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BRIEF REPORT

Reusing cytostatics in a centralised pharmacy preparation unit

S. Ramos Linares,* J. Merino Alonso, N. Román González, E. Tévar Alfonso, P. Díaz Ruíz, M. Gorchs Molist

Servicio de Farmacia, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain

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KEYWORDS
Intravenous preparations;
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Waste disposal

Abstract
Objective: To measure and provide an economic assessment of the preparations returned to a centralised cytostatic drug preparation unit, analyse reasons for their return, propose measures for minimising returns and assess their impact on the Medical Oncology division's outpatient services.
Methods: This prospective study contained two phases. During the first, we registered all returns, motives, cases of reuse and costs. In the second phase, we analysed returns at the Oncology outpatient division after having adopted measures to minimise the returns.
Results: During the first phase, 218 preparations (worth € 51,131) were returned. The Oncology Day Hospital returned 1%of the preparations worth 1%of the total value; during the second phase, these figures were 0.56% of the preparations and 0.14% of the total value.
Conclusions: Favouring reporting on and identifying expensive treatments with little stability and using returned preparations as a quality indicator for Oncology has improved management of the central cystostatic preparation unit

PALABRAS CLAVE
Mezclas intravenosas;
Citostáticos;
Evaluación económica;
Optimización recursos;
Eliminación residuos

Reutilización de citostáticos en una unidad centralizada de mezclas

Resumen
Objetivo: Cuantificar y evaluar económicamente las mezclas devueltas a una unidad centralizada de preparación de citostáticos, analizar causas de devolución, proponer medidas para minimizarlas y valorar su impacto en el hospital de día de oncología médica.
Métodos: Estudio prospectivo en 2 periodos. En el primero se registraron todas las devoluciones, motivos, reutilizaciones y costes. En el segundo periodo se analizaron las devoluciones del hospital de día de oncología tras adoptar medidas para minimizarlas.
Resultados: 218 mezclas (51.131 €) fueron retornadas en el primer periodo. El hospital de día de oncología devolvió el 1% de mezclas e importe solicitado, y en el segundo este valor fue del 0,56% de mezclas y del 0,14% del importe total.

*Corresponding author.
E-mail address: sramlin@gobiernodecanarias.org (S. Ramos Linares).

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Conclusiones: Favorecer la información e identificación de tratamientos de elevado coste y escasa estabilidad, e introducir las preparaciones devueltas como indicador de calidad de oncología han mejorado la gestión de la unidad centralizada de cistostáticos.

Introduction

In Spain, the preparation of cytostatics is centralised in most hospital pharmacy (HP) units, exceeding the European average.[1] The preparation of these compounds under the supervision of a pharmacist ensures that the expiration period and stability, storage and administration conditions are met as well as appropriate handling, thus reducing the risk of exposure of handlers and environmental contamination. Pharmaceutical intervention reduces the occurrence of negative outcomes associated with these drugs, improving the quality of care for cancer patients.[2,3] Additionally, centralisation of the preparation of intravenous compounds reduces costs by optimising human and material resources, making full use of the vials and re-allocating unused compounds,[4-11] which in other studies is around 1.3%[12,13] On the other hand, a study is needed on whether the centralisation of these compounds leads to efficient compound preparation and avoids mismanagement of prepared and unused compounds. In addition, the computerisation of the unit allows for the integration of data on the hospital's chemotherapy treatments, facilitating studies on their use.[14]

The aim of this study is to quantify and assess the economics of returned compounds to a centralised cytostatic preparation unit (CCPU), analyse the reasons for returns, the reasons that preclude reuse, and propose measures for minimising them, assessing the impact of measures adopted in an oncology outpatient centre (OOC).

Method

Prospective study performed in two periods. The first study period was conducted for one year in a tertiary hospital with an HP that prepares all compounds required by the different units in the CCPU. The preparation of treatments takes place after telephone confirmation with the unit nurses. Prior to this, the doctor assesses the analytical data and the patient's condition, except in the OOC where the nurses inform the doctor about any abnormal parameter detected. The unused preparations are collected, discarding those that were improperly stored in the medical units. Optimal preparations are stored pending use, in part or in whole, by another patient.

In March 2008, a database was developed for registering this activity. The date, unit, active ingredient, dose and reason for not administering the preparation were recorded (Table 1). For those cases where the drug was used for another patient, the destination unit and the dose requested were included. The amount recovered was subsequently calculated. When the drug could not be reused, the reason was recorded.

The first study period analysed preparations returned between March 2008 and March 2009. The cost calculation (€) for these compounds was performed using the cost per dose, given that the use of commercial vials is optimised in the unit by reusing whole vials.

