ORIGINAL ARTICLE

Prognostic Role of Cathepsin D as a Tumor Marker in a Comparative Study of Two Chemotherapy Regimens used in Node Positive Breast Cancer

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ABSTRACT

Objectives: To assess the level of Cathepsin D in the selected chemotherapeutic regimens used for breast cancer and to compare the effectiveness of two common chemotherapeutic regimens on the basis of Cathepsin D levels.

Setting: The present research was carried out in the department of Oncology, Sir Ganga Ram Hospital and INMOL Hospital Lahore.

Materials & methods: A total of 50 female patients with breast cancer were included in this study. Patients were divided into two groups. Each group consisted 25 patients. Each group received either TAC or FAC chemotherapy regimen. Blood levels of Cathepsin D were compared between each group.

Results: Data was analyzed on the basis of their age, socioeconomic status, family history, menstrual history, use of contraceptives & body mass index. Cathepsin D levels were analyzed prior, mid & post treatment using two chemotherapy regimens.

Conclusion: Both chemotherapy regimens i.e TAC & FAC are clinically effective. Although TAC therapy has reduced the level of Cathepsin D more as compared to FAC therapy which suggests regimen TAC is more effective in the treatment of breast cancer.

Keywords: TAC = Texanes**,** Doxorubicin, Cyclophosphamide, FAC= Fluorouracil, Cyclophosphamide

INTRODUCTION

Cancer is currently a leading cause of death worldwide. The most commonly diagnosed cancer among men is prostate cancer and among women is breast cancer.[1] Cancer mortality can still be improved by early diagnosis and employing better therapeutic methods.[2] .

It has been proposed that proteases secreted by cancer cells facilitate metastasis by degrading extra-cellular matrix. An increased activity of the lysosomal enzymes both in blood and in tumor tissues was revealed in cancer. Over the past few years, a particular attention has been paid to the fact that the high activity of some lysosomal enzymes i.e. Cathepsin B and D is connected with the increased cancer invasiveness.[3] Since elevated expressions of Cathepsins have been observed in several human cancers, including breast cancer, Cathepsins have been suggested to be biological markers of malignant tumors and are useful for prognosis of the disease.[4]

For more than 30 years clinicians caring for patients with breast cancer have struggled to reach on the conclusion that combination therapy is more effective as compared to single agent treatment for breast cancer patients.[5] From 1980's to 1990, popular chemotherapy for breast cancer was Anthracyclines. In 2000s Taxanes gained importance. Anthracyclines, Fluorouracil, Doxorubicin, and Cyclophosphamide (FAC) have been used in combination for node positive breast cancer patients.[6] Many studies establish that Taxanes (Paclitaxel/Docetaxel) in combination with Doxorubicin and Cyclophosphamide (TAC) have major clinical value in the combination therapy of women with early node positive breast cancer. [7]

The present study was designed to compare these chemotherapies by estimating the level of Cathepsin D. This will be helpful to choose the best and most responsive chemotherapeutic combination for the patients.

MATERIALS & METHODS

Fifty female patients with breast cancer were included in this study.

Inclusion Criteria

1. Women with breast cancer stage II and III.
2. Estrogen receptor positive patients.
3. Patients who have not yet received radiotherapy or chemotherapy.

Exclusion Criteria

1. Estrogen receptor negative patients.
2. Patients who have already received radiotherapy or chemotherapy.

Treatment Groups

50 patients were divided randomly into two groups of 25 patients each.

Group -A

25 patients included in this group were given the following chemotherapy.

1. Inj 5Flourouracil 500mg/ body meter square (m2) I/v Day 1 and Day 8.
2. Inj Doxorubicin 50 mg/m2 I/V Day1.
3. Inj Cyclophosphamide 500mg/m2 I/V Day1.

To be repeated every 21 days x 6 courses.

Group-B

25 patients included in this group were having the following chemotherapy:

1. Inj Docetexel 75mg/m2 I/V Day 1.
2. Inj Doxorubicin 50mg/m2I/V Day1.
3. Inj Cyclophosphamide 500mg/m2 I/V Day1.

To be repeated every 21 days x 6 courses.

Methodology

Five ml blood was drawn from patients and Cathepsin D was assessed before starting chemotherapy, in the middle of chemotherapy that is after third course and then at the end of chemotherapy that is after sixth course.

