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Original Research

Study of the Excess Cost Associated with Drug Wastage Due to Limited Vial Size Options of the Intravenous Drugs for Anti-cancer Treatment, Among Patients Receiving Such Treatment at Tata Memorial Hospital

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Aims and Objectives: To evaluate the drug wastage and additional costs (in INR) resulting from leftover or unused drugs due to limited vial strength options, and to propose vial size recommendations to pharmaceutical companies tailored to Indian requirements.

Material and Methods: A total of 500 adult patients attending daycare oncology were prospectively evaluated. Mean, median, mode and left over or unused drug dose for each

chemotherapy drugs were calculated. The economic loss estimation was done considering the unit cost for the drug.

Result: The overall drug wastage for 500 prescriptions was 57,836 mg, accounting for 8.67% of the total prescribed dose. This resulted in an economic loss of 1,02,562 INR, which is 6.26% of the total cost. The highest proportions of drug wastage were observed for vincristine (28.72%), etoposide (23.20%), bleomycin (18.5%), pemetrexed (17.10%), nab-paclitaxel (16.37%), vinblastine (14.70%), Adriamycin (11.76%), and carboplatin (11.36%). The maximum economic loss was attributed to carboplatin (19.66%), nab-paclitaxel (17%), etoposide (14.5%), oxaliplatin (9.45%), and pemetrexed (7%). In combination chemotherapy regimens, gemcitabine-cisplatin-nab-paclitaxel (18.52%), pemetrexed-carboplatin (11.82%), and carboplatin-etoposide (8.97%) were responsible for the highest monetary losses due to drug wastage.

Conclusion: Drug wastage due to oversized chemotherapy vials imposes significant financial and environmental burdens. We recommend offering additional vial size options for carboplatin, etoposide, gemcitabine, nab-paclitaxel, irinotecan, vincristine, and 5-FU. We hope this will reduce drug wastage to below 1-2%.

Introduction

The burden of cancer incidence is increasing both in India and globally. Cancer treatment has become a significant concern due to the associated costs and safety issues. With the rising number of cancer cases, there has been a corresponding increase in the expenses incurred for cancer treatment [1-4]. Systemic therapy is one of the primary therapeutic modalities for cancer treatment [5]. In countries like India, where the majority of patients belong to the lower-middle socioeconomic status, cancer treatment imposes a significant financial burden on families, as most of the treatment costs are borne by the patients and their families [6].

Cost is a major factor influencing both the choice of cancer treatment and patient compliance [7-10]. Consequently, 10% to 20% of cancer patients either do not start or complete the recommended treatment, or they modify their treatment plans to reduce the financial burden [11-12].

Chemotherapy drugs, whether used alone or in combination, are widely utilized for cancer treatment. The dosage regimen for chemotherapy is calculated based on various criteria, including height, weight, body surface area, renal and hepatic function, age, and sex. Consequently, chemotherapy drug doses can vary among patients even when following the same treatment protocol. Chemotherapy drugs are available in vials of specific strengths. Many existing cancer drugs come in doses that often exceed the prescribed amount for the average patient, leading to wastage of the leftover drug in the vial. Various studies have shown drug wastage ranging from 1% to 41% [13-15]. Additionally, leftover drugs from single-use vials must be discarded as they cannot be used for other patients due to concerns such as the risk of infection from the lack of preservatives in single-use vials [16]. The US Pharmacopeia recommends using single-dose vials exposed to ISO Class 5 or cleaner air within 6 hours of initial needle puncture, and those exposed to air lower than ISO Class 5 within one hour [17].

Another issue with chemotherapy drug wastage is the environmental and occupational health hazards it poses. Hospital waste materials present a wide range of health and safety risks for patients and healthcare workers [18]. Many anti-cancer drugs are mutagenic, carcinogenic, teratogenic, and/or toxic to reproductive systems, classifying them as highly hazardous compounds [19].

