Journal of BUON 17: 781-784, 2012

ORIGINAL ARTICLE

It is not only the empty vials that go into the garbage can during chemotherapy drugs preparation: A cost analysis of unused chemotherapy drugs in cancer treatment

A. Ata[1], H. Abali[2], E. Yengel[3], A. Arican[1]

[1]Mersin Public Health Hospital, Clinic of Medical Oncology, Mersin; [2]Baskent University School of Medicine, Department of Medical Oncology, Adana; [3]Mersin University School of Medicine, Department of Internal Medicine, Mersin, Turkey

Summary

Purpose: *Cancer therapy is a costly treatment. Costs of drugs used in cancer therapy are gradually increasing with the addition of new and expensive drugs. This fact imposes obligation on reasonable drug usage. Occasionally, all of the prescribed drugs are not used for various reasons, and a number of drugs can be left over. In this study, we aimed to calculate the costs of unused chemotherapeutic drugs in our oncology clinics.*

Methods: *A total of 117 patients with 17 different types of cancer were administered 32 cancer therapy protocols during 2 months. After administration of ideal doses of the prescribed drugs calculated on an individual basis, the number of unused drug doses in the packages was recorded and the costs of the unused drugs were calculated based on current prices of the drugs.*

Results: *The cumulative cost of the unused drugs calculated for all patients was US dollars (USD) 6406.93, and average cost of the drug per capita was USD 54.76. Minimal and maximal unused drug costs per drug were USD 0.29 for 5-fluorouracil, and USD 247.12 for bevacizumab, respectively. Minimal increase in drug costs per recipe was USD 0.50 for a prescription containing cyclophosphamide and 5-fluorouracil, while the total cost of bevacizumab plus irinotecan combination increased tremendously to USD 309.12. Among chemotherapeutic protocols the cheapest one was AC (adriamycin, cyclophosphamide) with USD 4.77, while the most expensive one (USD 116.02) was FOLFIRI-B (5-fluorouracil, calcium folinate, irinotecan, and bevacizumab).*

Conclusion: *The important financial burden of unused drugs goes unrecognized among routine chemotherapeutic applications. In order to be able to avoid this extravagance, drug industry, prescribing physicians, and practice nurses must assume important roles.*

Key words: cancer, chemotherapy, cost, unused drug

Introduction

Cancer therapy is a costly, exhausting, and frustrated therapy requiring multidisciplinary team approach. Every day a new development occurs in every part of the world in the treatment of cancer which is a common problem of humanity, and shared knowledge accumulates rapidly. However, the economic burden of cancer research is quite enormous. Therefore, the cost of cancer therapy and quotas reserved for cancer therapy in the national health care expenditures of the countries gradually increase [1-3]. This phenomenon is very annoying for the governments and health professionals, and economic parameters start to play larger-scale roles in the treatment choices and applications.

Drug therapies (chemotherapy, biotherapy, and immunotherapy) are more costly than the other two treatment modalities (surgical therapy and radiotherapy). In fact drug therapies are generally ongoing treatments. In other words chemotherapy is an open-end therapy unlike surgical therapy and radiotherapy with restricted durations. In recent years with increasing success rates in multidisciplinary treatment modalities and improved quality of patient care, longer survival times were achieved, and higher number of patients received chemotherapy. Besides, the number of first-line drugs, and those improving survival rates or slowing down the progression of the disease in patients with gradually deteriorating conditions, has increased. In addition, the number of drug therapies for each pa-

Correspondence to: Alper Ata, MD. Mersin Public Health Hospital, Clinic of Medical Oncology, Kuva-i Milliye, 33050 Mersin, Turkey. Tel: +90 3243363950, Fax: +90 3243360256, E-mail: dralperata@yahoo.com

Received 04-02-2012; Accepted 27-02-1012

tient has increased. With time, the number of oncology centers and medical oncologists has increased, cancer patients receive medical care within a shorter time and more easily, which naturally enhanced the total amount of medications. The gradually rising concern of the drug industry towards oncology should not be forgotten. This affinity has made the discovery of many new molecules, and enabled their clinical application. Especially, targeted treatments have been more widely used despite their high cost because of their marked beneficial effects.

