Tomoxifen Mono-Therapy for Breast Cancer in Elderly Women

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ORIGINAL STUDY

Tomoxifen Mono-Therapy for Breast Cancer in Elderly Women

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ABSTRACT

Background: Tamoxifen is an estrogen antagonist used as neo-adjuvant drug for breast cancer treatment in women.
Objective: To evaluate tamoxifen monotherapy on breast cancer for elderly women with estrogen positive, progesterone positive, and Her2/neu negative.
Materials and methods: Seventeen breast cancer women were examined. The age range of the patients was between 73 and 87 years (mean ± SD: 79.2 ± 3.8 years). The patients were examined and diagnosed by a surgeon, and histopathologic examination. The patients included in the study were estrogen positive, progesterone positive, and Her2/neu negative. The patients were treated with tamoxifen monotherapy 20 mg/day orally during the two-year study. The size of the tumor were measured by ultrasonic examination for each patient. Five milliliters (mL) of blood samples were taken from the patients and analyzed for CA15-3. The clinical and ultrasonic examination as well as blood investigations were carried out every 3 months for two years, while only clinical examinations were continued every six months up to 5 years.
Results: Treatment of breast cancer women by tamoxifen 20 mg/day gradually decreased serum CA15-3 significantly ($p \leq 0.01$) every 3 months. After two years of treatment with tamoxifen, serum CA15-3 was within normal range. The size of the tumor was decreased significantly and gradually every 3 months. After two years the tumor was completely disappeared. Each parameter was compared with that parameter measured before 3 months. Lymph node positive patients were 11 out of 17 patients; however, after 21 months of tamoxifen treatment, all patients were lymph node negative.
Conclusion: Tamoxifen monotherapy can be used for the treatment of women with breast cancer with estrogen +, progesterone + and Her2/neu–. The program can be applied for elderly breast cancer women or incompliance patients.

1. Introduction

Breast cancer is one the most common type of cancer causing death in women. Attempts have been made to control the disease in the developed counties where the incidence and mortality are high (Francies et al., 2020). Although the extent of breast cancer is low in developing countries, the mortality rate is elevated including that low- to middle-income coun-

tries. These countries have deficiency of resources for prevention and treatment of the cancer (Francies et al., 2020).

Several treatment programs have been used according to the stage of the tumor, and the patient condition. Mammary gland can be maintained either by adjuvant or neo-adjuvant therapies, with radiotherapy or surgery, and better quality of life (Albrand and Terret, 2008; Hamann and Ankel, 2018).

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In elderly women, the management of breast cancer is not clear, because of the high recurrence of the disease and cancer deaths (Fadda et al., 2016).

The term neo-adjuvant refers as to use systemic therapy in breast cancer disease in inoperable disease or before the main therapy (Shien and Iwata, 2020). However, adjuvant therapy indicates the use of a drug after the primary treatment of the disease (Burotto et al., 2019).

The role of endocrine therapy remains unclear. However, neo-adjuvant endocrine therapy can be considered as an option even as monotherapy. This endocrine therapy was associated with similar response rates as neo-adjuvant combination chemotherapy but with significantly lower toxicity (Spring et al., 2016).

Tamoxifen, a selective estrogen modulator, has been used for decades for the treatment of breast cancer (Shagufta, 2018). Tamoxifen is the gold standard of hormonal therapy for all stages of breast cancer in patients with estrogen positive (Jordan, 2011). Tamoxifen was confirmed by Food and Drug Administration (FDA) for the alleviation of breast cancer incidence in premenopausal and postmenopausal women at high risk (Jordan, Mar. 2003). In elderly breast cancer women with estrogen positive, tamoxifen is an adjuvant therapy in any stage of the disease, and chemotherapy should be used for patients with high risk of relapse (Marchei et al., Mar.-Apr. 1996). Breast cancer patients treated with tamoxifen for ten years or more than ten years had disease free survival than patients treated with tamoxifen for 5 years or less (Davies et al., 2013).

This study was conducted in order to evaluate the therapeutic effect of tamoxifen as a monotherapy in elderly breast cancer women.

2. Materials and methods

This study was conducted at a private clinic in Mosul, during the period from 1st January 2019 till 1st January 2021. The study was performed according to the declaration of Helsinki 1964, and written consents of the patients were obtained before the start of the treatment. Seventeen breast cancer women were involved in the study, since the only sample obtained during the study. Also, other 3 breast cancer women were excluded from the study, since they were lost during the study. The age range was between 73 and 87 years (mean ± SD: 79.2 ± 3.8 years). The patients were examined and diagnosed by a surgeon, and histopathologic examination. The patients included in this work were breast cancer elderly women with estrogen positive, progesterone positive, and Her2/neu negative (ER+, PR+, and Her2/neu–,

respectively). Ultrasound examination for the breast tumor of each patient was used to measure the size of the tumor. The lymph nodes were also measured by ultrasound. The patients were treated with tamoxifen monotherapy 20 mg/day orally during the two years of the study. Five milliliters (mL) of blood samples were taken from the patients and analyzed for CA15-3. The examination study by the physician and the measurements by ultrasonic and laboratory investigation were repeated every 3 months for two years. Clinical examinations were continued every six months up to 5 years. The measurement of the volume of the tumor was calculated by applying the following equation: Volume (V) = 0.5 × Lenght (L) × Width (W) × W (Tomayko and Reynolds, 1989).