Studies by Gopisankar et al. [20], Truong et al. [15], and Ghate et al. [21] indicate that drug wastage and its economic implications significantly increase the cost of cancer care without adding any incremental value to patients. Research in this field has proposed solutions such as vial sharing, dose rounding, and batching patients according to pathology to reduce wastage and lower costs [22].

Given that the majority of patients receiving treatment at Tata Memorial Hospital, Mumbai, belong to a low socio-economic status, our study aims to estimate drug wastage and the excess costs associated with large vial sizes of intravenous anti-cancer therapy among these patients.

Materials and Methods

This prospective, observational single-centre study was conducted over a period of 6 months at Tata Memorial Hospital, Mumbai. The study included twenty different intravenous chemotherapy protocols. A total of 500 adult cancer patients (twenty patients from each protocol) receiving intravenous anti-cancer treatment were enrolled consecutively. The mean, median, and mode for each chemotherapy drug were calculated.

Statistical Analysis

The average prescribed dose was determined by summing all the doses prescribed for each drug and dividing by the number of patients.

The median dose was identified as the middle value of the prescribed doses for each drug, arranged in ascending order.

The mode value of the prescribed dose was the dose most frequently prescribed.

The percentage of leftover drug was calculated for each drug based on the total leftover drug.

The total amount of drug wasted per hundred vials of each drug was calculated using the average prescribed dose for that drug.

Results

A total of 500 parenteral chemotherapy drug prescriptions from 25 commonly used protocols in solid and hematological malignancies were analyzed for drug wastage in our study. 20 prescriptions from each protocol were analyzed.

Drug wastage

In this study, the mean BSA was 1.57/m^2 (Range 1.11 - 2.12). The mean, median and mode of prescribed dose for each drug is summarized in Table 1.

Drug name	Total number of prescriptions	Commonest dose prescribed (mg)	Median dose prescribed(mg)	Mean dose prescribed (mg)	Formulations available in the Indian market (mg)	Frequency of administrations with vials matching the prescribed dose (%)
5 FU	80	2000	2000	2306.25	250, 500	18 (22.50)
Adriamycin	80	100	80	81.62	10, 50	20 (25)

Bleomycin	40	30	30	27.37	15	16 (40)
Carboplatin	80	600	600	520	150, 450	21 (26.25)
Cisplatin	80	50	50	45.87	10, 50	24 (30)
Cyclophosphamide	80	1000	1000	1168	200, 500, 1000	22 (27.50)
Dacarbazine	20	700	700	710	200, 500	4 (20)
Docetaxel	40	80	100	97.75	20, 80, 120	8 (20)
Epirubicin	20	150	150	145.5	10, 50, 100	12 (60)
Etoposide*	80	200*	200*	200*	100	11 (13.75)
Gemcitabine	100	1400	1400	1484	200, 1000	30 (30)
Irinotecan	60	240	240	275	40, 100	13 (21.66)
Leucovorin	60	350	350	340	50	60 (100)
Nabpaclitaxel	20	200	200	200	100	2 (10)
Oxaliplatin	100	150	150	166	50, 100	38 (38)
Paclitaxel	60	260	260	226	30, 100, 260, 300	22 (36.67)
Pemetrexate	20	1000	1000	965	100, 500	2 (10)
Rituximab	40	600	600	601.25	100, 500	40 (100)
Trastuzumab	40	440	440	395.25	150, 440	13 (32.50)
Vinblastin	20	10	10	11.5	10	9 (45)
Vincrestin	40	2 (4) **	2 (4)**	1.9 (4) **	1	18 (45)

Table 1. Mean, Median and Mode for the Prescribed Doses of Various Drugs.

* Per day drug doses; ** In REPOCH protocol

The results of drug wastage are summarized in Table 2. The drug wastage for individual chemotherapy drug varied from 4.90% to 29%. The overall drug wastage was 57,836 mg (8.67% of the total prescribed dose). The highest proportion of the drug wastage was for vincrestin (28.72%), etoposide (23.20%), bleomycin (18.5), pemetrexate (17.10%), nabpaclitaxel (16.37%), vinblastine (14.70), Adriamycin (11.76%) carboplatin (11.36%) and docetaxel (10.48). (Table 2).

