

QUALITY OF LIFE OF PATIENTS WITH METASTATIC BREAST CANCER TREATED BY DOXORUBICIN AND PACLITAXEL AT HUE UNIVERSITY OF MEDICINE AND PHARMACY

Nguyen Van Cau¹

ABSTRACT

Background: Metastatic breast cancer still remains essentially incurable. Palliative chemotherapy with doxorubicin-paclitaxel combination is to reduce the burden of disease, prolong overall survival and maintain quality of life for patients. The aim of this study is to assess the clinical response and benefits from this regimen on short-term quality of life of patients with metastatic breast cancer.

Patients and method: Included 26 patients with metastatic breast cancer received by first-line with doxorubicin-paclitaxel at the Hospital of Hue University of Medicine and Pharmacy from 2010 to 2014. Patient characteristics and clinical response were recorded. Quality of life forms were filled in by the patients at baseline, and at the fourth and eighth cycle of chemotherapy.

Results: Clinical response was achieved in 14 patients (53.8%), including 11.5% complete response, 43.4% partial remission and stable disease was 34.6%. The number of patients with response and stable disease lasted at least 4 months prior to progression. Quality of life changes statistically significant including: physical function decreased slightly (mean change 7.6 points) after 4 cycles of chemotherapy; cognitive function decreased slightly at the 8th cycle (8.1 points). Emotional function improved partially (7.7 points). However, the global quality of life was still maintained. Changes in body image can adversely affect patients with a decrease of 15.9 points. These symptoms have been reported in breast including pain, swelling and discomfort with little difference of 2.9 points. The toxicities of chemotherapy in organs such as the reduction or loss of appetite, headache and menstrual disorders vary in significance with an increase of 18.8 points. Distress associated with hair loss also increased significantly with 75.5 points.

Conclusion: Paclitaxel-doxorubicin combination for patients with metastatic breast cancer showed significantly clinical improvement and well-tolerated toxicities. Emotional function has been improved. Some aspects of quality of life slightly decreased such as physical, cognitive, and distress relating to body image changes, side effects of chemotherapy and hair loss. However, global quality of life of has no changes. Although sample in this study was still small but routinely assess the quality of life for patients with metastatic breast cancer receiving chemotherapy should be recommended.

I. INTRODUCTION

Breast cancer is one of the biggest medical as well as social problems worldwide. Metastatic breast cancer still remains mostly incurable and overall survival expectance is relatively short, therefore quality of life for patients with metastatic

breast cancer is one of the priority considerations [1]. At the metastatic stage, the cancer burden is quite serious and adversely impact on quality of life and survival time for patient. The real goals of treatment to relieve symptoms, to improve the quality of life and delaying disease progression

1. Hue University of Medicine and Pharmacy, Hue University

Corresponding author: Nguyen Van Cau
Email: nguyenvancau2009@gmail.com

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despite chemotherapy can prolong overall survival for some subtype patients [2]. Chemotherapy is the mainstay of treatment for metastatic breast cancer patients with hormonal receptor-negative disease [3]. In patients with hormonal receptor-positive disease or rapid progression and life-threatening, the chemotherapy is an irreplaceable indication [4]. Chemotherapy regimen combining 2 drugs paclitaxel and doxorubicin has shown the highest degree of response in metastatic breast cancer and taxane-containing regimens are associated with increased overall survival [5]. However, the impact of this combination on the quality of life of patients with metastatic breast cancer is one the issue need to be studied [6]. In Vietnam, the studies assessing the role of doxorubicin-paclitaxel on the clinical response and on quality of life in patients with metastatic breast cancer with the amount of clinical studies is still very modestly. The aim of this study was to:

1. Examine the clinical response of paclitaxel-doxorubicin for metastatic breast cancer patients.
2. Assess the impact of paclitaxel-doxorubicin combination on short-term quality of life outcome.

II. MATERIAL AND METHODS

2.1. Patients and treatment

This study was conducted at the Hospital of Hue University of Medicine and Pharmacy from March 2010 to June 2014. A total of 26 women diagnosed with metastatic breast cancer and treated by paclitaxel-doxorubicin were enrolled.