RESULTS

The study had two groups, one on treatment group FAC and other on treatment group TAC. There were 25 women in each group, out of those 6 were menstruating, 9 were peri-menopausal and 10 were post menopausal.

The trends of Cathepsin D levels were very clearly decreasing. The difference of absolute values were though giving a trend but made it noncomparable for the two groups at different stages. For this reason difference of values were calculated in terms of percentages while considering the base line levels as hundred percent. (table 1)

Table-1: Distribution of percent change in Cathepsin D levels among women in two treatment groups as per their menstruating status

	Before treatment		**Between treatment**		**After treatment**	
	Mean	**S.D±**	**Mean**	**S.D±**	**Mean**	**S.D±**
FAC						
Menstruating	100.0	0.0	80.3	8.4	60.1	12.3
Peri menopausal	100.0	0.0	74.9	10.0	40.0	10.9
Post menopausal	100.0	0.0	69.0	9.3	45.9	16.6
Total	**100.0**	**0.0**	**73.8**	**10.1**	**47.2**	**15.4**
TAC						
Menstruating	100.0	0.0	60.8	10.7	33.4	6.9
Peri menopausal	100.0	0.0	66.3	6.8	37.5	6.2
Post menopausal	100.0	0.0	66.5	11.1	36.4	7.2
Total	**100.0**	**0.0**	**65.1**	**9.6**	**36.1**	**6.7**

Table-2: Comparison of percent Cathepsin D of base line for three menstruating statuses at mid treatment and end treatment time

		Group				
		FAC		TAC		p-value
		Mean	S.D±	Mean	S.D±	
Menstruating	**Mid Treatment**	80.28	8.43	60.82	10.73	0.006
	End Treatment	60.09	12.26	33.39	6.86	0.001
Peri menopausal	**Mid Treatment**	74.95	10.04	66.27	6.77	0.047
	End Treatment	40.00	10.91	37.51	6.16	0.560
Post menopausal	**Mid Treatment**	68.95	9.30	66.50	11.10	0.599
	End Treatment	45.95	16.63	36.41	7.17	0.121

Table 2 shows that in mid treatment of menstruating women, the FAC group the level of Cathepsin D is reduced to 80.28% and with TAC it is reduced to 60.82%. In the mid treatment, level is more reduced significantly with TAC.(p value <0.05) In the end of treatment, FAC group the level of Cathepsin D is reduced to 60.09% and with TAC it is reduced to 33.39%. In the end of the treatment Cathepsin D level is more reduced with TAC. i.e. p value<0.05. In perimenopausal women in mid treatment, FAC group the level of Cathepsin D is reduced to 74.95% and with TAC it is reduced to 66.27%. In the mid treatment, level is more reduced with TAC. The p value (p value <0.05) is significant. In end of treatment, FAC group, the level of Cathepsin D is reduced to 40.00% and with TAC it is reduced to 37.51%. There is more reduction of Cathepsin D level with TAC group is noted at the end of treatment in perimenopausal women. In postmenopausal women in mid treatment, the FAC group, the level of Cathepsin D is reduced to 68.95% and with TAC it is reduced to 66.50% In the mid treatment, there is more reduction in the level of Cathepsin D with TAC group as compared with FAC group. In the end of treatment, FAC group, the level of Cathepsin D is reduced to 45.00% and with TAC it is reduced to 36.41%.In the end of the treatment Cathepsin D level is more reduced with TAC group as compared to FAC group.

It was observed that the difference at mid treatment and end treatment were both significantly different with p-values 0.006 and 0.001 respectively in menstruating women. The difference at mid treatment was also significant in perimenopausal women with p-value 0.047, and all remaining differences were found insignificant with p-values > 0.05.

DISCUSSION

Cathepsin D levels are generally increased in breast cancer patients. If the levels start decreasing with chemotherapy, it would suggest good prognostic sign.

In this study we compared the level of Cathepsin D in two treatment groups (FAC and TAC). It is seen that TAC has reduced the level of Cathepsin D more as compared with FAC. It means that TAC therapy is more effective than FAC in reducing the level of Cathepsin D[8].

This is consistent with many studies. According to them TAC is superior to FAC and the difference is statistically significant.[9]

CONCLUSION

The results of present study shows that there is significant reduction in the level of Cathepsin D in both treatment arms. TAC therapy has reduced the level of Cathepsin D more as compared to FAC therapy which suggests that treatment with regimen TAC is more effective as compared to regimen FAC in breast cancer patients in all three menstruating states.

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