

Treatment costs in Hodgkin's disease

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Little information is currently available on the effective use of hospital resources and the resulting costs of treating any childhood cancer in our country. The aim of this study was to estimate direct costs of medical care for Hodgkin's disease (HD). Between January 1989 and June 1998, direct medical cost (DMC) of 53 patients with HD was determined at Dr. Behçet Uz Children's Hospital, by chart review. Costs were estimated for initial, continuing, and terminal care. DMC of treatment per patient with HD, based on medicare charges, was calculated to be \$3,371. Chemotherapy was the major cost item in DMC. Additional cost items arose depending on the clinical stages of the disease and relapse ($p=0.0002$). Estimated direct medical costs reported here, may be useful in determining capitation rates, planning budgets, and estimating the aggregate medical care costs for HD. [Turk J Cancer 2000;30(3):105-110]

Key words: Direct medical costs, childhood cancers, Hodgkin's disease

Hodgkin's disease (HD) has the highest cure rate in childhood malignancy. Over the last 30 years, the prognosis of HD has improved impressively with the use of combination chemotherapy with or without radiotherapy (1-4). The aim of further studies will be to introduce new therapeutic modalities as effective but less toxic than the present ones in HD (1). This approach requires a rigorous assessment of the long-term cost and benefit of the various therapeutic modalities used for treatment of HD. However, little information is currently available on the effective use of hospital resources and the resulting costs of treating any childhood cancer. The aim of this study was to estimate direct medical cost of medical care for HD.

Patients and Methods

A retrospective analysis of medical records of 53 patients with HD, admitted to the Pediatric Oncology Unit between January 1989 and June 1998, was undertaken. Direct medical resource consumption patterns were determined by chart review. Together with the number of outpatient admissions, causes for admissions, the duration of in-patient stays, details of chemotherapy and

radiotherapy, and all laboratory investigations were recorded. Cost items for each of these activities were estimated using the Medicare Fee Schedule used in our department. Nonmedical costs were excluded.

For the clinical staging, chest X-ray, computed tomography (CT) of chest, abdomen, and pelvis, radionuclide scintigraphy of the bones, and bone marrow aspirations and biopsies were used. Ann-Arbor classification was used for staging of HD.

Until 1997, all patients in stage I and II were given three 28-day cycles of chemotherapy (COPP/MOPP or ABVD) followed by 25 Gy of radiation therapy (mantle or inverted-Y fields). Patients in stage III and IV received six 28-day cycles of chemotherapy, alternating between a cycle of COPP/MOPP and/or ABVD followed by 25 Gy of radiation therapy (mantle and inverted-Y fields) (3). After 1997, patients were treated according to the German/Austrian Hodgkin's Study (HD-90) protocol 2 x OPPA (OEPA) $\pm$ 2 (4) x COPP. Radiation dose was reduced to 20Gy (4).

Dosages for the chemotherapy cycles were as follows: MOPP/COPP: nitrogen mustard 6.0 mg/m² intravenous push on days 1 and 8 of each cycle; vincristine 1.5 mg/m² (maximum dose 2 mg) intravenous push on days 1 and 8 of each cycle; prednisone 40 mg/m² daily orally, divided into three doses, for 14 days; procarbazine 100 mg/m² daily orally divided into two doses, for 14 days; cyclophosphamide 500 mg/m² intravenous infusion over 30-60 minutes on days 1 and 8 of each cycle. ABVD: doxorubicin 25 mg/m² intravenous push on days 1 and 15 of each cycle; bleomycin 10 U/m² slow intravenous push on days 1 and 15 of each cycle; vinblastine 6 mg/m² intravenous push on days 1 and 15 of each cycle; and DTIC 375 mg/m² intravenous slow drip over 30 to 60 minutes on days 1 and 15 of each cycle. OPPA: Prednisone 60 mg/m² daily orally, divided into three doses, for 14 days; procarbazine 100 mg/m² daily orally divided into two doses, for 14 days; vincristine 1.5 mg/m² (maximum dose 2 mg) intravenous push on days 1, 8 and 15 of each cycle; adriamycin 40 mg/m² intravenous infusion over 4 hours on days 1 and 15 of each cycle. OEPA: Prednisone 60 mg/m² daily orally, divided into three doses, for 14 days; vincristine 1.5 mg/m² (maximum dose 2 mg) intravenous push on days 1, 8 and 15 of each cycle; adriamycin 40 mg/m² intravenous infusion over 4 hours on days 1 and 15 of each cycle; etoposide 125 mg/m² intravenous infusion over 2 hours on days 3-6 of each cycle.