Inclusion criteria:

- Patients who consent to participate in the study and have fully filled the questionnaires.
- Age 35 to 75.
- Received 8 cycles of paclitaxel-doxorubicin chemotherapy.
- The ECOG ≤ 2 .
- White blood cells $> 3000/\text{mm}^3$, platelets $> 100,000/\text{mm}^3$, hemoglobin $> 10\text{g/l}$.
- The liver and kidney functions are in normal limits

- Prior treatment with CMF regimen, hormonal therapy and radiotherapy were also allowed

Exclusion criteria:

- Patients with brain metastasis.
- Patients have been adequately treated with anthracycline and/or paclitaxel
- Infection with activated hepatitis B, C and other severe bacterial infections.

Chemotherapy: Patients were treated with doxorubicin ($50\text{mg}/\text{m}^2$, 10-minute infusion) follow three hours infusion of paclitaxel ($175\text{mg}/\text{m}^2$) every 21 days. Tests for white blood cell and platelet were taken on day 10 and day 11 of mid-cycles. If the patient with $\geq$ grade 3 neutropenia and thrombocytopenia, the dose was reduced by 25%. If patient was hospitalized due to febrile neutropenia, stop chemotherapy and require large spectrum antibiotics. Premedication of dexamethasone 20 mg IV, ranitidine 50mg IV and diphenhydramine 50mg IM were given IV 30 minutes before paclitaxel. A prophylactic anti-emetic (24mg ondansetron IV) was given according to routine practice.

2.2. Response: Response was defined by RECIST criteria for solid tumor after the fourth cycle and at the end of chemotherapy [7]. Clinical benefit was calculated for responding and stable patients maintaining the same status for at least 4 months. The mean follow-up time was 37 months.

2.3 Quality of life evaluation: Quality of life assessed according to the questionnaires EORTC QLQ-C30, Vietnamese version+3 for cancer patient in general [8] and EORTC -BR23 specific to breast cancer [9]. These questionnaires were validated by European Organization for Research and Treatment of Cancer (EORTC). EORTC QLQ-C30 with 30 questions include:

1. Five functional scales: physical, role, emotional, social and cognitive.
2. Three scales of symptoms: fatigue, pain, nausea and vomiting.
3. Scale of global health status / quality of life.

EORTC QLQ-C30 also includes a string of single items which estimate additional symptoms that are often the subject of complaints of metastatic breast cancer patients: dyspnea, loss of appetite, insomnia, constipation, diarrhea and experiencing financial burden of the disease.

EORTC QLQ-BR23 consists of 23 questions and includes five multi points scale as follows: self-body image, sexual functioning, sexual satisfaction, future perspectives, and scales of

symptoms that encompass systematic therapy side effects, breast symptoms, arm symptoms, disturbance due to hair loss.

2.4. Statistical analysis: Comparisons of quality of life scores at different time points were carried out with the analysis of variance for repeated measurements. P-values less than 0.05 were considered statistically significant. The survival analysis was estimated by using the Kaplan-Meier on SPSS version 16.

III. RESULTS

3.1. Patient characteristics and treatment:

Table 1. Patient characteristics:

Characteristics	n	%
Number of patients	26	100
Age: Mean (range)	54 (37-75)	
ECOG, mean (range)	1 (0-2)	100
Prior treatment:		
1. CMF	3	11.5
2. Hormonal therapy	15	57.7
3. Postoperative radiotherapy	4	15.4
Number of metastatic organs involved		
- 1	22	84.6
- 2	4	15.4
Metastatic sites:		
- Liver	8	30.7
- Lung	13	50
- Bone	5	22.3
Number of doxorubicin-paclitaxel cycles 8	26	100%

The mean age was 54 years (range 37-75) and the mean ECOG performance status was 1 (range 0-2) before chemotherapy. Eighteen patients (69.9%) had prior treatment with CMF and hormonal therapy. Twenty-six patients (100%) with distant metastasis received all the planned eight cycles in which metastasis to the liver, lung and bone were 30.7, 50% and 22.3%, respectively.

3.2. Response to chemotherapy:

Table 2. Response to chemotherapy:

Clinical response	N	%	Stable for at least 4 months
Complete response (CR)	3	11.5	3
Partial response (PR)	11	43.4	10
Stable disease (SD)	9	34.6	9
Progressive disease	3	11.5	
Clinical benefit	N°/% = 22/84%		

Clinical response was achieved by fourteen patients (53.8%), including three (11.5%) complete responses and eleven (43.4%) partial responses. Twenty-two patients (84%) showed clinical benefit

with responding and no changed diseases (CR, PR and SD) for at least 4 months. The overall median survival time was 37 months.

