Reduction in Chemotherapy Order Errors With Computerized Physician Order Entry

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Abstract

Purpose: To measure the number and type of errors associated with chemotherapy order composition associated with three sequential methods of ordering: handwritten orders, preprinted orders, and computerized physician order entry (CPOE) embedded in the electronic health record.

Materials and Methods: From 2008 to 2012, a sample of completed chemotherapy orders were reviewed by a pharmacist for the number and type of errors as part of routine performance improvement monitoring. Error frequencies for each of the three distinct methods of composing chemotherapy orders were compared using statistical methods.

Results: The rate of problematic order sets—those requiring significant rework for clarification—was reduced from 30.6% with handwritten orders to 12.6% with preprinted orders (preprinted v handwritten, P < .001) to 2.2% with CPOE (preprinted v CPOE, P < .001). The incidence of errors capable of causing harm was reduced from 4.2% with handwritten orders to 1.5% with preprinted orders (preprinted v handwritten, P < .001) to 0.1% with CPOE (CPOE v preprinted, P < .001).

Conclusion: The number of problem- and error-containing chemotherapy orders was reduced sequentially by preprinted order sets and then by CPOE. CPOE is associated with low error rates, but it did not eliminate all errors, and the technology can introduce novel types of errors not seen with traditional handwritten or preprinted orders. Vigilance even with CPOE is still required to avoid patient harm.

Introduction

Safe prescribing and administration of chemotherapy remain priorities for all medical institutions and practitioners. Errors involving chemotherapy can occur at any stage of the process, including ordering, preparation, administration, and monitoring. Communication from physicians to other members of the treatment team takes place primarily through the ordering process, which is complex because of the need for precision with regard to the drug, dose, diluent, infusion sequence, and duration and the need to modify doses based on current laboratory values or toxicity assessment. Errors in chemotherapy have a high potential for patient harm because of the narrow therapeutic margin of many antineoplastic agents, especially in physiologically compromised patients.

Estimates of ordering errors vary with definition and measurement methodology. Table 1 summarizes some recent studies of ordering error rates, the likelihood that such errors reached patients, and the estimates of harm.1-4

In recognition of ordering complexity and risk, professional societies have created standards for the ordering of chemotherapy, among other aspects of chemotherapy practice. Despite the occasional media accounts of deaths resulting from chemotherapy errors5 and well-publicized calls to adopt safe standards from professional societies,6,7 a 2011 survey of National Cancer Institute–designated cancer centers indicated that only 41% of responding institutions had fully adopted the four American Society of Clinical Oncology (ASCO)/Oncology Nursing Society (ONS) standards regarding chemotherapy ordering, which include 16 elements constituting a complete order.8

We studied the number and type of errors associated with three distinct methods of chemotherapy prescribing employed sequentially: handwritten orders, preprinted order sets that were compliant with ASCO/ONS and American Society of Health-System Pharmacists (ASHP) standards but required physician completion, and order sets embedded within a computerized physician order entry (CPOE) system. The study documented a dramatic decrease in the frequency of all types of errors associated with both handwritten and preprinted order methods with the use of CPOE. However, it also documented that CPOE introduces new ways to make familiar errors and allows the creation of novel types of errors.

Materials and Methods

This project was performed as part of a quality improvement initiative and as such was not formally supervised by the institutional review board per its policy.

Clinical Setting

Anne Arundel Medical Center is a 383-bed acute care hospital that hosts a multidisciplinary cancer institute. Approximately 1,600 new analytic patient cases of cancer are seen annually. Three separate medical oncology-hematology practices direct patients to the outpatient infusion center of the medical center; two practices use it exclusively. The infusion center consists of 42 chairs and treats an average of 90 patients daily, approximately 50% of whom have an oncologic diagnosis. The infusion center is staffed by three full-time equivalent (FTE) pharmacists who also dispense investigational medications, two
Registered pharmacy technicians, and 17.25 FTE nurses. No physician or mid-level practitioner has a routine clinical presence in the infusion center. No trainees were involved in the preparation of chemotherapy orders.