The radiation therapy (XRT) was given to supradiaphragmatic and/or infradiaphragmatic sites, and to involved extranodal sites. The dose was 25 Gy given in 1.8 Gy fractions, 5 days a week. Patients with residual nodal enlargement after chemotherapy were given a booster dose of 14. In those cases the overall radiation dose was achieved to 34-40Gy.

Serial physical examinations were performed at the beginning of each cycle of chemotherapy and before XRT. Complete blood counts were obtained before each course of chemotherapy and twice a week during XRT. Serum levels of liver function tests were evaluated both at the beginning of the third and fifth cycles and at the end of the chemotherapy and every 4 weeks during XRT. Chest X-rays were obtained at the beginning of the third and fifth cycles of the chemotherapy, before starting XRT and every 4 weeks during XRT. A CT scan of the chest as well as bone marrow aspiration and biopsy (if initially positive) were performed on completion of chemotherapy. Echocardiograms were obtained after three cycles of ABVD and on completion of the chemotherapy and every 4 weeks during XRT.

Pulmonary function studies were done in patients older than 5 years at completion of the chemotherapy and every 4 weeks during XRT. Chest X-ray and CT scan, bone scan, and any other tests positive at diagnosis were conducted at the end of therapy to evaluate overall response.

To assess the late effects of therapy the following processes were used: physical examination, complete blood counts, serum levels of liver function tests, and chest X-rays every 4 weeks during therapy; physical examinations and chest X-rays at the 9th month, the first year, the 18th month, the second year of the therapy, and every year thereafter for a period of five years; endocrine assessments (thyroxine, TSH, LH, FSH) at the 6th month after completion of the therapy and at yearly intervals; echocardiograms and pulmonary function tests at the 3rd and the 6th months after completion of the therapy and at the 5th, 7th and 10th year.

Statistical Analysis: Candidate prognostic factors were identified as those with a significance level of ≤ 0.05 . The predicting factors for DMC were assessed using regression analysis.

Results

Fifty-three patients were evaluated by chart review. There was male predominance (2,5:1) with a median age of 7 (1,5-14) years. The clinical stages of patients were as follows: Sixteen patients in stage I, 14 in stage II, 10 in stage III and 13 in stage IV (Table 1).

Table 1
Patient characteristics

Characteristics	Group 1*	Group 2†
Total no. of patients	43	10
Sex		
Male/Female	32/11	6/4
Clinical stage		
I/II	15/11	1/3
III/IV	7/9	3/3
Relapse	7	1
Outcome		
Follow-up	25	9
Lost to follow-up	15	1
Death	3	-

*Group 1 COPP (cyclophosphamide, vincristine, prednisone, procarbazine) MOPP (nitrogen mustard, vincristine, prednisone, procarbazine) $\pm$ ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine)+XRT

†Group 2: OPPA (vincristine, prednisone, procarbazine, adriamycin) OEPA (vincristine, etoposide, prednisone, adriamycin) $\pm$ COPP + XRT

The median follow-up period was 30 months. The 5-year overall survival (OS) and event-free survival (EFS) were 95% and 78%, respectively. The 5-year OS was 100% in stage I and stage II, and 89% in stage III and stage IV. The

3-year EFS was 96% in stage I and stage II, and 72% in stage III and stage IV. Relapses developed in eight patients.

The direct medical costs (DMC) of treatment per patient for Hodgkin's disease, based on medicare charges, was calculated to be \$3,371 and the annual cost was \$12,456.

The cost of chemotherapy and radiotherapy, which were the major cost items, accounted for 37.7% and 27.6% of the DMC, respectively. The cost of in-patient stay was 4.5%, and that of laboratory investigations was 6.6% of DMC (Table 2).

The DMC changed depending on the stages of HD as follows: \$3,773 for stage I, \$3,277 for stage II, \$2,837 for stage III; and \$3,388 for stage IV. The costs of radiotherapy and treatment of a recurrence were higher for patients with advanced disease. The cost of chemotherapy was also higher in stage IV, but the difference between those four stages were not significant ($P>0.05$) (Table 3).

