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Analysis of the return profile of intravenous chemotherapy protocols at a philanthropic hospital in Salvador-BA

Análise do perfil de devoluções de quimioterapias endovenosas em um hospital filantrópico de Salvador-BA

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ABSTRACT

Introduction: The increase in the costs of cancer treatments is configured as a relevant problem for health services linked to the constant incorporation of new drugs for cancer treatment. This growth in expenses reflects the challenge of managing resources to meet the needs of the oncologic area. It is necessary to optimize resources in view of the growing demand and associated costs. In the scenario where patients receive personalized treatments, changes in therapy are possible, causing some returns of antineoplastic drugs and increasing costs in health services. **Objective:** To analyze the profile of returns of chemotherapy drugs handled by the Pharmacy sector and the relationship with costs in a philanthropic hospital in Salvador. **Method:** This was a cross-sectional, retrospective, and analytical study conducted between August 2019 and August 2020. Data were collected through forms obtained after the return of chemotherapy. Information such as the drug name, dose, reuse status, and reason for return were evaluated. Data were tabulated using SPSS software. **Results:** 171 chemotherapy bags were returned involving 19 active ingredients. The clinical factor accounted for 59.1% of the returns. Cisplatin accounted for 14.6% of the returns. Carboplatin was the most discarded drug, representing 16.9% of the lost bags, whereas Cisplatin had the highest rate of reuse. In pharmacoeconomics, the returns represented the value of R$ 13,887.87. The hospital lost R$ 7,475.61 with the discarded products but saved R$ 6,412.21 through reuse. **Conclusions:** Oncology needs to be linked to pharmacoeconomics and to minimize discards, strategies should be adopted.

KEYWORDS: Pharmacoeconomics; Aantineoplastics; Chemotherapy

RESUMO

Introdução: O aumento dos custos dos tratamentos oncológicos se configura como uma problemática relevante para os serviços de saúde atrelada à incorporação constante de novos medicamentos para o tratamento do câncer. Esse crescimento de gastos reflete no desafio de gerir recursos para atender as necessidades na área oncológica. É preciso otimizar os recursos, visando a crescente demanda e os custos associados. No cenário em que pacientes recebem tratamentos personalizados, são possíveis alterações na terapia ocasionando algumas devoluções de antineoplásicos, elevando custos nos serviços de saúde. **Objetivo:** Analisar o perfil de devoluções de quimioterápicos manipulados ao setor de Farmácia e a relação com os custos em um hospital filantrópico de Salvador. **Método:** Estudo de corte transversal, retrospectivo e analítico realizado entre agosto de 2019 e agosto de 2020, cuja coleta foi realizada por meio de formulários obtidos após a devolução da quimioterapia. Foram avaliadas informações como nome do medicamento, dose, *status* do reaproveitamento, motivo de devolução. Os dados foram tabulados no programa SPSS. **Resultados:** Foram devolvidas 171 bolsas de quimioterapias, envolvendo 19 princípios ativos. O fator clínico justificou 59,1% dos retornos.

A cisplatina foi responsável por 14,6% das devoluções. A carboplatina foi o medicamento mais descartado, representando 16,9% das bolsas perdidas, enquanto a cisplatina teve o maior índice de reaproveitamento. Na farmacoeconomia, as devoluções representaram o valor de R$ 13.887,87. O hospital perdeu R$ 7.475,61 com os descartes efetuados, porém economizou R$ 6.412,21 por meio do reaproveitamento. **Conclusões:** A oncologia precisa estar atrelada à farmacoeconomia e, para minimizar as devoluções, estratégias devem ser adotadas.

PALAVRAS-CHAVE: Farmacoeconomia; Quimioterapia; Antineoplásicos

INTRODUCTION

Cancer is a group of diseases characterized by the disordered growth of cells, which can invade various tissues and organs, even at a distance, compromising their functions. According to estimates, in 2020, the various existing neoplasms were responsible for the emergence of 626,030 new cases in the Brazilian population, while in 2018 they caused 224,712 deaths in the country, revealing the high incidence and mortality from cancer in Brazil[1].