Chemotherapy Ordering and Error Classification
This study examined error rates over three time periods in which different methods of composing chemotherapy orders were used. Every 10th (handwritten and preprinted) or every fifth (CPOE) order set was selected for analysis. During each of the three distinct phases of the ordering process, the same pharmacist (R.R.W.) reviewed the order sets for completeness and accuracy using the ASCO/ONS and ASHP standards. Data were reported quarterly to the performance improvement program of the medical center. For analysis, a new method of classification of possible problems and errors was created. We recognized a category of orders with problems, which we identified as mistakes unlikely to cause patient harm, because they lacked essential information such as dose, demographics, or signature and thus could not have been translated into actual infusions. Problem orders did require staff to contact the prescribing physician for clarification and/or completion. Errors were defined distinctly as those mistakes with potential for harm, including errors involving drug, dose, or schedule, among other aspects. Table 2 lists the classifications of both problems and errors.

Handwritten Orders
Data for this method were analyzed for the calendar year 2008, the 12-month period before order format was shifted to preprinted. Physicians wrote orders on blank order sheets. Only physicians with oncology privileges were allowed to sign orders sets, but often nurses or nurse practitioners composed orders for a physician’s signature.

Preprinted Order Sets With Comprehensive Orders and Nursing Instructions
Beginning in 2009, preprinted, regimen-specific order sets were developed in iterative collaboration with pharmacists, nurses, and oncologists and were compliant with the ASCO/ONS and ASHP guidelines. Order sets were posted on the medical center intranet. They included the standard dose and appropriate supportive care measures. Handwritten changes were allowed as clinically appropriate. Prescribers had to accurately complete the form with handwritten patient demographics, dates of therapy, cycle number, and final desired dose based on their own calculations of body-surface area and creatinine clearance, as necessary. To encourage compliance, the pharmacy stopped accepting handwritten orders for any regimens for which order sets had been created. Over the first few months, the number of available order sets rapidly increased, and compliance rapidly exceeded 90%. Data for this study included 12 months beginning in June 2009, when the compliance rate with preprinted order sets was > 90%. Only physicians were allowed to sign orders, but nurse practitioners were allowed to compose orders for a physician’s signature.

CPOE
In 2009, the medical center purchased a comprehensive electronic health record system from Epic Systems (Verona, WI) for both inpatient and ambulatory settings. Two of the three medical oncology practices began using Epic in the ambulatory setting in 2011 and began using Beacon for CPOE of chemotherapy in January 2012. Use of the Beacon system has been described previously, most comprehensively by Brockstein et al9 and Harshberger et al10 Each regimen has to be built to include chemotherapy drugs, nursing instructions, and supportive care medications and fluids as appropriate. The goal was to ensure that the content would be identical to the preprinted order, even if the display was not. Physicians reviewed each order set before it was finalized. To allow time for oncologists to become accustomed to the system, we analyzed only orders written after a 2-month run-in time, which proved adequate for gaining competency. Unlike with handwritten or preprinted order sets, only physicians were permitted to create an order set.

Statistical Analysis
The overall rate of problem order sets and order sets with errors was calculated. Two sets of comparisons were made: handwritten versus preprinted and preprinted versus CPOE. The results were compared using a two-sample normal theory test for binomial proportions. CIs were calculated using the Wilson score.
Results
We reviewed 2,216 handwritten, 2,480 preprinted, and 5,142 CPOE order sets. On average, each order set had 8.6 separate medication or fluid orders, a number that did not change over the three study time periods. The random selection of order sets for quality review successfully produced a representative sample of all orders with respect to diagnosis and ordering physician (data not shown). Table 2 lists the number and type of problem orders and orders with errors for each of the three methods of prescribing. There were highly statistically significant reductions in the incidence of both problems and errors as the shift occurred from handwritten orders to preprinted orders and then to CPOE (Table 3).

CPOE provided 100% compliance and accuracy with certain elements of the order, including demographics, required signature with date and time, dose calculations, and creatinine clearance—information that was missing or inaccurate in 10% to 44% of orders with the other ordering methods. Illegibility was also eliminated by CPOE, although human-computer interfaces can still be troublesome.