The cost of drug therapies in the treatment of cancer is generally calculated during the post-marketing period. Analyses of treatment and cost-effectiveness performed using the sources of the country's economic facilities are rapidly increasing in number. In cost analyses, usually the association between effectiveness and cost of the drug has attracted attention. We have heard concepts of ICER (incremental cost-effectiveness ratio) or QALY (quality- adjusted life year) more frequently. However, higher costs of drugs can not be attributed only to increased prices of the drugs.

For instance, discordance between calculated drug dosages and commercial presentation of the drug for an individual patient *per se* is one of the important points usually overlooked. Cancer therapy is individualized for each patient. For each patient, drug dosage can be modified according to patient's body weight, body surface area (BSA), renal or hepatic functions, performance status, and even age. Therefore, it is not possible for a drug industry to present ideal individual dosage inside only one single package. Pharmaceutical firms offer the most possible proprietary dosage forms by coupling effective doses extrapolated from phase the most possible proprietary dosage forms by coupling effective doses extrapolated from phase I-II studies with ideal human body measurements. In these calculations mean BSA is accepted as 1.70-1.80 m^2 [4-6]. For instance, ideal drug doses determined after phase I-II studies for adriamycin and cyclophosphamide (AC) combination to be used in a breast cancer patient are 60 mg/m^2 and 600 mg/m^2, respectively. In a woman with ideal body measurements of nearly 1.7 m^2 the final doses are approximately 100 mg and 1000 mg. These drugs are marketed in Turkey as 50 and 1000 mg commercial vial formulations. Therefore, with vial formulations it is possible to administer ideal individual dosages without any amount of surplus drug left over. What if BSA of the patient is 1.55 m^2? This is the subject of this study. We know that most of our patients have not golden ratios of Leonardo da Vinci and Le Corbusier [7,8].

In this study we intended to analyze the costs of ideal doses that are required by cancer patients, and those of unused, and so wasted drug formulations because of unrealistic commercial dosage forms.

Methods

Our study enrolled patients treated for different cancers and management protocols, who were referred to Medical Oncology Clinic of Mersin University Faculty of Medicine between April 15, 2008 and June 15, 2008. During the study period, repetitive therapeutic cycles of the same regimen of each patient were excluded from analysis. During drug prescription process, body weight and height of each patient were measured again to calculate current and ideal BSA. Individual drug dosing to be prescribed was calculated based on the patient's BSA or body weight. Unit prices of each drug were estimated in Turkish Liras (TL) based on the reimbursement rates of the relevant healthcare payers [1]. These calculated amounts were then converted to US currency rates valid on 07.14. 2008 (1 USD = 1.216 TL). On every prescription the difference between ideal drug dose required for the individual patient, and the marketed dosage form of this drug was noted and multiplied by previously calculated unit price to estimate costs of unused and wasted drug forms *per se*, and for each prescription and therapeutic protocol in USD. Besides, the total cost of the prescribed drugs and cost percentage of unused drugs to that total amount were estimated. In addition, total daily cost of all the drugs used in our clinics was calculated.

Results

Within the time frame of the study, 32 different chemotherapy protocols were used in 117 (68 women, 49 men) patients with 17 distinct cancer types. Mean age was 53.3 ± 12.4 years in women, and 57.2 ± 11.1 years in men. Mean BSA was 1.71 ± 0.15 m^2 in women, and 1.81 ± 0.18 m^2 in men. Mean body weight was 69.01 ± 12.60 kg in women, and 71.44 ± 14.22 kg in men (Table 1). Considering the different cancer types' distribution, breast cancer prevailed (30 cases; 25.6%), while malignant melanoma, head and neck cancer, esophageal cancer, and renal cell carcinoma had the least number of patients (n=1; 0.9% each). Mostly FOLFOX (5- fluorouracil, calcium folinate, oxaliplatin) protocol was used in 16 patients with colorectal cancer, while only one patient received one of 13 different chemotherapy protocols.

