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# Pharmacists role in cost saving and waste minimization study on antineoplastic drugs: A multi-central study in Turkey

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**ABSTRACT**: Cancer diseases are the most common cause of death and chemotherapeutics used in cancer treatment have an important place in the budget allocated to health due to their high costs. This study aims to reduce disposal costs and reduce chemotherapy drug expenses through cost savings. Our study was conducted between November 2017 and July 2018 (1st semester) and between August 2018 and April 2019 (2nd semester) in three hospitals using a common chemotherapy drug preparation center. Chemotherapy sessions were rearranged in accordance with the drugs included in the treatment plans to reduce drug costs. The drug quantities billed through hospital automation programs and the disposal costs of unused drugs were reported by the pharmacists on a milligram (mg) basis. The obtained data was analyzed by the GraphPad Prism program. $P<0.05$ was considered significant. While the total amount of waste medicine in the 1st. period was reported as 371,866 mg, it was reported as 303,056 mg in the 2nd. period ($p<0.05$). While the total disposal cost was calculated at € 87,867.02 in the 1st. period, it was calculated € 26,392.48 in the 2nd. period under the control of pharmacists ($p<0.01$). In this study, it was observed that providing and monitoring drug preparation services by well-equipped pharmacists specialized in the field of oncology gave positive results in terms of reducing both drug expenditures and drug disposal costs. Further studies are needed to determine the safety of chemotherapy pharmacists and patients.

**KEYWORDS**: Pharmacists; waste management; antineoplastic drugs; drug disposal cost; pharmacoeconomics.

## 1. INTRODUCTION

Cancer is a significant public health problem and the second leading cause of death worldwide [1]. It is projected that by 2050, the population of the world is expected to be 9.7 billion and the number of new cases per year is estimated to increase to 35.2 million new cancer cases annually, resulting in 18.4 million deaths from cancer. These figures indicate a rise in the number of newly diagnosed cancer cases to 75 million in the past five years [2,3].

The rapid increase in the burden of cancer poses a significant challenge to public health and healthcare systems worldwide. Expenditures on cancer drugs are escalating at a concerning rate globally becoming a major concern for consumers, healthcare professionals, insurance companies, and governments [4]. Industrialization and population aging are considered the primary factors contributing to the rise in cancer patients. Budget allocation for the treatment of cancer patients, as well as palliative-supportive care and end-of-life care, presents a significant challenge [5]. Various strategies have been developed to reduce costs in oncology treatments, such as utilizing healthcare system resources for disease prevention or early detection,

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embracing evidence-based medicine, conducting studies on the stability durations of medications, and waste reduction based on package leaflet information [6]. Treatment protocols are personalized and tailored to each patient based on the clinical efficacy, safety, toxicity, and cost of the treatment [7]. The number of selected antineoplastic drugs and the frequency of administration vary depending on the implemented protocol. Oncology patients are predominantly treated with surgery, radiation therapy, and/or chemotherapy.

The number of antineoplastic drugs used in treatment, the available dosage forms, and the frequency of administration affect both the cost of treatment drugs and the cost of waste disposal [8]. If the available dosage form contains more than what is required for a single patient and cannot be used for another patient within its stability period, there is a need to discard the remaining dose once the stability period expires. In Turkey, reimbursement for antineoplastic drugs is covered by the Social Security Institution (SGK). Due to the high cost of drugs used in cancer treatment, the financial burden on the government is also significant. In a study, the direct cost allocated to cancer drugs by the Social Security Institution in 2012 amounted to approximately 197 million euros [9]. The expenses in cancer treatment have been increasing each year due to factors such as the rise in cancer prevalence, demographic changes, and the inclusion of new and expensive drugs in treatment regimens. With scientific advancements, there has been an increase in the licensing of biologic and cytotoxic new agents with good efficacy; however, these new drugs also come with high costs [6].