At the same time as the high incidence of cancer, treatment costs are also high, because they are personalized, since a single patient may use a combination of antineoplastics for several cycles, or even need to change chemotherapy protocols in order to contain the progression of the pathology[2]. Added to this is the constant incorporation of new drugs for the treatment of cancer, which also have high costs. This implies both increased spending for the health system and the challenge of managing limited resources for the vast demand present in oncology[3].

On the other hand, it is also common for cancer patients not to comply with the treatment as previously established, which can be caused by the occurrence of adverse reactions, changes in tests or lack of response to treatment, for example. These variables can lead to changes in doses, protocols, or cycles which, ultimately, result in the possibility of chemotherapies that have already been manipulated being returned to the Pharmacy department[4].

The role of the professional pharmacist is essential in oncology, as it guarantees the patient a safe and effective treatment, with the aim of ensuring quality of life in line with the care provided. It is their role to advise patients on treatment, possible reactions, management, the use of supportive medication, and the search for drug interactions. The pharmacist is also responsible for properly storing medicines, validating prescriptions, checking the dose, diluent, route, concentration, preparation method, and using the appropriate techniques for handling. The pharmacist is also responsible for managing the stock of medicines, reporting adverse reactions or technical complaints and carrying out pharmacotherapeutic monitoring. In the case of chemotherapy returns, it is the pharmacist's job to check that the bags can be reused, in order to guarantee effective and safe treatment, as well as saving money[5].

When treatment with a chemotherapy drug is prescribed, the patient must periodically undergo laboratory tests in order to assess cell recovery, as chemotherapy tends to affect cells that are constantly dividing (red blood cells, leukocytes, platelets). The nurse checks these results and if they are within the expected values, the patient continues with the treatment. But this check doesn't always take place before the chemotherapy is ordered from the pharmacy, a process that sometimes leads to improper manipulations.

In this sense, this study aimed to analyze the profile of returns of manipulated chemotherapy drugs to the Pharmacy sector, the causes pointed out, whether the manipulated bag was reused, and finally to evaluate the costs involved in this process at a Philanthropic Hospital in Salvador, Bahia.

METHOD

This is a descriptive, observational, and retrospective study, a method that has already been described[6]. It was carried out in the oncology pharmacy sector of a philanthropic hospital located in the city of Salvador, between August 2019 and August 2020. The study was approved by the Ethics and Research Committee of the State University of Bahia, under opinion number 4.888.973/2021.

To collect the data, we used forms from the hospital service with information on the return of the chemotherapy products handled. The variables analyzed were: name of the chemotherapy, dose, reason for return, reuse status, and average cost of the bag handled.

Chemotherapies handled and returned between August 2019 and August 2020 were included, considering those handled for patients over the age of 18. Forms that indicated the start of administration of the chemotherapy bag to the patient were excluded, as there was no possibility of reuse. Forms without information on the reuse status or cause of return and returned oral therapy drugs were also excluded.

The data obtained was tabulated in the Statistical Package for the Social Science (SPSS) Statistics 23 and, in order to analyze it, it was necessary to systematize it in a table: the name of each chemotherapy drug used in the hospital, the dose of the vial, the average purchase price of this vial, and the average price per milligram. The bags returned, discarded, and reused were separated. In this way, it was possible to calculate the total amount of milligrams involved in disposal

