

Implications of dose-rounding intravenous chemotherapy at a community-based hospital

ABSTRACT

OBJECTIVES: To quantify and evaluate the total number of pharmacist interventions completed for dose-rounding of IV chemotherapy medications, calculate cost savings due to dose-rounding of IV chemotherapy medications, and identify the 5 most commonly prescribed medications yielding the greatest cost-savings. **METHODS:** Prospective, single-center, IRB-approved interventional study conducted at South Miami Hospital from December 14th 2013 to March 14th 2014. All oncology patients 18 years of age and older receiving single-dose vial intravenous (IV) chemotherapy agents during the study period were included. On a daily basis, the primary investigator (PI) checked the IV room in the morning and evening for chemotherapy orders. In addition, the IV room pharmacist notified the PI regarding orders involving single-dose vial chemotherapy for IV use. On the other hand, a list with the names of the chemotherapy outpatients was provided to the PI by the oncology department on the afternoon prior to the day of the scheduled cycle. The PI reviewed orders to **evaluate** feasibility of dose rounding to the nearest vial. If the order met the specified 5% dose-rounding criteria, the PI contacted the prescriber to make the recommendation of dose-rounding. Once the 3 month study period was completed, the amount of orders meeting the specified 5% limit criteria for dose rounding was recorded; the top 5 most commonly prescribed antineoplastic agents yielding the most cost-savings were identified, and the overall cost-savings associated with dose-rounding of chemotherapy medications during the study period was calculated. **RESULTS:** Eleven percent (14 of 123) of the orders analyzed met the 5% dose-rounding criteria. All orders (100%) were rounded after obtaining approval from the prescriber. A total of 9634.51 dollars were saved by

rounding the 14 orders to the vial size. The 5 most commonly prescribed medications yielding the most cost-savings at our institution were, in order of potential savings: Doxorubicin (liposomal), bevacizumab, rituximab, cyclophosphamide, and pemetrexed.

INTRODUCTION

Although dosing based on body surface area (BSA) is used as the standard method for the administration of chemotherapy medications, it is well documented that this is not a dosing approach devoid of drawbacks^{1,2}. This is primarily because inter-patient variability of systemic medication exposure involves several factors not controlled by BSA-based dose calculations. Dose-rounding of antineoplastic agents is increasingly being incorporated in several institutions within the United States and worldwide^{3,4}. This is usually done with the ultimate goal of improving delivery of oncological agents in busy oncology departments without compromising the efficacy of the chemotherapeutic regimen. In most cases, the intervention entails calculating the dose of a chemotherapeutic agent based on the patient's BSA and then rounding the dose within defined ranges to the nearest vial size. Substantial cost-savings associated with the implementation of a dose-rounding protocol of antineoplastic agents have been previously described in the literature^{5,6}. In addition, unnecessary wastage of these medications is not uncommon due to the fact that most of these medications are preservative free⁷. At the present moment, there are several chemotherapeutic agents on the national drug shortage list (Table 1). Adopting the idea of dose-rounding can lead to an increase in the hospital inventory of medications that are in shortage. Thus, rounding the dose of antineoplastic agents to the vial

size is expected to result in significant cost-savings, minimization of waste disposal⁸, and increase in the institution's inventory. In this prospective, interventional study conducted at a not-for profit community hospital, we hypothesized that rounding the dose of single-dose IV chemotherapy is a feasible process resulting in significant cost-savings for our pharmacy department.

METHODS

Study Design

This Prospective, single-center, interventional study was conducted at South Miami Hospital (SMH), a licensed 467 bed facility. The study protocol was approved and conducted in accordance with the ethical standards of the facility's Institutional Review Board (IRB).

Patient selection

All oncology patients 18 years of age and older receiving single-dose vial IV chemotherapy agents during the period of December 14th 2013 to March 14th 2014 were included. The PI provided an in-service to the pharmacists explaining the rationale of the study and the process for contacting the PI when IV chemotherapy orders were received at the pharmacy (Appendix 1). A similar in-service was provided to clinicians prescribing chemotherapy (Appendix 2), and to nurses administering such medications (Appendix 3). All of these scripts were posted in each

department as reminders. Patients' information was collected by several mechanisms. The PI checked the IV room daily in the morning and evening for chemotherapy orders. In addition, the IV room pharmacist notified the PI regarding orders involving single-dose vial chemotherapy for IV use. The majority of the chemotherapy at our facility is administered to patients who come to the hospital to receive their chemotherapy cycle as outpatient. For these patients, the PI obtained a list of patients receiving chemotherapy from the oncology floor on the afternoon of the day prior to patients receiving the chemotherapy.