The total cost of unused surplus drugs calculated for all patients was USD 6406.93, and the mean cost of surplus drugs per capita was USD 54.76. Minimal sur-

Table 1. Patient characteristics

Sex	*Age (years)*	*Body surface area (m^2)*	*Weight (kg)*
Male (n=49)	57.2 ± 11.1	1.81 ± 0.18	71.44 ± 14.22
Female (n=68)	53.3 ± 12.4	1.71 ± 0.15	69.01 ± 12.60

Table 2. Costs of the unused drugs for each drug commonly used in cancer patients

Name of drug	*Number of patients*	*Total cost of drug (USD)*	*Cost of unused drug per patient (USD)*
5-fluorouracil	33	99.46	3.01
Cyclophosphamide	21	68.63	3.26
Cisplatin	11	61.61	5.60
Irinotecan	6	93.94	15.65
Bleomycin	11	321.24	29.20
Paclitaxel	10	600.38	60.03
Gemcitabine	6	412.45	68.74
Docetaxel	7	653.38	93.34
Oxaliplatin	12	1390.18	115.84
Bevacizumab	6	790.8	131.8
Rituximab	6	884.7	147.45

plus drug cost was USD 0.29 for 5-fluorouracil, and most expensive for bevacizumab (USD 247.12). The cheapest surplus drug cost per prescription was USD 0.50 for cyclophosphamide-5-fluorouracil combination, while the most expensive one amounted to USD 309.12 for bevacizumab-irinotecan combination. Surplus drug cost was at a minimal level for AC protocol (USD 4.77), while it was highest for FOLFIRI-B protocol (USD 116.02). Surplus drug costs of some frequently used drugs are shown in Table 2. Mean surplus drug costs for each prescription used in some frequently used chemotherapy protocols are shown in Table 3. Surplus drug costs varying according to the different cancer types are shown in Table 4. Based on these calculations, in our unit where everyday an average of 25 patients are receiving various chemotherapy protocols, the daily surplus drug expenditure rises to nearly USD 1369.

Discussion

Cancer therapy is an expensive treatment modality. As is the case for every drug therapy, unfortunately some portion of the prescribed drugs is left over and discarded for various reasons. However, when compared with other medications, the relatively expensive cancer therapy results in higher surplus drug expenditures. Based on our findings we came to several conclusions on how to decrease the amount of unused drugs and their costs, which are cited below.

Unfortunately, some drugs available in Turkey are not marketed in different dosage forms. For instance bleomycin can be only purchased as single 15 mg vials. Ideal bleomycin dose in the ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) protocol used in the treatment of Hodgkin's lymphoma is 10 mg/m^2. Since for a patient with a BSA of 1.8 m^2, total bleomycin dose amounts to 18 mg, thus 2 packages of bleomycin

Table 3. Costs of unused drugs in some chemotherapy protocols commonly used in cancer patients

Chemotherapy protocol	*Number of patients*	*Cost of prescription per patient (USD)*	*Total cost of unused drug (USD)*	*Cost of unused drug per patient (USD)*	*Ratio of unused drug cost to prescription*
AC	6	55.84	28.65	4.7	8.5
CAF	5	61.66	32.13	6.4	10.41
FUFA	9	100.63	186.29	20.69	20.56
CEF	6	130.28	153.12	25.52	19.58
CARPAC	7	1474.3	291.07	41.58	2.8
ABVD	10	159.47	722.06	72.2	45.27
FOLFOX	17	1101	1342.48	78.9	7.1
R-CHOP	5	2685.2	404.84	80.96	3.0
FOLFIRI-B	6	2969.6	696.16	116.02	3.9

AC: adriamycin, cyclophosphamide, CAF: adriamycin, cyclophosphamide, 5-fluorouracil, FUFA: 5-fluorouracil, calcium folinate, CEF: epirubicin, cyclophosphamide, 5-fluorouracil, CARPAC: carboplatin, paclitaxel, ABVD: adriamycin, bleomycin, vinblastine, dacarbazine, FOLFOX: 5-fluorouracil, calcium folinate, oxaliplatin, R-CHOP: rituximab, adriamycin, cyclophosphamide, vincristine, prednisone, FOLFIRI-B: 5-fluorouracil, calcium folinate, irinotecan, bevacizumab

Table 4. Cost of unused drugs in some types of cancer

Types of cancer	*Number of patients*	*Total cost of unused drug (USD)*	*Cost of unused drug per patient (USD)*
Breast	30	1094.42	36.48
Colorectal	29	2767.86	95.44
Lung	13	410.26	31.55
Hodgkin lymphoma	10	722.06	72.20
Non-Hodgkin lymphoma	9	438.39	48.71
Ovarian	7	613.28	87.61

should be prescribed, and 12 mg bleomycin remaining from the second package are not used, and discarded. Proportionally higher drug cost of ABVD regimen in total cost of prescribed drugs is clearly associated with bleomycin. Lack of intermediate dosage forms for many marketed drugs complicates adjustment of ideal drug dosages, compels physicians to overprescribe, and surplus drugs increase treatment expenditures. Every effort should be exerted to encourage the pharmaceutical industry to manufacture the drugs in various dosage forms.

