Mahidol University Journal of Pharmaceutical Sciences 2006; 33(1-4): 9-14.

Original Article

Cost of Breast Cancer Treatment with Adjuvant Therapy in Thai Women

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Abstract This study aimed to investigate the patient outcomes and cost of breast cancer patients treated with chemotherapy. A retrospective-cohort study was performed in patients who were diagnosed with breast cancer and received cytotoxic drugs at the National Cancer Institute (NCI), Thailand, since 2001 with 2-year follow-up. Of 1,088 patients, 296 were selected. Most patients were between 41-45 years old (21.3%), in agricultural sector (36.5%), with stage II disease (71.3%) and used FAC (5-fluorouracil, adriamycin and cyclophosphamide) regimen (47.3%). Duration of treatment and number of laboratory tests ranged between 90-120 days and 21-30 tests, respectively. In this study, for stage I, regimen AC (adriamycin and cyclophosphamide) consumed the least resource use, i.e. 80.73 days of treatment, 21.09 laboratory tests and 25.09 patient visits, and therefore resulted in the lowest total cost of treatment, $249.67. A similar result was demonstrated for stage II that was regimen AC had minimal duration of treatment (95.67 days), laboratory tests (24.91), number of patient visits (30.31), cost of cytotoxic drugs, ($106.95) and total cost of treatment ($290.34). All patients were discharged with no node positive and some patients continued follow-up with laboratory tests or continued hormonal therapy. From this study, it can be concluded that patients with stage I and II adjuvant breast cancer who have no risk of heart disease can therefore start the treatment with AC regimen.

Keywords: adjuvant breast cancer, chemotherapy, cost

INTRODUCTION

Cancer is a major problem facing health care systems worldwide. About 12.5% or more than 7 million people died from cancer every year. Cancer incidence by the year 2020 is estimated as 16 million people. Projection by the World Health Organization (WHO)[1] states that more than 11 million people will die from the cancer by the year 2020 and 7 million come from developing countries. Cancer was the first cause of death in 2004 in Thailand with the death rate of 81.3 per 100,000 populations (94.9 in men and 67.9 in women).

Lung cancer, stomach cancer, breast cancer, colon cancer, liver cancer and cervical cancer are the 6 leading types of cancer in the world. Among these, cervical cancer (6,228 per 100,000 populations), breast cancer (5,592 per 100,000 populations) and liver cancer (4,696 per 100,000 populations) were the 3 major types of cancer among Thai women.[2] The DALY (Disability Adjusted Life Year) indicated that cancer was the third major cause of DALY loss for Thai people (10.8% of the total burden).

There are different methods in breast cancer management such as surgery, radiotherapy, endocrine therapy and chemotherapy. Some regimens are used as adjuvant chemotherapy treatment. CMF, FAC and AC are the recommended cytotoxic regimens used by the National Cancer Institute (NCI), Ministry of Public Health, Thailand. The CMF regimen consists of cyclophosphamide (C) 600 mg, methotrexate (M) 40 mg and 5-fluorouracil (F) 600 mg. The AC regimen consists of adriamycin (A) 60 mg and cyclophosphamide

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600 mg. The FAC regimen consists of 5-fluorouracil 500 mg, adriamycin 50 mg and cyclophosphamide 500 mg. All drugs are given intravenously. Patients with hormone-receptor-positive tumors also receive tamoxifen for 5 years.[3-10] These regimens are different in expenditures and period of treatment.

The choice of chemotherapy regimen depends on recurrent risk, co-morbid illness and patient status. The absolute advantage of anthracyclines over CMF is small but shows a significant improvement in survival; a unique toxicity of anthracycline-based chemotherapy is the risk of cardiomyopathy. Anthracycline-based chemotherapy should be considered for women with node-negative high risk and node-positive disease, and CMF should be considered for women with low-to-moderate relapse risk or high risk of cardiac toxicity.[6,9-11]