By the increasing number of cancer cases in Turkey, as well as worldwide, the importance of oncology units that can control and manage the processes involving the preparation and administration of antineoplastic agents has grown due to the potential side effects, mutagenic, and carcinogenic effects resulting from the exposure of preparing and administering personnel to these drugs [10]. In recent years, there has been a rising presence of pharmacists in the treatment team [11]. A study investigating the impact of pharmacist control before dispensing of chemotherapeutic drugs showed that pharmacist checking of anticancer drug orders decreased the waste drug costs by 80.48% [12]. Previous plenty of studies stated that supervising of pharmacists during preparation of anticancer drugs reduced in unused or discarded volumes of antineoplastic drugs [13,14].

The aim of this study, by comparing the first (no pharmacist management) and the second (pharmacists management) periods, is to demonstrate the role of the pharmacists in ensuring the maximum utilization of the antineoplastic drug prepared from the current dosage form, thereby reducing waste quantity and lowering waste costs.

## 2. RESULTS

The comparison of amount (mg) and cost of disposed drugs used in all three hospitals was presented in Table 1. When the drugs used by all three hospitals were examined, chemotherapy drug disposal approximately amounted to € 87,867.42 at the end of the first period; while it approximately amounted to € 26,515.22 at the end of the second period. As it can be seen, at the end of the second period, under the supervision and control of pharmacists; the disposal cost significantly decreased by approximately € 61,352.20 ($p<0.01$).

**Table 1.** Comparison of disposed drug amounts and drug costs in terms of two periods

| Active ingredient | 1st. period Total Disposal amount (mg) | 2nd. period Total Disposal amount (mg) | 1st. period Total Disposal Cost (€) | 2nd. period Total Disposal Cost (€) |
|---|---|---|---|---|
| **Total** | 366,350.10 mg | 303,055.90 mg | € 87,867.42* | € 26,515.22* |
| | **The difference is based on the amount of disposal** | | | **€ 61,352.20*** |

*The data was taken from the thesis of the student who works at the Ministry of Health and could access the data source (Hastane Bilgi Yönetim Sistemi (HBYS)). The first and second periods' average costs for mg/euro were determined as € 4,88 and € 6,51, respectively. The total amounts were calculated based on 38 active ingredients.

In addition, the total cost of disposed drugs in the first and the second periods was evaluated and shown in Fig. 1. After the pharmacist assignment, disposal cost and ratio significantly decreased by approximately € 61,352.20 (69.83%) when compared to the first part of the study.

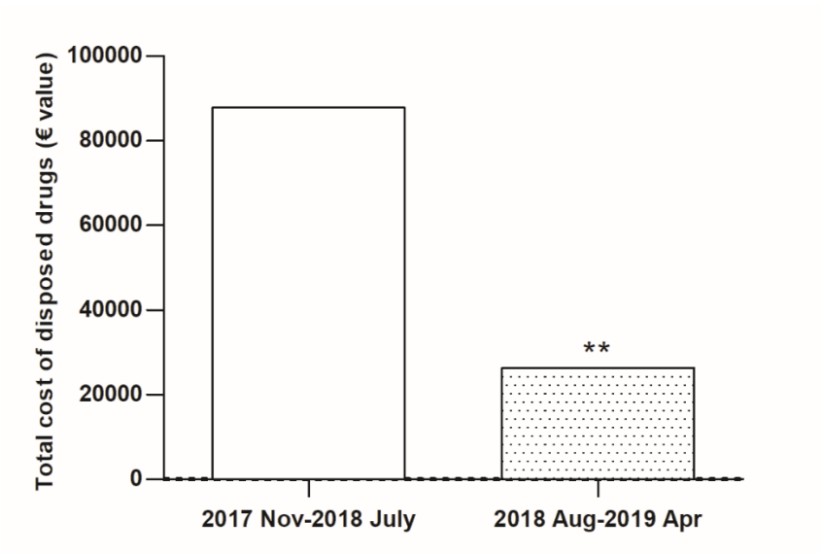


**Figure 1.** Cost of disposed drugs in the first and second periods

The ratios of the total disposal costs to the total consumption amounts were examined cumulatively in separate periods, presented in Table 2. Findings showed that while the ratio of the total disposal cost to the total consumption amount in the first period was 4.19%, this ratio decreased to 1.39% in the second period when pharmacists were assigned.