3.3. Quality of life: Twenty-six patients (100%)

have completed the interview according to the items of the study forms at the baseline, 4th and 8th cycle. Results of quality of life are shown in tables 3, 4 and 5.

Table 3. Comparison of mean scores of EORTC QLQ-C30 function scales at baseline and prior to the 4th and 8th cycle of chemotherapy.

Functional scales		At baseline Mean ± SD	4 th cycle Mean ± SD	8 th cycle Mean ± SD	P-values 1-4 cycle 1-8 cycle
1	Physical	78.2 ± 27.4	70.6 ± 21.2	74.3 ± 25.9	0.044* 0.22
2	Role	75.8 ± 16.4	72.4 ± 25.5	79.6 ± 24.3	0.33 0.44
3	Cognitive	90.2 ± 16.4	95.3 ± 14.7	82.1 ± 21.2	0.22 0.033*
4	Emotional	70.8 ± 23.2	78.5 ± 19.1	76.2 ± 21.4	0.002* 0.082
5	Social	82.2 ± 25.1	74.3 ± 26.8	79.2 ± 23.4	0.34 0.14
6	Global quality of life	70.0 ± 20.6	68.8 ± 21.5	64.4 ± 18.8	0.47 0.72

SD: standard deviation, * statistically significant difference. The clinical changes with statistical significance shown in table 3 as follows: from the baseline to the 4th cycle, the physical functioning slightly decrease (change of mean by 7.6 points), cognitive functioning decrease slightly after the 8th cycle (8.1 points). Emotional functioning improved partially (change of mean by 7.7 points). However, the global quality of life remained unchanged.

Table 4. Comparison of mean scores of EORTC QLQ-C30 symptom scales at baseline and at the 4th and 8th cycle of chemotherapy.

Symptom scales		At the baseline Mean ± SD	4 th cycle Mean ± SD	4 th cycle Mean ± SD	Giá trị P 1-4 cycle 1-8 cycle
1	Fatigue	27.8 ± 17.1	30.3 ± 22.2	32.1 ± 24.9	0.082 0.18
2	Nausea & vomiting	8.5 ± 16.6	7.4 ± 12.0	7.8 ± 20.1	0.71 0.73
3	Pain	21.2 ± 24.0	19.7 ± 20.3	17.5 ± 19.7	0.24 0.45
4	Dyspnea	24.1 ± 26.5	20.0 ± 27.5	19.8 ± 21.3	0.22 0.45
5	Insomnia	31.2 ± 24.8	27.5 ± 28.2	30.1 ± 32.2	0.33 0.42
6	Loss of appetite	9.5 ± 14.4	11.2 ± 15.6	10.4 ± 21.6	0.19 0.52
7	Constipation	7.5 ± 12.2	8.6 ± 14.8	6.5 ± 15.9	0.33 0.56
8	Diarrhea	7.5 ± 12.2	10.4 ± 18.8	9.4 ± 16.7	0.11 0.42
9	Financial difficulties	12.4 ± 18.5	15.3 ± 25.0	10.5 ± 18.8	0.32 0.88

There were no both statistically and clinically significant changes in table 4, however there was a trend towards increased fatigue after chemotherapy ($P=0.082$).

Table 5. Comparison of mean scores of EORTC QLQ-BR23 breast cancer items at baseline and the 4th and the 8th cycle of chemotherapy.

Functional scales		At baseline Mean $\pm$ SD	At the 4 th Mean $\pm$ SD	At the 8 th Mean $\pm$ SD	Giá trị P 1-4 cycle 1-8 cycle
1	Body imaging	69.2 $\pm$ 24.8	59.2 $\pm$ 28.8	53.3 $\pm$ 29.6	0.039* 0.008*
2	Sexual enjoyment	26.5 $\pm$ 21.8	29.4 $\pm$ 18.8	22.8 $\pm$ 16.9	0.67 0.54
Symptom scales					
1	Breast symptoms	10.3 $\pm$ 22.5	7.7 $\pm$ 18.9	7.4 $\pm$ 17.5	0.048* 0.33
2	Arm symptoms	12.5 $\pm$ 14.4	12.9 $\pm$ 15.1	14.6 $\pm$ 16.2	0.88 0.33
3	Systematic chemotherapy toxicities	14.8 $\pm$ 9.5	38.9 $\pm$ 15.2	33.6 $\pm$ 9.8	0.0003* 0.0007*
4	Distress due to hair loss	24.5 $\pm$ 17.8	44.9 $\pm$ 38.5	100 $\pm$ 0	0.0049* 0.0022*