The selection of systemic adjuvant therapy is based on prognosis and predictive factors. Predictive factors and molecular markers are associated with likelihood of benefit from a specific therapy and also disease free interval and overall survival. These factors may be tumor size, tumor stage, age, blood hemoglobin level, estrogen receptor (ER) and progesterone receptor (PgR), HER-2, p53, CerbB2, Ki-67.[10-18] The HER-2-positive might be resistant to adjuvant treatment with CMF while p53 expression seemed to have an important role in tumors over expressing HER-2.[16] Tumor size and tumor stage are directly correlated with survival.[17]

The recommendation for adjuvant chemotherapy is derived from the Oxford overviews of polychemotherapy and the St Gallen consensus on prognosis factors.[6] When compared with non-anthracycline-containing regimens, four to six courses of treatment (3-6 months) of adjuvant chemotherapy with CMF or an anthracycline-based regimen, is associated with highly statistical significant 15-year absolute reductions in death for young women (< 50 years) with node-negative (7%) and node-positive (11%) breast cancer, and 4% absolute risk reduction for recurrence and death after 10-year follow-up (11%, $p = 0.0005$ and 16%, $p < 0.00001$, respectively).[7-9,11]

In comparing adjuvant chemotherapy with no adjuvant chemotherapy treatment for breast cancer patients, researchers found that for the 45-59, 60-74, 75-79 and 80+ years old node-negative breast cancer patients, incremental costs per year QALY of US$15,400, 18,800-28,200, 44,400 and 57,100 respectively.[19] The average undiscounted lifetime cost per case of treating women diagnosed with breast cancer varied by stage, from $36,340 for stage IV to $23,275 for stage I patients in Canada.[20] These costs consist of costs associated with diagnosis, treatment and follow-up in local currency. The use of Q-TWIST method shows that the incremental lifetime utility derived from the adjuvant treatment with CMF is 127.5 QALYs for every 100 patients. The incremental cost of treatment versus no treatment was around $160,000 for every 100 subjects.[21]

The number of breast cancer patients treated at the Thai National Cancer Institute according to the 1997-2000 statistics are 611, 555, 660 and 723 respectively.[22-25] Many patients do not have access to the services, the possible reasons may be the high cost of treatment, and that a limited number of health care settings for cancer treatment are available.

There is a lack of basic information about breast cancer in Thailand. For examples, epidemiological data, efficacy of cytotoxic drug regimens and also cost of treatment are missing. So we do not have a basic guideline to determine which regimen is the most appropriate for Thai patients.

This study aimed to investigate the cost of breast cancer patients treated with adjuvant chemotherapy, taken the perspective of healthcare providers.

METHODS

A retrospective-cohort study was conducted by using available patient profile of women who were diagnosed as adjuvant breast cancer and received cytotoxic drugs at the National Cancer Institute (NCI), the Ministry of Public Health, Thailand, since 2001 with 2 year follow-up.

Inclusion Criteria

The following criteria were set for patient selection. Thai women who were diagnosed with adjuvant breast cancer that had completed the treatment plan. Only 3 regimens, CMF, AC and FAC, and of stage I and II adjuvant breast cancer were studied in detail from the patient profile available within the study period.

Data Collection

Data were collected by manual review. They were divided into 3 parts: (1) personal data (date of diagnosis, age), (2) treatment data (type of breast cancer, number of visits, disease stage, cytotoxic drug regimen, all of laboratory tests), and (3) direct medical cost (or charge) of treatment including cytotoxic and supportive drugs for nausea/vomiting or pain relief, and laboratory tests.

Data Analysis

SPSS 10 and Microsoft Excel 2003 were used to analyze demographic and descriptive data such as epidemiological data, pattern of adjuvant breast cancer treatment and direct medical cost.

Total cost of the treatment was calculated from cost of drug chemotherapy, supportive drug therapy and laboratory cost. Chemo-therapy drug cost was calculated by summation of each drug for each regimen (CMF, AC and FAC). Supportive drugs were used to prevent side effects and other conditions associated with chemotherapy and total cost of supportive drugs was estimated by chemotherapy unit of NCI. All laboratory costs were provided by NCI.