**Table 2.** The ratio of total cost of drug disposed to total cost of drug consumed

| Active ingredient | 1st. period Total Disposal Cost (€) | 2nd. period Total Disposal Cost (€) | 1st. period Total Consumption Cost (€) | 2nd. period Total Consumption Cost (€) |
|---|---|---|---|---|
| **Total** | € 87,867.42* | € 26,515.22* | € 2,092 293.65 * | € 1,906 800.94 * |
| | **Total disposal / Total consumption (%)** | | **4.19 %** | **1.39 %** |

*The data was taken the thesis of the student who works at the Ministry of Health and could access the data source (Hastane Bilgi Yönetim Sistemi (HBYS)). First and second periods average costs for mg/euro were determined as € 4,88 and € 6,51, respectively. The total amounts were calculated based on 38 active ingredients.

To exhibit the effect of pharmacist-controlled and -managed drug use, the total disposal/consumption ratio (%) was also calculated for the first and second periods as shown in Figure 2. It was observed that while the total disposal/consumption ratio was found 4.19% from November 2017 to July 2018, this ratio was calculated at 1.39% in the second period (from August 2018 to April 2019) ($p<0.01$). When the first and the second periods were compared, it was demonstrated that there was a dramatic decrement (66.83%) in the disposal/consumption ratio shown in Figure 2.

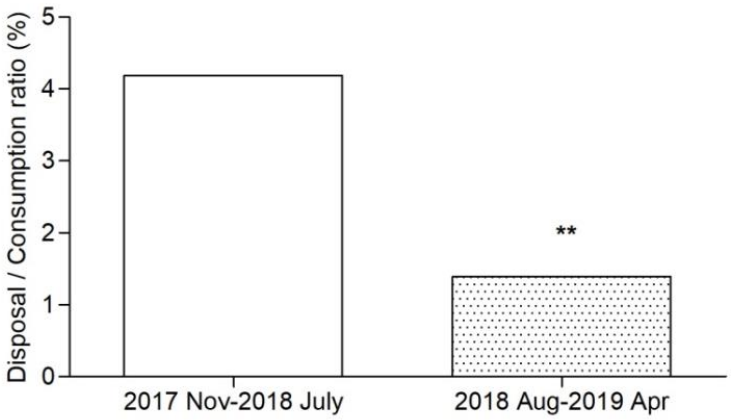


**Figure 2.** Change in the total disposal/consumption ratio between periods

In the current study, amounts and cost of drugs that were prepared but not used and destroyed due to patient-related conditions (patient did not come, patient had an allergy to a chemotherapeutic drug, and patients with influenza, gastroenteritis-like health problems) were analyzed. It is shown in Table 3. When the cost of disposed drugs was € 3,282.02 in the first period, it was calculated € 4,831.25 in the second period.

**Table 3.** Amounts and cost of drugs that were prepared but not used and destroyed

| Active ingredient | 1st. period Total Destroyed and disposed amount (mg) | 1st. period Total Disposal Cost (€) | 2nd. period Total Destroyed and disposed amount (mg) | 2nd. period Total Disposal Cost (€) |
|---|---|---|---|---|
| **Total** | 52,388.60 mg | € 3,282.02 | 154,524.00 mg | € 4,831.25 |

*The data was taken the thesis of the student who works at the Ministry of Health and could access the data source (Hastane Bilgi Yönetim Sistemi (HBYS)). First and second periods average costs for mg/euro were determined as € 4,88 and € 6,51, respectively. The total amounts were calculated based on 38 active ingredients.