Table 5 shown a few statistically and clinically significant changes clinically and statistically were observed as follows: the distress related to body imaging changes increased modestly (15.9 points). The breast symptoms included pain; swelling and discomfort had little changes (2.9 points). The chemotherapy toxicities such as the reduction or loss of appetite, headache, and menopausal symptoms increased significantly (18.8 points) throughout the chemotherapy cycles. Discomfort associated with hair loss also increased significantly by 75.5 points.

IV. DISCUSSION

The combination of paclitaxel and doxorubicin showed a high degree of clinical benefit with manageable toxicities in patients with metastatic breast cancer without adverse impact on global quality of life throughout the entire treatment process. The clinical effect was noted including: fourteen patients (54.9%) with response and clinical benefit achieved is 22/84%, median overall survival

time is 37 months. During the treatment, some positive effects on quality of life were observed. Although some functional scales decreased slightly as physical and cognitive functioning but emotional functioning was improved. According to Ramirez *et al* [10], the improvement in emotional functioning might merely reflect the fact that patients always hope that the treatment will bring clinically beneficial results and patients feel more optimistic in the face of life-threatening disease. During the treatment, quality of life is adversely affected due to the side effects of chemotherapy. In addition, quality of life of patients also declined in terms of physical functioning, distress related to body image changes and hair loss in which is very common with regimen of doxorubicine and paclitaxel [11]. Cognitive functioning decline slightly. Reduced cognitive functioning partly caused by anxiety, depression and fatigue after chemotherapy. Many other functional scales were also changes but no clinical and statistical significance and not affected

adversely the global quality of life of patients. In a previous study, Yeo *et al* assessed the quality of life in patients with metastatic breast cancer treated with 6 cycles of chemotherapy by combination epirubicin and docetaxel and in patients with response received additional 3 cycles of docetaxel [12]. They used other functional scale with the aspects such as emotional, physical functioning and a number of other selected symptoms. Yea *et al* observed these items affected adversely quality of life after 3th cycle of chemotherapy but then these functional scales and symptoms were improved. However, quality of life was still declining but did not return to baseline level although there was a trend towards improved emotional functioning at the end of treatment. In this study, we adhere to the questionnaires assessing quality of life standardized by European Organization for Research and Treatment of Cancer including EORTC QLQ-C30 for cancer patients in general and EORTC-BR23 specific to breast cancer with the best objectivity and the accuracy for assessment of quality of life. However, in this study, we also encountered some difficulties during comparing results with other studies. The slight decline of physical functioning and increased emotional functioning are similar to the results of other authors, while other items such as appetite, nausea / vomiting, pain, fatigue, and financial difficulties were no statistically significant

difference. It was noted that 100% of patients in this study possessed medical insurance to cover the cost of treatment, so patients mostly did not complain about the cost of treatment.

One limitation of this study is that the sample size was small. Some other limitations are due to disease progression (3 patients) that contributed affecting adversely the desired results of the study. I think that these questionnaires validated by EORTC might have some inappropriate items to cultural and health of the Vietnamese people. However the data of quality of life in patients with breast cancer in Vietnam is still very rare to build complete questionnaires for Vietnamese patients with cancer in general and for breast cancer.

V. CONCLUSION

Chemotherapy with combination of paclitaxel and doxorubicin in patients with metastatic breast cancer showed significantly clinical improvement and well-tolerated toxicities. In the course of treatment, emotional function has been improved. Some aspects of quality of life decreased slightly including physical, cognitive functioning, and distress related to body image changes, hair loss and other side-effects of chemotherapy. However, global quality of life in patients is maintained. Although patients in the study sample was small but routinely assess the quality of life for patients with metastatic breast cancer receiving chemotherapy should be recommended.

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