RESULTS

Demographic Data

Of patients, 296 from 1,088 were met the inclusion criteria. Most of them were 41-45 years old (21.3%), working in the agricultural sector (36.5 %) (Table 1) and came to NCI with stage II adjuvant breast cancer (71.3%) (Table 2). FAC regimen was the most-frequently used chemotherapy (47.3%) followed by AC regimen (25.7%) and CMF (19.9%). For most of the patients, duration of treatment plan was

Table 1. Demographic data of 296 breast cancer patients at the National Cancer Institute

Demographic	Number of patients (%)
Age (years)	
≤ 35	33 (11.1)
36-40	41 (13.9)
41-45	63 (21.3)
46-50	50 (16.9)
51-55	42 (14.2)
56-60	30 (10.1)
> 61	37 (12.5)
Total	296 (100.0)
Occupation	
Civil servants	53 (17.9)
Employees	7 (2.4)
State enterprise	33 (11.1)
Agriculture	108 (36.5)
Private employers	93 (31.4)
Not specified	2 (0.7)
Total	296 (100.0)

Table 2. Breast cancer disease data at the National Cancer Institute

Condition	Number of patients (%)
Stage of disease	
I	56 (18.9)
II	211 (71.3)
III	24 (8.1)
IV	5 (1.7)
Total	296 (100.0)
Drug regimen	
CMF	59 (19.9)
AC	76 (25.7)
FAC	140 (47.3)
Others	21 (7.1)
Total	296 (100.0)
Duration of treatment (days)	
≤ 90	44 (14.9)
91-120	87 (29.4)
121-150	70 (23.6)
151-180	56 (18.9)
> 180	29 (9.8)
Not specified	10 (3.4)
Total	296 (100.0)
Number of laboratory tests	
0-10	20 (6.8)
11-20	55 (18.6)
21-30	98 (33.1)
31-40	64 (21.6)
41-50	37 (12.5)
>51	22 (7.4)
Total	296 (100.0)

CMF = cyclophosphamide, methotrexate, 5-fluorouracil
AC = adriamycin, cyclophosphamide
FAC = 5-fluorouracil, adriamycin, cyclophosphamide

91-120 days (29.4%) and number of laboratory tests was 21-30 (33.1%). Most of patients with age under 55 years old were treated with FAC regimen while age over 56 years old were treated with other regimens in a similar proportion (Table 3).

Table 3. Distribution of cytotoxic drugs regimen by patient age

Age (years)	Regimen			Total
	CMF	AC	FAC	
≤35	1	6	25	32
36-40	9	13	19	41
41-45	13	13	36	62
46-50	7	12	29	48
51-55	10	15	15	40
56-60	10	9	7	26
> 61	9	8	9	26
N/A	-	-	-	21
Total	59 (19.9)	76 (25.7)	140 (47.3)	275/296

Cost of Treatment

For stage I adjuvant breast cancer (as shown in Table 4), regimen AC consumed the minimal duration of treatment (80.73 days), number of laboratory tests (21.09 times) and number of patient visits (25.09 times) while CMF used a maximal duration of treatment (159.38 days), laboratory tests (33.44 times) and number of patient visits (45.44 times). Regimen AC also had a minimal cost of the cytotoxic drugs ($106.95) and cost of laboratory tests ($110.82) while FAC had a maximal cost of cytotoxic drugs ($295.35) and CMF had a maximal cost of laboratory tests ($197.58). Overall, regimen AC showed the lowest total cost of treatment ($249.67).

For stage II adjuvant breast cancer, regimen AC had a minimal duration of treatment (95.67 days) while CMF had a maximal duration of treatment (162.13 days) (Table 5). Regimen FAC had minimal laboratory tests (24.91 times) but the average number of laboratory tests for 3 regimens was slightly different. Regimen AC had a minimal number of patient visits (30.31 times) while CMF had a maximal number of patient visits (40.95 times). Regimen AC had a minimal cost of the cytotoxic drugs ($106.95) while regimen FAC had a minimal cost of the laboratory tests ($136.91). Regimen AC showed a minimal total cost of treatment ($290.34).