Table 2
Estimated direct medical costs of treatment per patients

Cost variable	Estimated cost (US \$)	%
Chemotherapy	1270	37.7
Radiotherapy	932	27.6
Follow-up	795	23.6
Laboratory	221	6.6
Hospitalization	153	4.5
Total	3371	100.0

Table 3
Estimated direct medical costs of treatment per patients by stages

Cost variable	Costs (US\$)				p
	Stage I	Stage II	Stage III	Stage IV	
Radiotherapy	926	916	945	982	0.03
Chemotherapy	875	693	624	1132	
Hospitalization	178	154	154	111	
Follow-up	980	873	433	758	
Laboratory	814	641	681	405	
Total	3773	3277	2837	3388	

Univariate and multivariate prognostic factor analysis: The extent of disease was associated with the cost of radiotherapy, and also with the cost of follow-up. The costs of chemotherapy and radiotherapy, which were heavily influenced by the recurrence of disease, had an impact on the DMC (Table 4). LDH levels were also associated with DMC ($p=0.03$).

Table 4
Significant factors contributing to the direct medical costs of treatment per patients by multivariate analysis

Cost variable	r	p
Relapse	0.9181	0.0002
Follow-up	0.7385	0.003
Chemotherapy	0.5772	0.003
Radiotherapy	0.2224	0.01

Discussion

The DMC of treatment per patient was estimated to be \$3,371. Using our estimated DMC and the number of the patients registered in one year (supplied from the registry of the Ministry of Health) the total estimated DMC of HD was calculated to be approximately \$505,650. Since we couldn't find any study reported by the Ministry of Health, we couldn't have the chance to compare our results with the actual costs of the Ministry of Health. Besides that, many cancer patients, who did not have health insurance, couldn't take medical care and therefore were not registered.

In our country, however, the ratio of the Budget of the Ministry of Health to the Consolidated Budget of the Government was reported to be 2.65% and that of the Department of Cancer Control was 0.01% (5).

Bloom et al. (6) reported that, about 95% of all medical costs had been paid by private, public, or charitable payers. Hospital programs that reimbursed out-of-pocket costs, transportation costs to obtain services, and lodging accommodations were available. Additional services were also offered through cancer advocacy groups, such as the cancer societies to assist patients with managing costs and overcoming barriers to care.

Norum et al. (7) reported the mean total cost of treatment in HD as approximately \$7,820 (12,512 £). They noticed that the total treatment costs were significantly higher in patients with advanced clinical stages of the disease ($p=0.0006$), B-symptoms ($p=0.0027$) and relapse ($p<0.0001$) (7). Similarly, we found that, the cost of radiotherapy and the cost of treatment of a recurrence were higher in advanced stages of disease. Although, it was not statistically significant, the cost of chemotherapy was also higher in advanced stages of disease. This might be attributable to the intensive treatment regimens previously used, even in early stages of disease, and also to relapses occurred in three patients with early stages of disease. Multivariate analyses indicated that the excess cost was associated with relapse of the disease. Since, Norum et al. (7) estimated the total treatment costs, including medication, hospital stay, hospital hotel stay, radiotherapy, travelling, loss in production, i.e. work, it was not possible to compare their costs with that of ours.

Corder et al. (8) reported that 30% of the total charges were identified as perceived excess. Hospitalization was accounted for 68% and laboratory charges for 22% of the perceived excess charges. They recommended that attempts to reduce the expense of HD staging should be directed at decreasing

hospitalization (8). The DMC for hospitalization and laboratory investigations in our study were lower than the costs reported in that study.

Fireman et al. (9) reported the DMC for non-Hodgkin's lymphoma to be \$48,000. The mean cost of cancer care and treatment per patient-year for lymphoma was \$8,969 in the study of Gülen et al. (10). There was another study estimating medical costs and family out-of-pocket expenses over time for 569 children with malignant neoplasms (6). In this study, the mean cost of cancer care and treatment per patient-year was \$29,708 with variation by diagnosis, prognosis, and time from diagnosis. As we have showed, the DMC of HD was lower than the DMC of non-Hodgkin's lymphoma.

This study will serve to highlight some of the difficulties involved in assessing treatment costs and to provide a basis for future studies. However, future collection of more specific data at the country level would greatly assist policymakers dealing with cancer issues.

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