Data analysis

The PI reviewed orders for feasibility of dose rounding to the nearest vial. If the order met the 5% criteria for dose-rounding, the PI contacted the prescriber to make the recommendation of dose-rounding. A clarification of the accepted recommendation was documented in the patient's chart using a physician's order form (Appendix 4). In addition, each nurse administering the medication was verbally informed of the change in dose. The intervention, and other data variables from the intervention were documented in a password-protected data collection sheet (Appendix 5). At the end of the 3-month period, the percentage of evaluated orders meeting the specified 5% dose-rounding criteria was calculated. The top 5 most commonly prescribed chemotherapeutic agents yielding the most potential cost-savings were identified by multiplying the doses prescribed by the price of the vial. Last, the overall cost-savings associated with dose-rounding of antineoplastic agents during the study period was calculated as follow: The cost of each product vial was obtained from our pharmacy buyer. The

total number of vials required based on the rounded dose was subtracted from the total number of vials required if the originally prescribed dose would have been used. The difference was multiplied by the cost of the vial to obtain the cost saved per dose. Multiplying this by the total number of doses rounded allowed the investigators to find the total cost-savings for that regimen.

RESULTS:

A Total of 123 orders met criteria to be analyzed. Of those, 14 (11%) actually met criteria for dose rounding (Figure 1). All 14 orders (100%) were rounded after obtaining approval from the prescriber. A total of 9,634.51 dollars were saved by rounding the 14 doses to the vial size (Figure 2). The 5 most commonly prescribed medications yielding the most cost-savings at our institution were, in order of potential savings: Doxorubicin (liposomal), bevacizumab, rituximab, cyclophosphamide, and pemetrexed.

DISCUSSION

Antineoplastic agents are the top medication class for expenditure in nonfederal hospitals, and oncology products accounted for 32.2% of medication expenditure in the clinical setting throughout 2012. This trend continues as there is an increase in the number of new molecular entities approved by the Food and Drug Administration (FDA) to treat oncological disorders¹⁰. In

this study, we have shown that the concept of dose-rounding single-dose IV chemotherapy is not only feasible, but also results in significant cost savings.

Several important aspects related to this study are noteworthy mentioning. Although a reasonable proportion of the orders prescribed at our facility met the specified 5% limit criteria, this outcome could have been improved by using a 10% dose-deviation. We decided to be conservative in our study using a 5% dose-rounding criteria and rounding down to the vial size, as it was our first interventional study involving dose-rounding of antineoplastic agents. Nevertheless, the available literature supports a 10% dose deviation, which would result in significantly more interventions and cost-savings. For all 14 orders meeting the specified 5% dose-rounding criteria, the prescriber was comfortable with us rounding the dose to the vial size. This implies that our prescribers are aware of the benefits of this intervention and are receptive to pharmacist-based recommendations related to cost-containment. Some patients had more than 1 dose rounded. This is because those patients came back for subsequent cycles of chemotherapy. For bevacizumab, we had 1 patient receiving 3 cycles, 1 receiving 2 cycles, and a third patient receiving a single cycle. The cost of the vial was used to determine the top 5 most commonly prescribed medications yielding the most potential cost-savings. Although some of the medications in this study are available in multiple vial sizes, this does not affect this particular outcome because the cost per milligram of medication remains constant. As an example, cyclophosphamide 500 mg vials cost \$258 and therefore the 1000 mg vials cost \$516 which is twice the cost.

Several limitations were evident upon culmination of this study. First, not every chemotherapeutic agent in our study is dosed on the basis of BSA. As an example, bevacizumab is dosed in milligrams per kilograms. This would be inconsistent with the rationale behind using BSA to dose chemotherapy specified in this study. However, several studies have shown that rounding the dose of this agent to the vial size results in cost-savings without affecting clinical outcomes. Our study was conducted over a relatively short amount of time. This may explain the small sample size collected and the relatively small, although substantial, amount of money saved. Implementation of an automatic dose-rounding protocol using the presented data may confirm the much bigger benefit of dose-rounding single-dose IV chemotherapy at our institution.

CONCLUSION

The results of this prospective, interventional study, were consistent with our hypothesis that dose-rounding antineoplastic agents would result in significant cost-savings for our pharmacy department. This is consistent with others studies which have targeted similar endpoints^{6,7}. It is evident from this study that dose-rounding chemotherapy is feasible and that oncologists are receptive to the idea of dose-rounding. We identified the 5 most commonly prescribed chemotherapeutic agents at our institution, and we intend to obtain approval for an automatic dose-rounding protocol for these agents based on the results of this study. Nevertheless, the data presented in this study would support the implementation of a dose rounding protocol involving any single-dose IV antineoplastic agent.