Drug name	Total number of prescriptions	Total amount of prescribed drug in vials (mg)	Total amount of drug wasted (mg)	Percentage of drug wastage (%)	Total cost of drug wastage INR	Percentage of cost of drug wastage (%)
Vincrestin	40	118	33.9	28.72	1685.02	1.65
Etoposide	80	53600	12435	23.2	14922	14.55
Bleomycin	40	1095	203	18.5	6191.5	6.05
Pemetrexate	20	19300	3300	17.1	7236.76	7.05
Nabpaclitaxel	20	4000	655	16.37	17615.85	17.17
Vinblastin	20	230	33.8	14.7	710.47	0.7
Adriamycin	80	6530	768	11.76	2539.8	2.46
Carboplatin	80	41610	4730	11.36	20171.66	19.66
Docetaxel	40	3910	410	10.48	911.68	0.9
DTIC	20	14200	1480	10.42	3239.88	3.15
Cisplatin	80	8450	786	9.3	3450.5	3.36
Oxaliplatin	100	16600	1472	8.86	9671.08	9.45
Cyclophosphamide	80	92290	7380	8.65	413.22	0.4
5 FU	80	221000	14250	6.45	470.2	0.45
Irinotecan	60	16530	945	5.7	4656.24	4.54
Epirubicin	20	2910	155	5.32	1612	1.57
Gemcitabine	100	150800	7980	5.3	4364.81	4.25

Paclitaxel	60	13560	665	4.9	2699.4	2.64

Table 2. Drug Wastage and Cost Wastage for Individual Drugs.

There was no drug wastage for trastuzumab, rituximab and leucovorin.

BEP (19.4%), Carboplatin-etoposide (18.40%), Cisplatin-etoposide (17.40%), Pemetrexed-carboplatin (14.2%), REPOCH (13.15%), ABVD (11.50%), and Paclitaxel-carboplatin (10.60%) were the combination chemotherapy protocols with more than 10% drug wastage of the total prescribed doses (Table 3).

Chemotherapy regimen name	Total number of prescriptions	The total amount of available drug in vial (mg)	Total amount of drug wastage (mg)	Percentage of drug wastage
BEP	20	24100	4678	19.41
Carboplatin etoposide	20	23100	4250	18.4
Cisplatin etoposide	20	14970	2604	17.4
Pemetrexate carboplatin	20	31200	4440	14.2
REPOCH	20	48650	6401.2	13.15
ABVD	20	15925	1832.8	11.5
Paclitaxel carboplatin	20	14530	1540	10.6
Gemcitabine	20	34200	2920	8.5
Adriamycin cyclophosphamide	20	22860	1740	7.6
Docetaxel	20	2190	165	7.5
Docetaxel oxaliplatin 5 FU (DOF)	20	78020	5265	6.75
Gemcitabine cisplatin Nabpaclitaxel	20	31600	2030	6.4
Mfolfirinox	20	66470	4210	6.3
Irinotecan	20	6370	385	6
Epirubicin Cyclophosphamide	20	22710	1215	5.35
Gemcitabine cisplatin	20	32980	1757	5.3
Capecitabine Oxaliplatin	20	4300*	215	5
Gemcitabine Oxaliplatin	20	35500	1775	5
Gemcitabine carboplatin	20	35310	1630	4.6
RCHOP	20	39428	1585.7	4
mFolfox	20	104550	4032	3.9
Paclitaxel	20	5040	175	3.5
Paclitaxel trastuzumab	20	11450	290	2.5
mFolfiri	20	107340	2560.25	2.4
Trastuzumab	20	8250	0	0

Table 3. Drug Wastage for Combination Drug Regimen.