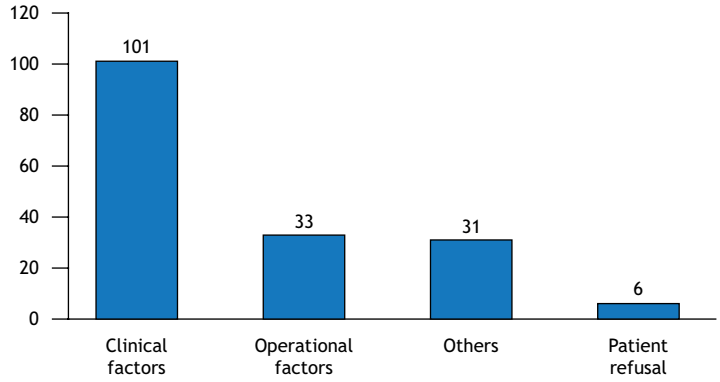
or reuse and, finally, through the average value per milligram, to estimate the average value present in the return, disposal, and reuse of each chemotherapy drug computed in the research.

RESULTS

Between August 2019 and August 2020, 171 chemotherapy bags were returned to the handling center with 19 drugs involved. Among the reasons given on the forms, the majority were related to the clinical factor, as shown in the Figure.

Clinical factors accounted for 101 (59.1%) of the returns, justified by lack of venous access, altered clinical condition, adverse reaction to the drug, and altered tests. On the other hand, operational factors, i.e. service-related errors, accounted for 33 (19.3%) chemotherapy returns. Incorrect request, change in prescription, suspension of treatment, and hospital discharge were the reasons given.

The "other" option, present in 31 (18.0%) of the forms, involved variables such as: failure to administer pre-chemotherapy drugs, inadequate time to start chemotherapy, and patients taking



Source: Prepared by the authors, 2023.

Figure. Factors associated with the returns of chemotherapy manipulated in a philanthropic hospital in Salvador-BA.

Table 1. Chemotherapies returned, discarded and reused in the handling center at a philanthropic hospital in Salvador-BA.

Medicines	Bags returned		Discarded bags		Reused bags	
	N	%	N	%	N	%
Cisplatin	25	14.6	7	9.1	18	19.1
Paclitaxel	21	12.3	11	14.3	10	10.6
Gencitabine	20	11.7	5	6.5	15	16.0
Carboplatin	14	8.2	13	16.9	1	1.1
Doxorubicin	13	7.6	3	3.9	10	10.6
Cyclophosphamide	12	7.0	4	5.2	8	8.5
Oxaliplatin	12	7.0	3	3.9	9	9.6
Fluorouracil	9	5.3	4	5.2	5	5.3
Cytarabine	7	4.1	6	7.8	1	1.1
Etoposide	6	3.5	5	6.5	1	1.1
Vimblastine	6	3.5	3	3.9	3	3.2
Dacarbazine	5	2.9	3	3.9	2	2.1
Docetaxel	5	2.9	1	1.3	4	4.3
Vincristine	4	2.3	2	2.6	2	2.1
Bleomycin	3	1.8	1	1.3	2	2.1
Ifosfamide	3	1.8	2	2.6	1	1.1
Methotrexate	3	1.8	3	3.9	-	-
Irinotecan	2	1.2	-	-	2	2.1
Pemetrexed	1	0.6	1	1.3	-	-
TOTAL	**171**	**100.0**	**77**	**100.0**	**94**	**100.0**

Source: Prepared by the authors, 2023.

antibiotics. Among the 171 bags returned to the handling center, cisplatin was responsible for 14.6% of the returns, while paclitaxel and gemcitabine were reported in 11.7% of the returns each, as shown in Table 1. On the other hand, irinotecan and Pemetrexed were the bags with the lowest rates of return to the handling center during the study period.

When the manipulated bags were returned to the pharmacy, some went on to be reused, while others had to be discarded. In the period studied, 77 bags were discarded, which represented a loss of 45.0% of all returns. Carboplatin was the most discarded chemotherapy drug, with 16.9% of bags lost, followed by paclitaxel, responsible for 14.3% of discards. Cisplatin (9.1%) and cytarabine (7.8%) also had high discard rates, as described in Table 1.