In August 2009, after analysing the results, the preparations returned to the CCPU were introduced as an indicator of the quality of the OOC. Moreover, the HP reported on high-cost treatments with reduced stability (<3 days), informing of the economic impact of inappropriate conservation. The second study period analysed returns to the OOC during August and September 2009.

Results

During the first study period, 18 005 cytostatic preparations were made (€4 909 863). The most demanding units were the oncology unit, with 11 889 preparations (10 570 in the outpatient centre) and haematology unit, with 3206. The outpatient centres requested 89%of oncology preparations

Table 1 Possible causes for returns

Patient complications	Patient medical problems after treatment confirmation
Confirmation error	Confirmation of treatments that should not be administered or that cannot be administered due to patient medical problems that were present before going to the hospital
Treatment modification that was not reported to the pharmacy unit	Changes in treatment or dosage schedules that are not reported to the pharmacy
Technical complications	Technical problems with radiation therapy equipment
Not specified	Return was made without providing a reason

and 48% of haematology preparations, the other treatments being prepared for hospitalised patients.

During the year under study, 218 preparations with 35 active ingredients were returned (€51 131). The OOC returned 114 compounds, a figure that exceeds 1% of those requested. A similar percentage was observed in the haematology outpatient centre, while hospital units from both specialities returned over 0.74% of the required compounds. However, in terms of economic value, the compounds returned by the haematology outpatient centre corresponded to 1.31% of the total value requested, 1.08% for the OOC and around 0.3% for both hospital units.

The main reasons for returns were patient complications (41.3%), errors in treatment confirmation (29.8%) and changes in treatment that were not reported to the HP (14.7%). The first two reasons accounted for approximately 90% of the value returned. The preparation of compounds returned due to confirmation errors and changes in treatment that were not reported to the HP could have been avoided.

Table 2 shows the compounds returned and re-allocated by active ingredient and cost. The centralisation of returns of compounds made it possible to reuse around 40% of their value (€19 187).

Four active ingredients (bevacizumab, rituximab, trastuzumab and pemetrexed) constituted 69% of returns in terms of value but only 8% of the total compounds returned.

There were three causes that prevented reusing the returned preparations: conservation under improper conditions in the medical units (28.1%), return of compounds beyond the expiry period (7.5%) and expiration of these drugs in the CCPU (64.4%). The first two were considered avoidable. Some 11.93% of returned preparations could not be reused partially or wholly in other patients. This fact

Table 2 Active ingredients returned and reused

Drug	Return		Reuse	
	€	No. compounds	€	No. compounds
Bevacizumab	11 364	5	3.98	1
Bleomycin	54.64	3	18.21	1
Bortezomib	2528	4	2464	4
Carboplatin	363.81	53	168.84	48
Carmustine	388.77	1	388.77	1
Cyclophosphamide	29.67	9	15.57	5
Cisplatin	18.02	3	6.61	1
Cytarabine	10.38	3	–	–
Dacarbazine	41.66	2	15.66	1
Docetaxel	910	1	–	–
Doxorubicin	115.71	8	62.37	5
Pegylated liposomal doxorubicin	2773	2	–	–
Non-pegylated liposomal doxorubicin	814	1	–	–
Epirubicin	410	3	223	2
Etoposide	14.08	3	–	–
Fluorouracil	128.2	28	102	24
Ganciclovir	92.9	10	28.99	3
Gemcitabine	3914	21	2332	14
Idarubicin	87.25	1	87.25	1
Ifosfamide	49.96	3	-	–
Irinotecan	173.85	1	-	–
L-asparaginase	317.29	3	79.33	2
Dactinomycin	39.78	1	–	–
Methotrexate	139.89	1	–	–
Mitomycin	2.55	1	–	–
Mitoxantrone	178.3	4	–	–
Oxaliplatin	769.17	9	542.54	7
Paclitaxel	1006	9	855.5	8
Pemetrexed	6192	3	2028	1
Rituximab	10 973	6	6534	4
Topotecan	329.98	3	60	1
Trastuzumab	6729	4	3006	2
Vinblastine	7.39	1	7.39	1
Vincristine	21.41	5	21.41	5
Vinorelbine	141.92	3	134.82	3

– indicates compounds not reused.