* Only parentral chemotherapy drug

Cost expenditure

The overall drug wastage in 500 drug administrations was 57,836 mg, (8.67% of the total

prescribed dose). This drug wastage resulted in an economic loss of 1,02,562 INR (6.26% of the total cost) in 500 prescriptions.

Carboplatin (19.66%), nabpaclitaxel (17%), etoposide (14.5%), oxaliplatin (9.45%) and Pemetrexate (7%) were responsible for the maximum drug cost wastage (Table 2). For combination chemotherapy protocols, the highest cost wastage was observed with gemcitabine-cisplatin-nabpaclitaxel (18.52%), followed by pemetrexate- carboplatin (11.82%), carboplatin-etoposide (8.97%), BEP (7.58%), ABVD (6.84%), and paclitaxel-carboplatin (6.40%) (Table 4).

Chemotherapy regimen name	Total number of prescriptions	Total cost of drug wastage INR (USD)	Percentage of cost of drug wastage
Gemcitabine cisplatin Nabpaclitaxel	20	18996.6	18.5
Pemetrexate carboplatin	20	12130.62	11.8
Carboplatin etoposide	20	9210	8.97
BEP	20	7782.65	7.6
ABVD	20	7020.05	7.15
Paclitaxel carboplatin	20	6560.6	6.4
REPOCH	20	6225.3	6
mfolfirinox	20	4206.3	4.1
Gemcitabine carboplatin	20	4185.45	4.07
Docetaxel oxaliplatin 5 FU (DOF)	20	4193	4.01
Cisplatin etoposide	20	3632	3.5
Gemcitabine Oxaliplatin	20	2446.55	2.4
mfolfox	20	2303.24	2.25
Irinotecan	20	1894.2	1.85
Epirubicin Cyclophosphamide	20	1671.36	1.6
Gemcitabine cisplatin	20	1641.26	1.6
Gemcitabine	20	1597	1.55
Capecitabine Oxaliplatin	20	1412.55	1.37
Docetaxel	20	1304.38	1.27
Paclitaxel trastuzumab	20	1177.4	1.15
mfolfiri	20	1114.04	1.08
Paclitaxel	20	710	0.7
RCHOP	20	625.72	0.6
Adriamycin cyclophosphamide	20	521.76	0.5

Table 4. Drug Cost Wastage in Various Chemotherapy Protocols.

Chemotherapy drug dose and vial size matching

The frequency of prescribed doses exactly matching the available dose strengths of chemotherapy drugs is summarized in Table 1. For leucovorin and rituximab, all the prescribed doses match the available dose strengths.

Discussion

Tata Memorial Hospital is a large tertiary cancer center that caters to approximately 400 patients (both General and Private categories) per day at its day care center for intravenous anti-cancer therapy. Given that the majority of patients receiving treatment at TMH belong to low socio-economic status, drug wastage has a significant financial impact, along with environmental

hazards.

In our study, 500 patients from 25 different chemotherapy protocols were analyzed. The mean BSA was 1.58 m² (range 1.11 – 2.12). Ninety percent of the patients had a BSA ranging from 1.30 m² to 1.90 m². Overall, 57,836 mg (8.67% of the total prescribed dose) was wasted. This drug wastage resulted in an economic loss of 102,562 INR (6.26% of the total prescribed drug cost). Considering this loss across 500 prescriptions, and extrapolating to all daily prescriptions over a month, the monetary and total loss nationwide would be substantial. In this study, drug wastage for various chemotherapy drugs varied from 4.9% to 29%. Various studies on drug wastage have shown a range from 1% to 41% [13-15, 23-25]. Similar to our findings, a study by Fasola et al. [26] reported that drug wastage accounted for 8.3% of the annual drug expenditure. In another study by D'Souza et al. [13], 6.1% of the reconstituted drugs were wasted, with the cost analysis amounting to 11.1% of the total drug cost. Adede et al., in a study from Morocco, reported drug wastage of 7.2% and an economic loss of 13.9% [27]. In the same context, two other similar Indian studies by Ghate et al. [21] and Gopisankar et al. [20] reported drug wastage of 19.61% and 17.72%, respectively. The cost expenditure for these studies was 28.98% and 17.14%, respectively. Drug wastage and cost expenditure in these studies were higher than in our study. The study by Ghate et al. was conducted in a pediatric population. The reason for the lower wastage in our study may be the availability of more vial sizes at our institute. Our study uniquely evaluated drug wastage within combination drug regimens. We found that regimens containing carboplatin and etoposide had particularly high levels of wastage. This was primarily due to the limited vial size options available.