Of the total returned, 94 (55.0%) chemotherapy bags were reused, covering 16 different active ingredients. The reuse of cisplatin accounted for 19.1% of the total, followed by gemcitabine, responsible for 16.0% of the reuses and lastly doxorubicin with 8.5%. Carboplatin, cytarabine, ifosfamide, and etoposide had the lowest reuse rates, around 1.1% each.

In the context of pharmacoeconomics, returns amounted to R$ 13,887.87, with gemcitabine being the drug that contributed most to this amount, accounting for R$ 2,037.03. The hospital incurred a loss of R$ 7,475.61 from discards during the period. However, it saved R$ 6,412.21 with bags that were reused, as shown in Table 3.

Table 2. Average price per milligram of medicines used in a handling center of a philanthropic hospital in Salvador-BA.

Medicines	Average price per milligram (R$)
Cyclophosphamide	0.04
Bleomycin	17.29
Carboplatin	0.23
Cisplatin	0.50
Cytarabine	0.04
Dacarbazine	0.14
Docetaxel	1.00
Doxorubicin	0.76
Etoposide	0.17
Fluoruoracil	0.03
Gencitabine	0.07
Ifosfamide	0.04
Irinotecan	0.35
Methotrexate	0.16
Oxaliplatin	0.72
Pemetrexed	0.48
Paclitaxel	0.31

Source: Prepared by the authors, 2023.

Table 3. Amounts in Brazilian Reais referring to the return, reuse, and disposal of chemotherapy bags at a philanthropic hospital located in Salvador-BA.

Medicines	Return (R$)	Reused (R$)	Disposal (R$)
Cyclophosphamide	434.83	339.88	94.95
Bleomycin	1,011.50	778.08	233.42
Carboplatin	1,485.75	146.06	1,339.69
Cisplatin	784.30	455.31	328.99
Cytarabine	158.64	6.41	152.23
Dacarbazine	334.76	86.49	248.27
Docetaxel	380.49	280.15	100.34
Doxorubicin	652.21	556.47	95.73
Etoposide	155.30	26.96	128.34
Fluorouracil	348.07	90.13	257.93
Gencitabine	2,037.03	1,660.11	376.92
Ifosfamide	518.27	201.77	316.50
Irinotecan	138.57	138.57	-
Methotrexate	1,959.93	-	1,959.93
Oxaliplatin	1,498.13	1,047.61	450.51
Pemetrexed	433.21	-	433.21
Paclitaxel	1,201.73	465.73	736.00
Vimblastine	251.65	80.71	170.94
Vincristine	103.52	51.76	51.76
Total	**13,887.87**	**6,412.21**	**7,475.61**

Source: Prepared by the authors, 2022.

Gemcitabine was the second most reused chemotherapy drug, saving the institution R$ 1,660.11, or around 25.0% of the total reused. On the other hand, methotrexate, an antineoplastic antimetabolite, had only three bags returned, but all were discarded, representing a loss of almost R$ 2,000.00 for the institution, i.e. it was characterized as the drug whose disposal generated the most costs. Despite the low cost per milligram, as shown in Table 2, protocols with methotrexate usually have a high dose, which led to the high amount lost.

DISCUSSION

Oncology is a sector marked by a high demand for drugs, most of which are expensive, with various therapeutic proposals and limited resources. Therefore, pharmacoeconomics is necessary for choosing the most appropriate technology to reduce costs. The tools of pharmacoeconomics make it possible to obtain the technical-scientific data used in evidence-based decision-making, bringing the best results[7].

In this study, the predominant factor for chemotherapy returns was the clinical factor and involved everything from adverse reactions to the drug to altered vital signs. In a study carried out in a hospital in Spain with the aim of quantifying and economically evaluating the return of manipulated

chemotherapy[8], the clinical factor was responsible for 54.4% of the returns, characterized by both adverse reactions to the treatment and changes in the patient's clinical condition. Another study[9] found that, of the 130 chemotherapies that were returned, 89 were for reasons more related to deterioration in clinical condition, corroborating the data obtained in this study.