Table 3 Compounds returned by the oncology outpatient centre during the two study periods and their reuse

Drug	Return € (no. compounds)		Reuse € (no. compounds)	
	First period	Second period	First period	Second period
Bevacizumab	11.361 (4)	–	–	–
Bleomycin	19.12 (1)	–	18.21 (1)	–
Carboplatin	241.20 (6)	125.63 (2)	98.49 (3)	129.31 (2)
Cyclophosphamide	21.93 (6)	–	7.83 (2)	–
Cisplatin	15.62 (2)	–	6.61 (1)	–
Dacarbazine	41.66 (2)	–	15.66 (1)	–
Docetaxel	909.96 (1)	–	–	–
Doxorubicin	73.50 (4)	–	51.66 (3)	–
Pegylated liposomal doxorubicin	2.774 (2)	–	–	–
Non-pegylated liposomal doxorubicin	813.60 (1)	–	–	–
Epirubicin	295.60 (2)	–	108.91(1)	–
Etoposide	−8.23 (1)	–	10.29 (1)	
Fluorouracil	128.20 (28)	9.40 (1)	102.06 (24)	9.40 (1)
Gemcitabine	3781 (20)	674.06 (4)	2332 (14)	547.48 (3)
Irinotecan	173.85 (1)	–	–	–
Oxaliplatin	769.17 (9)	–	542.54 (7)	–
Paclitaxel	871.06 (8)	294.42 (2)	720.91 (7)	292.32 (2)
Pemetrexed	6192 (3)	–	2028 (1)	–
Rituximab	3866 (2)	–	1422 (1)	–
Topotecan	329.98 (3)	–	60 (1)	–
Trastuzumab	6729 (4)	–	3006 (2)	–
Vinblastine	7.39 (1)	–	7.39 (1)	–
Vincristine	6.69 (1)	–	6.69 (1)	–
Vinorelbine	141.92 (3)	46.63 (1)	134.82 (3)	60.82 (1)
Total	39 562 (114)	1158 (11)	10 670 (74)	1049 (10)

– indicates compounds not reused.

meant that more than 60% of the value returned was discarded, which mainly consisted of bevacizumab preparations due to their short shelf life and conservation in suboptimal conditions in the medical units.

More than half of the value discarded due to expiration was monoclonal antibody preparations, which have a shelf life of less than two days.

Bevacizumab, pemetrexed and gemcitabine preparations constituted the majority of improperly conserved compounds.

In the first study period, the OOC returned 114 compounds with 23 active ingredients, including high-cost drugs. The main reasons were patient complications (54.4%) and confirmation errors (28.9%). Some 64.9% of preparations could be re-allocated while the others were discarded due to improper conservation by the unit that requested them (17.54%) or because of drug expiration.

During the second study period, the OOC requested 1980 compounds (€808 696) and 0.56% were returned (0.14% of the total value). The main reasons were confirmation errors (54.5%) and patient complications (27.2%). Some 90% of the compounds could be reused, discarding one preparation due to improper conservation.

Table 3 shows the compounds returned by the OOC during the two periods and their reuse.

Discussion

The collection of unused compounds is an indicator of quality in the CCPU, allowing for their reuse in other patients and, when not possible, assuring proper disposal. In this study, the collection of unused preparations in the CCPU allowed for the reuse of almost 40% of the value of returned compounds.

Although the percentage of returned preparations is lower than in other studies,[13] these drugs have a high economic impact and therefore higher costs. This makes it imperative to assess the causes and adopt measures to minimise returns.

The OOC was the unit that requested more than half of the prepared compounds and was responsible for the majority of returns, due mainly to clinical reasons similar to those described in other studies.[13]

However, unlike other studies,[12,13] in the initial study only 0.8% of cytostatics preparations were reused since most expired in the HP.

After analysing the results in the first period, certain measures were adopted to minimise returned compounds, achieving a significant reduction in both their quantity and economic impact.

In this period, the OOC did not return a single high-cost, short shelf life preparation. The number of compounds

discarded due to improper conservation was also reduced, although there is still room for improvement since the necessary information was already printed on the label of each preparation.

In the second period, the re-allocation of returned compounds was similar to the Yuste study,[13] maintaining a lower percentage of returns over the total.

In the second study period, the main reason for returns was confirmation error in the treatment. The OOC, which is characterised by dealing with a high workload that hinders medical evaluation prior to the confirmation of chemotherapy, is developing a health status questionnaire that the patient must fill out. This questionnaire will help detect situations that may preclude treatment administration.

Lastly, the implementation of electronic prescriptions in the oncohaematology area may minimise returns due to treatment changes thanks to updated drug therapy profiles.

This study did not assess the impact of these measures on the CCPU's workload.

In conclusion, the information and identification of high-cost, low stability treatments and the introduction of returned preparations as an indicator of quality in oncology has improved CCPU management.

Conflict of interest

The authors declare that they have no conflict of interest.

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