The mono-therapy treatment of tamoxifen was applied, since the patients either refused or could not tolerate cancer treatment because of comorbidity of the patients. The results were expressed as M±SD and were analyzed by using ANOVA and paired t-test. SPSS package version 26-2018 was used for analysis.

3. Results and discussion

In this work, the treatment of the breast cancer women was applied by tamoxifen monotherapy. The ages of those patients were more than 70 years. Accordingly, either the patients cannot tolerate chemotherapy treatment because of comorbidity or they refused the chemotherapy. Several studies showed that less than 3% to 19% of the cancer patients refused conventional chemotherapy treatment, partially or completely (Puts et al., 2010). Treatment with anticancer drugs should not be related to the age of the patients, since other factors, such as life anticipation, tolerance with the treated drugs, rated interest, patient aim, and priorities (Tesarova, 2013).

Table 1 has shown that treatment of breast cancer elderly women for tamoxifen 20 mg/day orally significantly decreased serum CA15-3 ($p \leq 0.01$). Comparison was made between each parameter compared with the parameter measured 3 months ago. After two years of treatment with tamoxifen, serum CA15-3 was within normal range.

The size of the tumor decreased significantly every 3 months. Comparison was made between each parameter and that parameter measured before 3 months. After 24 months the tumor had completely disappeared (Table 1).

Lymph node positive patients were 11 out of 17 patients before tamoxifen treatment, but after 21 months of the treatment all patients were lymph node negative (Table 1).

Table 1. Breast cancer patients treated with tamoxifen 20 mg/day for two years (n = 17).

Months	CA15-3 U/mL	Size of the tumor mm^3	Lymph node Positive	Negative
0	34.29 ± 1.83	158.8 ± 147.7	11	6
3	31.59 ± 3.04**	105.6 ± 129.9††	11	6
6	29.29 ± 2.80*	67.6 ± 86.6††	11	6
9	24.82 ± 6.29**	57.7 ± 88.2†	10	7
12	20.47 ± 8.83**	35.4 ± 69†	8	9
15	16.82 ± 9.51*	11.1 ± 2††	5	12
18	14.26 ± 7.89*	3.4 ± 6.6††	1*	16
21	12.00 ± 5.81*	0.17 ± 0.3††	0	17
24	8.76 ± 4.55*	0.0†	0	17

*$p \leq 0.01$, **$p \leq 0.001$, †$p \leq 0.05$, ††$p \leq 0.01$.
Paired t test was performed between each parameter and the parameter taken before 3 months.

Serum CA15-3 was gradually decreased $p \leq 0.01$ by tamoxifen every 3 months. After two years of treatment with tamoxifen, serum CA15-3 was returned to normal value. Serum CA15-3 can be routinely used for checking stages of breast cancer (Chourin et al., 2009). However, tumor markers including CA15-3 were of small value, mostly in patients with early stages of the cancer (Lumachi et al., 2010). The baseline level of serum CA15-3 cannot be predicted for relapses of breast cancer in elderly patients (Lumachi et al., 2010).

In this study, the selected patients, were ER+, PR+ and Her2/neu–, since they have a chance for survival compared with ER+, PR– and Her2/neu– patients. Patients with single hormone positive tumors and Her2/neu negative (ER+, PR– and Her2/neu– or ER–, PR+ and Her2/neu–) were related with bad prognosis compared with ER+, PR+ and Her2/neu– patients (Bae et al., 2015). Although genomic tests are developed, hormone receptors are still the most predictive and prognostic receptors (Yip and Rhodes, 2014). Patients with estrogen and progesterone positive had a long-term benefit with tamoxifen than patients with estrogen positive alone (Nordenskjöld et al., 2016). In addition, five years treatment with tamoxifen for breast cancer women with ER positive decreased recurrence of the cancer with concurrent decrease in the death rate (Tesarova, 2013). Multiple clinical trials also found that tamoxifen was equivalent in improvement and survival to other selective estrogen degraders (Howell and Howell, 2023).

4. Conclusion

Tamoxifen monotherapy can be applied for the treatment of women with breast cancer with ER+, PR+ and Her2/neu –. This program is recommended for elderly breast cancer women or incompliance patients. Further studies are needed with a significant sample size of patients.

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