Unfortunately, some chemotherapeutic drugs have been marketed as single-use disposable vials, and reuse of surplus drug is not recommended. Difference between two drugs in the group stems from this peculiar drug formulation. A single paclitaxel vial can be used repeatedly, but it is not the case for a docetaxel vial. Therefore surplus drug cost of docetaxel is higher than that of paclitaxel. If appropriate packaging techniques can be evolved enabling repeated uses of chemotherapy drugs, then surplus drug costs will decrease.

One of the methods of decreasing the economic impact of unused medications is to produce depot formulations for the utilization of more than one patient, and to develop new technologies to facilitate usage of pharmacologic formulations. Some equipments adjusting, and then pumping appropriate dosages for each individual patient from a common container into drug delivery sets are available only in scarce number of chemotherapy units [9]. With this approach dosages are delivered just in exactly calculated amounts without any surplus or deficit. However, usage of this costly equipment is not adequately applicable yet, and hence it is not widely employed. Necessary technologies should be developed for widespread usage of this equipment.

Physicians responsible for prescribing drugs in polyclinics should be cognizant of the treatment costs. Apart from this critical issue, prescribing physicians should spend much more time for prescription and know all formulations and prices of marketed proprietary drugs, and finally regulate drug dosages so as to minimize (or even eliminate) the number of any surplus unused drugs. When prescribing especially expensive drugs, one can be more flexible in observing ideal doses. In our polyclinics, meticulous obedience to this rule has been demonstrated as far as possible, and proportionally lesser expenditures related to surplus unused drugs could be achieved in protocols comprising expensive drugs such as bevacizumab or rituximab. However, the same meticulous care was not exerted in relatively cheaper treatment protocols, and the proportionally higher surplus drug costs incurred in these treatment regimens struck our attention. This issue was taken into consideration, and periodic informative meetings were arranged with our research workers.

In Turkey preparation of chemotherapeutic regimens is generally under the responsibility of nurses. It is important to raise the awareness of nurses about costs of therapeutic modalities. Nurses should be given an opportunity to propose solutions aiming at decreasing the costs of treatment regimens.

Conclusion

Higher costs of cancer chemotherapy are partially related to unused drugs. Avoidance of these higher expenditures, i.e. squandering expenses observed in varying degrees is under the joint responsibility of drug industry, physicians, and nurses.

References

1. American Cancer Society. Cancer Facts & Figures 2011. Atlanta, GA, 2011.
2. Yabroff KR, Lund J, Kepka D, Mariotto A. Economic burden of cancer in the United States: estimates, projections, and future research. Cancer Epidemiol Biomarkers Prev 2011; 20: 2006-2014.
3. Jemal A, Siegel R, Ward E et al. Cancer statistics 2008. CA Cancer J Clin 2008; 58: 71-96.
4. Pouliquen AL, Escalup L, Jourdan N, Cottu P, Faure P, Madelaine-Chambrin I. Dose standardisation of anticancer drugs. Int J Clin Pharmacol 2011; 33: 221-228.
5. Mosteller RD. Simplified calculation of body surface area. N Engl J Med 1987; 22: 317: 1098.
6. Gehan EA, George SL. Estimation of human body surface area from height and weight. Cancer Chemother Rep 1970; 54: 225-235.
7. Dunlap RA (Ed). The Golden Ratio and Fibonacci Numbers. World Scientific Publishing,1997.
8. Le Corbusier (Ed). The Modulor p. 25, as cited in Padovan, Richard, Proportion: Science, Philosophy, Architecture, 1999, p 316, Taylor and Francis.
9. Cotugno MC. Automating Chemotherapy Preparation with Robotic Technology. Pharmacy Purch Prod 2010; 18.