Overall, there was no drug wastage for leucovorin, rituximab, and trastuzumab. For trastuzumab, the mean leftover drug was 50 mg when used as a single-agent regimen and 72 mg in combination regimens. Due to its 28-day shelf life, the leftover trastuzumab was utilized in subsequent cycles, resulting in no wastage. A study by Ritesh M. Pabari et al. [28] supports this, showing that trastuzumab intravenous solutions remain physically and structurally stable when stored at 2-8°C for 28 days.

The most significant factor contributing to drug wastage is the available vial size. Other important factors include the patient's weight, height, and body surface area.

Future prospectives

Drug wastage increases financial burden and causes environmental and occupational hazards. Various mitigation strategies have been tried to decrease drug wastage. A study conducted in three hospitals in Toronto by Leung et al. demonstrated that these strategies reduced the cost of wasted drugs by 1% to 2% of the total drug cost [29]. Another study by Fasola et al. [26] found that rounding drug dosages within 5% of the calculated dose to match vial strength, sharing multidose vials between patients with 24-hour stability, and scheduling chemotherapy sessions by grouping patients according to pathology or drug type reduced drug cost expenditure by 45%. However, rounding up to the full vial quantity, also known as 'flat' or 'fixed' dosing, cannot be used as it may result in some patients receiving much higher or lower doses than the FDA-approved amount, potentially causing toxicity or underdosing.

Although vial sharing appears promising, most chemotherapy drugs are available as single-dose vials due to the lack of preservatives. Another issue with vial sharing is maintaining strict sterility and the associated risk of infection. Guidance on vial sharing is also inconsistent. The Centers for Medicare and Medicaid Services essentially encourage it, while the Centers for Disease Control and Prevention state that it is unsafe [30-31].

We suggest offering additional vial size options for drugs to reduce wastage. We recommend that manufacturers provide a reasonable range of vial sizes to minimize the amount of wasted medication.

We recommend additional vial size options for carboplatin (50 mg), paclitaxel (10 mg), etoposide (50 mg and 10 mg), 5-FU (50 mg and 100 mg), gemcitabine (50 mg and 100 mg), irinotecan (20 mg), nab-paclitaxel (10 mg and 50 mg), and vincristine (0.5 mg) as detailed in Table 5.

Drug name	Formulations available in the Indian market (mg)	Recommended vial size (mg)
Paclitaxel	30mg, 100mg, 260mg, 300mg	10mg
Etoposide	100mg	10mg, 50mg
Carboplatin	150mg, 450mg	50mg
Gemcitabine	200mg, 1000mg	50mg, 100mg
Nabpaclitaxel	100mg	10mg, 50mg
VCR	1mg	0.5mg
5 FU	250mg, 500mg	50mg, 100mg
Irinotecan	40mg, 100mg	20mg

Table 5. Recommended New Vial Size Option for Various Drugs.

We anticipate that the availability of these vial sizes will likely reduce drug wastage to below 1-2%. This reduction will mitigate environmental hazards and alleviate financial burdens on patients' families and the country. For every hundred prescriptions of these drugs, an estimated 1.51 lakh INR could be saved. Considering that approximately 20 million patients receive chemotherapy annually in India, this could have a significant impact on patients, their caregivers, families, and the national economy.

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Statement of Transparency and Principals:

• Author declares no conflict of interest

• Study was approved by Research Ethic Committee

of author affiliated Institute.

• Study's data is available upon a reasonable request.

• All authors have contributed to implementation of this research.

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