In addition to the reasons for the returns, it is necessary to know the epidemiology of neoplasms in the institution, as this makes it possible to characterize and understand the profile of the returned manipulated bags. In 2020, the most common types of cancer in the institution were prostate cancer, breast cancer, cervical cancer, and cancer of the trachea, bronchus, and lung. For these neoplasms, both surgical and chemotherapy treatment are recommended, and the modality to be used takes into account the tumor's stage, the patient's clinical condition, the aim of the treatment, and the therapeutic options available at the Hospital[10].

Among the various regimens used, the combined use of carboplatin and paclitaxel is one of the main alternatives for the treatment of metastatic or recurrent cervical cancer[11]. Concomitant cyclophosphamide and doxorubicin, followed by paclitaxel, are the most widely used regimen for breast cancer[12], while the combination of gemcitabine and cisplatin is widely used in tumors affecting the nasopharynx[13]. Carboplatin and cisplatin are also widely used in the treatment of non-small cell lung cancer[14].

It is important to note that the drugs used to treat the most frequent tumors are precisely those with the highest rates of return to the pharmacy. Carboplatin and gemcitabine, which are among the five most returned drugs to the center, also featured in a study[8], in which many returns were counted, occupying first and third place in that study, respectively.

Of all the manipulated bags discarded, carboplatin was the drug with the highest discard rate. The dose calculation for this drug uses the area under the curve (AUC) measure, which can vary from 2 to 6, which results in doses with high variability, making it difficult to reuse the manipulated chemotherapies[15]. This difficulty has also been identified in the use of methotrexate, which is widely used in hematological neoplasms and whose dose ranges from 40 mg/m^2 to 8 g/m^2 in some regimens[16,17].

In addition to the variability of doses, other variables can prevent the reuse of chemotherapy, such as the possibility of inadequate storage on the wards, return to the pharmacy outside the stability period, and finally the expiry of the bag at the handling center itself[8].

When analyzing the reuse made on returns, this reached a rate of 55.0%. Cisplatin, the most reused antineoplastic, represented a saving of R$ 455.31, a lower figure when compared to gemcitabine, due to the lower number of milligrams used. On the other hand, if we look at methotrexate, whose 5g vial has an average cost of R$ 815.00, although only three bags were discarded, they all had high doses, which increased the cost of losses.

Some high-cost drugs, such as pemetrexed, rituximab, and trastuzumab, which could be responsible for driving up waste in oncology, were not included in this study. When patients undergo treatment with these antineoplastics at the institution, the flow is altered. There is a prior assessment by the nursing staff and then the request for chemotherapy is sent to the pharmacy, a practice that helps to optimize resources.

CONCLUSIONS

In view of the above, it is notable that oncology needs to be linked to pharmacoeconomics, considering the dynamics of the area and the need to establish the best treatment on a limited budget, whether in the public or private sector.

Due to the large number of patients treated at the institution, many bags that have already been handled are reused, reducing the waste rate. However, the ideal would be to create mechanisms to avoid undue requests. This would not only reduce the burden on the service but also save money for the institution and ensure patient safety.

In order to minimize this problem, it would be interesting to adopt a prior assessment of the patient by the nursing staff before ordering chemotherapy, especially when handling methotrexate and carboplatin, the return of which represented a high cost and a low rate of reuse.

It is also important to promote educational activities that warn both about the costs present in the oncology sector and the attention that should be paid to bags with reduced stability, which would help to reduce returns. Lastly, promoting greater integration of the multi-professional team should also be encouraged to improve healthcare.

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Authors' Contribution

Santos MS, Bacelar LS, Félix SS - Conception, planning (study design), acquisition, analysis, data interpretation, and writing of the paper. Araújo PL, Azevedo RMHS - Conception, planning (study design), writing of the paper. Bendicho MT, Xavier RMF - Writing of the paper. All the authors approved the final version of the paper.

Conflict of Interest

The authors declare that there is no potential conflict of interest with peers and institutions, political or financial, in this study.