In Table 4, the ratio of the total amount of disposed drugs in three hospitals to the amount of consumption was examined. Results demonstrated that pharmacist-controlled and -managed drug use reduced the total amounts of disposed drugs from 366,350.10 mg to 303,055.90 mg. At the management of pharmacists, the ratio of total disposed drugs to total consumed drugs decreased to 1.42% from 1.88%. Although the disposal/consumption rates usually decreased in the second period, this ratio increased for active ingredients like azacitidine, bleomycin, fluorouracil, gemcitabine liposomal doxorubicin, and trabectedin.

**Table 4.** The ratio of the amounts of disposed drugs to the amounts of consumption*

| Active ingredient | 1st. period Total Disposal amount (mg) | 1st. period Total Consumption amount (mg) | 1st. period Disposal / Consumption ratio | 2nd. period Total Disposal amount (mg) | 2nd. period Total Consumption amount (mg) | 2nd. period Disposal / Consumption ratio |
|---|---|---|---|---|---|---|
| **Total** | 366,350.10 | 19,465 487.1 | 1.88% | 303,055.90 | 21,307 890.40 | 1.42% |

*The data was taken the thesis of the student who works at the Ministry of Health and could access the data source (Hastane Bilgi Yönetim Sistemi (HBYS)). The total amounts were calculated based on 38 active ingredients.

## 3. DISCUSSION

Cancer is the second most common cause of death worldwide and is a major public health problem that imposes a significant economic burden on society [16]. Pharmacists' role in oncology settings has increasingly been recognized as crucial, not only for ensuring the safe administration of chemotherapy but also for achieving pharmacoeconomic benefits. The integration of pharmacists into the drug preparation process allowed for adjustments based on stability data, enabling precise drug allocations tailored to patient schedules and needs. The current study was conducted to decrease the number of disposed drugs and provide a pharmacoeconomy in antineoplastic drugs.

In this study, regarding physical and chemical stability dates were reported in RxMedia Pharma and the package inserts of drug regimen rearrangements were made for the drug administration dates, and commonly used drugs were collected on the same days for patients admitted to three hospitals. After the rearrangement of drug treatments, the drugs commonly used on the same days at three different hospitals were prepared at one center by the pharmacist control and management. By closely monitoring drug preparation, the pharmacists minimized the amount of unused drugs, reducing disposal rates from 1.88% to 1.42%, as shown in the study's findings. This cost-saving measure supports previous research indicating that pharmacist-supervised drug management can lower healthcare expenses by enhancing resource utilization and reducing waste. Supporting our findings, Yamada et al conducted a study investigating the effect of pharmacist checking of orders before dispensing of antineoplastic drugs and showed that pharmacist checking of anticancer drug orders reduced waste drug costs from $ 18,562 to $ 3,622 [12]. In another study, clinical pharmacists played an active role in the preparation of oncology medications, and the waste drug was significantly reduced. The median price value for the cost of drug wastage was detected as 237.30 INR [17].

The supervision of pharmacists in the preparation of antineoplastic drugs has exhibited essential benefits in decreasing waste drug costs associated with these high-cost medications. By optimizing drug preparation protocols and managing dosing more precisely, pharmacist involvement is shown to minimize drug disposal costs. In addition, the intervention of pharmacists in a large volume ambulatory-based chemotherapy preparation unit provided a positive economic impact on the healthcare budget. Several studies noted reductions in unused or discarded antineoplastic drug volumes when pharmacists have supervised preparation processes [13,14,18,19]. Similar to the findings of the previous studies, the current study demonstrated a marked reduction in disposal costs, by the management of pharmacists resulting in enhancing the pharmacoeconomic efficiency of chemotherapy services.