Outcomes

All patients were discharged with no node positive and some patients continued follow-up with laboratory tests or continued hormonal therapy with tamoxifen for 5 years as shown in Table 6.

DISCUSSION

Many patients were excluded from our study because of loss of follow-up. There were many causes for this such as expensive drug cost, transportation, occupation because most of them were poor and worked in agricultural sector, and NCI's location is in the capital city, Bangkok.

Table 4. Treatment cost of stage I adjuvant breast cancer

	CMF	AC	FAC	Others
No. of patients	16	11	22	7
Average duration of treatment (days)	159.38 (149-185)	80.73 (61-126)	123.95 (64-168)	344.29 (0-757)
Average number of lab. tests	33.44 (22-44)	21.09 (0-49)	31.14 (18-45)	19.86 (15-27)
Average number of visits	45.44 (34-56)	25.09 (4-53)	43.14 (30-57)	-
Cytotoxic drug cost, $	148.50	106.95	295.35	
Supportive drug cost, $	95.70	31.90	95.70	-
Average lab cost, $	197.58 (96.50-355.00)	110.82 (0-275.25)	191.44 (51.00-331.00)	-
Average total cost, $	441.78 (340.70-599.20)	249.67 (138.85-414.10)	582.49 (442.05-722.05)	-

CMF = cyclophosphamide, methotrexate, 5-fluorouracil
AC = adriamycin, cyclophosphamide
FAC = 5-fluorouracil, adriamycin, cyclophosphamide

Table 5. Treatment cost of stage II adjuvant breast cancer

	CMF	AC	FAC	Others
No. of patients	39	58	99	14
Average duration of treatment (days)	162.13 (121-219)	95.67 (46-196)	126.10 (63-196)	452.00 (0-961)
Average number of lab. tests	28.95 (0-50)	26.21 (0-71)	24.91 (0-45)	16.64 (0-27)
Average number of visits	40.95 (12-62)	30.31 (4-75)	36.91 (12-57)	-
Cytotoxic drug cost, $	148.50	106.95	295.35	-
Supportive drug cost, $	95.70	31.90	95.70	-
Average lab cost, $	152.53 (0-364.25)	151.49 (0-542.25)	136.91 (0-531.50)	-
Average total cost, $	396.73 (244.20-608.45)	290.34 (138.85-681.10)	527.96 (391.05-761.80)	-

CMF = cyclophosphamide, methotrexate, 5-fluorouracil
AC = adriamycin, cyclophosphamide
FAC = 5-fluorouracil, adriamycin, cyclophosphamide

Table 6. Hormonal therapy (tamoxifen) after chemotherapy

Regimen/Stage	Yes (%)	No (%)	Total
CMF, stage I	10 (62.5)	6 (37.5)	16
CMF, stage II	22 (56.4)	17 (43.6)	39
AC, stage I	9 (81.8)	2 (18.2)	11
AC, stage II	36 (62.1)	22 (37.9)	58
FAC, stage I	10 (45.5)	12 (54.5)	22
FAC, stage II	48 (48.5)	51 (51.5)	99
N/A	-	-	51
Total	135	110	296

Cost of cytotoxic drugs and supportive drugs were the same for stage I and II patients because they were calculated from each drug of each regimen (CMF, AC and FAC) and the duration of the treatment plan were the same. Laboratory costs were higher in stage II because patients required more tests to verify their tumor size and status.

From this study it can be concluded that patients with stage I and II adjuvant breast cancer who have no risk of heart disease can start the treatment with AC regimen because of minimal necessary laboratory tests and lower costs of treatment, and they show the same outcomes as other regimens. Furthermore, other factors such as estrogen markers, number of node positive breast cancer and patient compliance must be considered.

However, many limitations were found during the study. For examples, patient data were only available in the medical records, no electronic databases, only new patients in the year 2001-2002 were selected and followed-up for 2 years, only patients who completed the treatment plan were included into the study, only direct medical cost of cytotoxic drugs (limited to CMF, AC and CMF regimens) and supportive drugs were calculated, and only patients in stage I and II breast cancer were studied. So the results from this study may not cover all breast cancer situations in Thailand.

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