We identified six types of errors associated with CPOE that could potentially add ambiguity and introduce errors. Some of these may be unique to the brand of CPOE used in our center; others are common to the CPOE process. These hazards include:

1. **Unintended re-escalation of doses.** To add additional cycles of a regimen in the Beacon CPOE, prescribers copy any previous cycle and paste it at the bottom of the screen to create a new cycle with the same content. However, if there have been dose reductions or other changes, this method of propagating a regimen may result in inadvertent errors if the wrong cycle is copied forward. The CPOE lacks a safety mechanism to detect this human error.

2. **Creating confusion among care team members when adding or deleting drugs.** Adding or deleting drugs from a named regimen such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) without changing the title of the regimen creates a mismatch between the expected order and the actual order. The system does allow comments to be sent to the treatment team, but this section is more than one click away and may not be used as often as necessary.

3. **Incorrect supportive care medications remain after deleting a specific chemotherapy drug.** The CPOE system allows the prescriber to delete an antineoplastic drug (eg, cisplatin) without deleting its associated supportive medications or hydration.

4. **Overdosing by not propagating intended deletion of treatment days.** When physicians change a dose of a drug, they are offered the choice of making a onetime change only or a change to all

### Table 2. Categorization and Incidence of Problems and Errors in Chemotherapy Order Sets

<table>
<thead>
<tr>
<th>Type of Issue</th>
<th>Handwritten (n = 2,216)</th>
<th>Preprinted (n = 2,480)</th>
<th>CPOE (n = 5,142)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Problems</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing or incomplete patient identifiers or diagnosis</td>
<td>124</td>
<td>53</td>
<td>0</td>
</tr>
<tr>
<td>Missing or undated signatures</td>
<td>245</td>
<td>114</td>
<td>0</td>
</tr>
<tr>
<td>Missing or partial height, weight, or BSA information</td>
<td>131</td>
<td>33</td>
<td>0</td>
</tr>
<tr>
<td>Missing dose</td>
<td>75</td>
<td>40</td>
<td>6</td>
</tr>
<tr>
<td>Missing or unclear dates of treatment or cycle number</td>
<td>86</td>
<td>62</td>
<td>22</td>
</tr>
<tr>
<td>Mismatch between name of order set and drugs ordered</td>
<td>1</td>
<td>3</td>
<td>66</td>
</tr>
<tr>
<td>Mismatch between chemotherapy and supportive care</td>
<td>11</td>
<td>3</td>
<td>21</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total orders sets with problems</strong></td>
<td>678</td>
<td>312</td>
<td>115</td>
</tr>
<tr>
<td><strong>Errors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrong or illegible patient name identifiers</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Illegible drug name</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wrong dose or dose calculation</td>
<td>23</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Incorrect BSA calculation</td>
<td>27</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Incorrect calculation of creatinine clearance</td>
<td>8</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Wrong dose units (eg, gm for mg)</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wrong treatment frequency or infusion time</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Omission of chemotherapy drug or supportive care medication</td>
<td>8</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Wrong diluent</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Unintended dose escalation after previous reduction</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Dangerous abbreviation</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Duplication of drug class (eg, 5HT-3 antagonists)</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total order sets with errors</strong></td>
<td>94</td>
<td>37</td>
<td>3</td>
</tr>
</tbody>
</table>

Abbreviations: BSA, body-surface area; CPOE, computerized physician order entry; 5HT, 5-hydroxytryptamine.
future occurrences of the same drug. However, when deleting entire days (eg, day 8), this same option is not offered, and prescribers can be misled into thinking they have adjusted all future cycles.

5. Overdosing by mistyping. The system does not include hard stops for inadvertent overdose, such as mistyping a digit or adding a zero. Because the same chemotherapy drug can be prescribed at widely varying doses depending on the indication, a single-dose limit hard stop is not feasible for all drugs. To provide protection from this type of error, each institution must therefore build individualized, regimen-specific dose limits that appear as soft stops. In our experience, these have been effective. But some users, afflicted by alert fatigue, may click through these warnings, a phenomenon that has been well described.11

6. Inadvertent omission of drugs. Beacon allows prescribers to sign for all or parts of the regimen and for all drugs or individual drugs. Because of the design and display factors of Beacon, practitioners can inadvertently sign in the wrong place, mistakenly signing only for one of the drugs when they meant to sign for all. Because of another design feature, these unsigned orders are not always visible to the rest of the treatment team, so the error may not be caught.