Waste of unstable drugs can be prevented by rounding the doses of chemotherapy agents to the nearest dosage form of reasonable volume. Rounding the dose of antineoplastic agents by 10% was acceptable and did not affect the safety and effectiveness of cytotoxic agents [15]. Before dose rounding, medical oncologists were consulted. Then, the procedure was carried out with the knowledge of medical oncologists and considering the patient's benefit. A study conducted to reduce chemotherapy costs showed a significant reduction of waste and healthcare costs when rounding of the dose entered the system by the medical oncologists by approximately 10% [14]. In a previous study performed to examine pharmacist effect on antineoplastic drug disposal and their pharmacoeconomic contributions, it was shown that pharmacist analysis of injectable antineoplastic prescriptions provided a crucial reduction in waste drug cost and improved patient safety with an overall benefit to the healthcare system [20].

The current study suggests that the pharmacist-controlled and –managed preparation process of antineoplastic medications has a positive economic impact from hospitals' perspective by reducing direct disposed drug costs. Disposal drug cost decreased € 61,352.20 (69.83%) when pharmacists played a role preparation of antineoplastic drugs. These results are consistent with previous studies. In a study evaluating the pharmaceutical examination of injectable chemotherapeutic medications, Nerich et al. found that 31.7% reduction in disposed drug costs [21]. In the same study, due to the pharmaceutical interventions carried out over one year, € 25,136 savings were generated.

In our study, we also found that savings significantly increased by 66.83% in a nine-month interval for three hospitals, although the investigation time was short. Therefore, it can be said that the pharmacist-managed preparation process of antineoplastic drugs causes a positive pharmacoeconomic result. Previous studies also stated similar findings that the contribution of the clinical pharmacist provided cost reduction [22,23,24].

Pharmacists also play a crucial role in implementing vial-sharing protocols, which allow the distribution of remaining drug amounts among multiple patients who need the same drug. It is a very beneficial strategy, particularly for high-cost biologics and targeted therapies. Pharmacist supervision in antineoplastic drug

preparation has been demonstrated not only to reduce waste costs but also to reduce drug disposal-to-consumption ratios significantly. In a study conducted more than one year, the authors reported that approximately € 92,907 cost avoidance was provided with the help of the pharmaceutical analysis done by pharmacists [25]. Moreover, in another study, it was exhibited that pharmacist-controlled vial sharing in oncology services leads to more efficient resource utilization, resulting in the reduction of waste and disposal drug costs [6,26]. A study highlighted pharmacists' role in reducing waste costs by 20-40% in high-volume oncology centers [8]. Aligns with the findings of previous studies, the findings of our study showed the disposal/consumption ratio was reduced from 4.19 to 1.39 at the end of the investigation. That meant both utilization and disposal of antineoplastic drug costs were significantly reduced.

Furthermore, previous study evaluating the impact of oncology and non-oncology pharmacists in the reduction in disposal of drug costs, significant results were obtained. According to the findings of the study, while oncology pharmacists provided a JY 6,355 (€ 38,69) reduction in cost, non-oncology pharmacists provided only JY 3,604 (€ 21,94) savings. However, the authors stated that both savings were essential compared to previous costs [27].

## 4. CONCLUSION

The assignment of pharmacists, especially oncology pharmacists, in the antineoplastic drug preparation process has been confirmed to be a beneficial strategy for controlling waste, reducing disposal costs, and ensuring the most effective utilization of drugs in oncology clinics in hospitals. Pharmacists' expertise benefits not only pharmacoeconomic outcomes but also enhances the sustainability of cancer treatment by minimizing the environmental impact associated with drug disposal. Pharmacists must be fully integrated into oncology teams. Their interventions provide a crucial balance between cost savings, patient safety, and environmental stewardship. Future large-scale and comprehensive studies should be planned and conducted to increase effective antineoplastic drug utilization and reduce waste drug costs not only in İstanbul but also in Turkey.

## 5. MATERIALS AND METHODS

### 5.1. Design and settings

The current study was conducted between November 2017 and April 2019. The study was separated into two periods. The first period continued from November 2017 to July 2018 (nine months), and the second period continued from August 2018 to April 2019 (nine months). While there was no pharmacist management in the preparation process of the antineoplastic drugs in the first semester, in the second semester of the study, three specialist pharmacists (one from each hospital) from three different Training and Research hospitals were assigned to plan rational drug use in the unit where drugs are prepared.

