferred in post-menopausal women. ASCO guidelines recommend that tamoxifen should be given to pre-menopausal women for 10 years while in post-menopausal women both therapies are recommended.

MATERIAL AND METHODS

The prescription data of 143 patients (2006-2013) was reviewed for evaluation of letrozole, anastrazole and tamoxifen utilization. Clinical performa was utilized for data collection regarding MR number, name, age and gender of each individual. Their treatment history was checked forTamoxifen vs. AI use. Hormonal status of patients was checked and recorded by checking estrogen receptor (ER) test, Progesterone receptor (PR) test andHuman epidermal growth factor receptor (HER2Neu) test. Menstrual history of patients was also recorded and they were labeled as either in pre-menopausal stage, post-menopausal stage. It was also enquired that whether endocrine therapy was recommended before aromatase inhibitors or not and if yes, was it already given before aromatase inhibitor use or not? Duration of Tamoxifen therapy before aromatase inhibitors were introduced was also checked. Use of the drugs was compared against latest NCCN guidelines. Switching between letrozole to anastrazole and anastrazole to letrozole was also monitored. After getting all the data prescribing trends were checked and utilization evaluation was done. Hospital information system software (HIS) was used for data collection.

RESULTS& DISCUSSION

Tamoxifen upfront use in pre-menopausal women with breast cancer was 93.3%, while that of AI was 6.7%. Tamoxifen was used as second line therapy in pre-menopausal women in 6.7% while aromatase inhibitor was used as second line therapy in pre-menopausal women in 93.3%. Tamoxifen upfront use in post-menopausal cases was 18.6%. Aromatase inhibitor upfront use in post-menopausal cases was 81.4%.

The institute majorly complies with the latest guidelines of oral chemo use in breast cancer. In a few cases, physicians prefer to use AI over tamoxifen to avoid tamoxifen related adverse effects of hot flashes, decreased bone density and thrombo-embolic events.

Table 1: AI use trend in breast cancer patients (2006-2013)

	Total (92)		
	Pre-menopausal	**Post-menopausal**	**Unknown**
AI used upfront	1	90	1
AI as second line therapy	1	89	1

Table 2: Tamoxifen use trend in Breast Cancer patients (2006-2013)

	Total (52)	
	Pre-menopausal	**Post-menopausal**
	29	23
Tamoxifen upfront	28	20
Tamoxifen upfront	97%	87%

Table 3: Tamoxifen vs. AI use trend in breast cancer patients (2006-2013)

	Total 144				
	Pre-menopausal	**%age**	**Post-menopausal**	**%age**	**Unknown**
	30		113		1
Tamoxifen Upfront	28	93.3	21	18.6	
AI used upfront	2	6.7	92	81.4	1
Tamoxifen used as 2nd Line therapy	2	6.7	92	81.4	
AI used as 2nd Line therapy	28	93.3	21	18.6	

CONCLUSION

With few exceptions, tamoxifen is the treatment of first choice for pre-menopausal breast cancer cases, while Aromatase inhibitors are the preferred treatment in post-menopausal cases at the institute.

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