Discussion
Our study documents that the rate of both problems and errors fell with the use of both preprinted order sets and CPOE because both formats enforce compliance with the standards recommended by professional societies.6,7 Both preprinted and CPOE ordering ensured correctly spelled and legible medications without dangerous abbreviations, proper drug sequence, infusion rates, diluents, nursing instructions, and laboratory parameters, among other processes. However, preprinted order sets still required physicians to complete aspects of the order and perform calculations. These aspects continued to generate both problems (12.6%) and errors (2.2%). Our retrospective methodology did not allow us to perform metrics around the time wasted and extent of dissatisfaction among patients, nurses, pharmacists, or physicians regarding all the rework. Nor could we estimate the loss of confidence that occurred if a patient became aware that his or her chemotherapy prescription was flawed. The findings of enhanced accuracy with CPOE are consistent with those of Harshberger et al,10 who observed improved completion of chemotherapy orders with the same CPOE system used in this study compared with paper, although the type of paper order used (ie, preprinted or handwritten) was not specified. We know of only two prescribing errors reaching a patient with potential to harm: an error of omission caused by an inadvertent failure to sign one of the three chemotherapy drugs in a regimen on the CPOE user screen and an unintended dose escalation caused by copying forward a previous dose that had been reduced for toxicity. This latter type of error also occurred in handwritten orders but was caught and prevented by a pharmacist who was transcribing the order with knowledge of past dose reduction. In CPOE, the order gets transmitted without this intermediate step.

Comparison of error rates and the harm they cause across studies is difficult because of a lack of standard definitions and data gathering tools. In published studies, estimates of chemotherapy error frequency vary based on clinical setting, type of medication included in the analysis, and chemotherapy ordering system (Table 1). Some studies include all medications delivered in multipurpose infusion centers, and others confine their analyses to antineoplastic agents. This is an important distinction because the therapeutic index of chemotherapy may be narrower than that of other medications, leading to different estimates of harm rates. Another problem with harm estimates is that unintentional underdosing may not be registered as a harm, because it does not cause immediate toxicity. Comparisons among studies are also hindered by the lack of a standard definition or categorization of errors. The broadest definition of error includes any order in violation of professional society recommendations.6,7 However, such a system would inappropriately give equal weight to mistakes such as, for example, missing time of signature and miscalculated cisplatin dose. Our own study created a novel categorization schema to include both problems and errors, the latter defined as having the potential to cause harm.

Weaknesses of our study include its quasi-experimental, interrupted time sequence design. This may have allowed for other factors, such as heightened awareness of the danger of chemotherapy ordering or a change in physicians over time, to account for some of the improvement. However, during the years of our study, there were no departures and only one addition. Another potential source of improvement indirectly related to CPOE is that nurses and nurse practitioners were no longer able to prepare orders for physician signature. Although not specifically addressed by ASCO/ONS or ASHP guidelines,
the practice of shared responsibility for chemotherapy orders is fraught with opportunities for miscommunication. Again, the size of improvement is likely too large to be accounted for by this factor alone. It is also possible that the prescribers became aware of increased performance improvement scrutiny occurring at the same time CPOE was being introduced. However, during the period of data collection, there was no enhanced effort to provide comprehensive feedback to the prescribing physicians other than their own burden of calls.

Another potential problem of this CPOE system is that in our institution, Epic imports medication safety data from Medispan, a third-party vendor. Drug interaction and maximum dose warnings are preset and are not always clinically relevant (eg, dexamethasone doses > 4 mg cause a warning). Customized adjustments can be built for specialized uses but are time consuming to create and maintain.

We have demonstrated that CPOE creation of chemotherapy orders has clear advantages over handwritten and preprinted ordering methods. Additional advantages outside the scope of this study include cumulative dose tracking, the capability to create a shared and visible chemotherapy flow sheet, and remote access to order writing, which allows a reduction of verbal orders. However, as our study shows, clinical personnel should not lower vigilance thresholds, because the opportunity for errors remains significant. The safe administration of chemotherapy still requires independent diligence from nurses, pharmacists, and physicians. As a previous warning has sounded, “attention must be paid.”

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References