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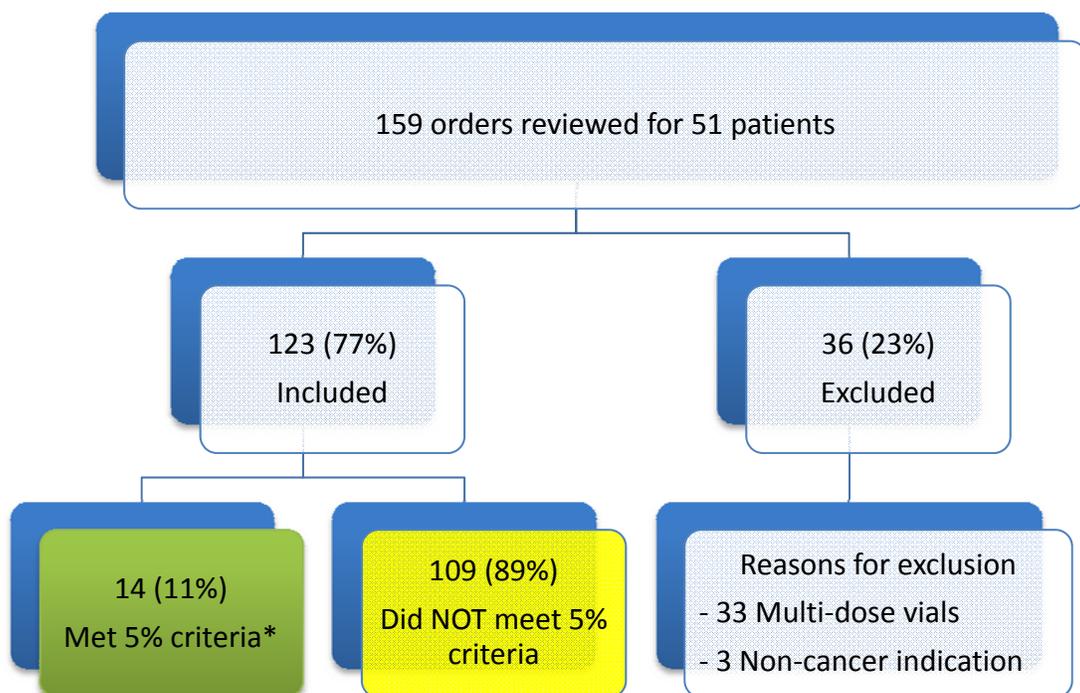
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Figure 1. Percentage of patients meeting the specified 5% dose-rounding criteria



*All interventions were made by phone and were accepted by the prescriber

Figure 2. Total amount of US dollars saved by dose-rounding 14 orders to the vial size

Medication	Doses Rounded	Amount of patients rounded	Amount Saved (US Dollars)
Avastin (Bevacizumab)	6	3*	3,739.02
Alimta (Pemetrexed)	1	1	2,831.76
Rituxan (Rituximab)	2	1	1,317.30
Doxil (Liposomal Doxorubicin)	1	1	1,131.00
Cytoxan (Cyclophosphamide)	2	1	516.98

Taxotere (Docetaxel)	1	1	94.21
Adriamycin (Conventional Doxorubicin)	1	1	4.24
			9,634.51

* Patient 1 received 3 doses, patient 2 received 2 doses, and patient 3 received 1 dose

Figure 3. Top 5 most commonly prescribed medications yielding the most potential cost-savings

Medication	Doses prescribed	Vial price (US dollars)	Potential Savings (US dollars)
Doxorubicin (Liposomal)	17	1,132	19,244
Bevacizumab	11	623	6,853
Rituximab	7	659	4,613
Cyclophosphamide	16	258	4,128
Pemetrexed	1	2,832	2,832
Docetaxel	19	94	1,786
Doxorubicin (Conventional)	11	4	44

Table 1 – List of chemotherapy medications currently in shortage status*

IV Drug Name	Revision Date
Cytarabine	August 05, 2003
Dacarbazine	October 07, 2013
Daunorubicin HCL	September 30, 2013
Doxorubicin	October 09, 2013
Doxorubicin Liposomal	September 27, 2013
Fludarabine	August 28, 2013
Methotrexate	September 12, 2013
Mitomycin	August 29, 2013
Paclitaxel	October 10, 2013
Vinblastine	September 04, 2013

* A comprehensive list of current drugs in shortage is found at: <http://ashp.org/menu/DrugShortages>