Pharmacists, in collaboration with the attending physicians, played a role in the coordination of the treatment planning process to align the administration of antineoplastic medications on the same days. This strategy was implemented to minimize drug wastage and prevent any potential delays or disruptions in patient care. Furthermore, physicians and pharmacists performed dose rounding within an accepted range of approximately 5–10% [15], adjusting doses to the nearest available vial size. This practice aimed to optimize drug utilization while maintaining therapeutic efficacy and ensuring patient safety.

Chemotherapeutic drugs used in the three different Training and Research Hospitals were prepared in the same robotic drug preparation unit. Amounts of disposed drug doses, amounts of drugs used in the treatment of patients, and amounts of prepared drugs but not used, thus had to be disposed of due to a variety of reasons (patient did not come and cannot be administered) were obtained from Hospital Automation Program named Hastane Bilgi Yönetim Sistemi (HBYS). These amounts were reported separately for each hospital and analyzed through a pivot table.

The unit price of the drugs was obtained from the business intelligence package program used in the hospitals. In addition, hospital cost price was used in the study. Then, this data was reported and analyzed in the Microsoft Excel program. The first and second periods' average euro (€) costs were calculated for mg/euro and found € 4,88 and € 6,51, respectively.

In this study, drugs were evaluated based on active ingredients. There were different commercial preparations of the same active ingredient. Additionally, unit prices of different dosage forms varied. To examine the data more accurately, an average value was taken for the drugs that were entered and issued in stock for each period. The study did not include drugs that were used in complete doses in hospitals and did not need to be destroyed. In all three hospitals, the treatment planning of the patients was carried out on the

same days in a way that would not cause any patient victimization for drugs with a short stability period and high costs. In addition, taking into account the patient benefit, the appropriate dose rounding about 5-10% [15] was made to the bottle in the nearest dosage form by consultation with the physicians who follow up with the patients. Ethical approval was obtained from the Local Ethics Committee of Sağlık Bilimleri Üniversitesi (S.B.Ü.) İstanbul Training and Research Hospital (27 June 2019 / E.1974).

### 5.2. Active ingredients examined

This study included a comprehensive analysis of 38 active pharmaceutical ingredients commonly used in chemotherapy and supportive cancer treatments. The selected drugs encompassed a broad range of antineoplastic agents including alkylating agents, antimetabolites, anthracyclines, monoclonal antibodies, and targeted therapies. These agents were azacitidine, bendamustine, bevacizumab, bleomycin, bortezomib, cabazitaxel, carboplatin, cetuximab, cisplatin, cyclophosphamide, cytarabine, dacarbazine, decitabine, doxorubicin, docetaxel, epirubicin, etoposide, fludarabine, fluorouracil, gemcitabine, idarubicin, ifosfamide, irinotecan, liposomal doxorubicin, mesna, methotrexate, mitoxantrone, oxaliplatin, pamidronate, panitumumab, rituximab, topotecan, trastuzumab, trastuzumab + emtansine, vinblastine, vincristine, vinorelbine and trabectedin. The agents were included based on their usage in clinical oncology and their disposal rates observed in hospital settings. The selection criteria focused on drugs with high procurement and wastage rates, providing insight into cost efficiency and resource utilization during the study period.

### 5.3. Statistical analysis

Statistical analysis was carried out using GraphPad Prism statistical program version 5.04 (GraphPad Software, San Diego, CA, USA). Obtained data was analyzed using one-way analysis of variance (ANOVA) followed by post hoc Tukey's multiple comparisons tests. Student-t test was performed to compare two groups. The results were expressed as mean euro value (€) ± standard error of the mean (SEM). Values of $p < 0.05$ were regarded as significant.

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