Original Contribution

Improving Electronic Oral Chemotherapy Prescription: Can We Build a Safer System?

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Abstract

Introduction: To prevent oral chemotherapy prescription errors, we enhanced a prescription-writing module in an ambulatory electronic medical record. We sought to describe the enhancement, examine its performance to date, and identify opportunities for improvement.

Methods: Enhancements to the oral chemotherapy writing module included weight- and body surface area–based dosing, fields for cancer diagnosis and intent of therapy (curative *v* palliative), and dose-limit warnings. We studied all prescriptions for 18 oral chemotherapies generated by oncology clinicians during the first 17 months after the safe prescribing enhancements were introduced, from May 1, 2010, to October 1, 2011. We examined the frequency with which clinicians used the new features, the number and type of alerts generated, and clinician actions in response to alerts.

Results: Six hundred clinicians generated 6,673 prescriptions for 2,043 patients. Six drugs—temozolomide, capecitabine, lenalidomide, hydroxyurea, imatinib, and erlotinib—accounted for 5,512 of all oral chemotherapy prescriptions (83%). Prescribers indicated the intent of therapy 13% of the time and listed the patient's cancer diagnosis 46% of the time. Prescribers customized their instructions using a free-text field in 64% of prescriptions. Clinicians' 6,673 prescription attempts triggered 395 dose-limit warnings (5%), mostly for temozolomide. Clinicians ignored most (96%) warnings, because current dosing recommendations exceeded the dose-limit warnings for the alerted medications.

Conclusion: Oncology clinicians readily accepted features designed to enhance oral chemotherapy safety. Additional enhancements are needed to facilitate prescriptions with complex dosing regimens and to provide dose-limit warnings that reflect current clinical practice.

Introduction

Oral chemotherapy is a widely used treatment, with more than 25 million doses administered per year in the United States for a variety of cancer diagnoses.[1] Although oral chemotherapy offers patients the convenience of home administration, this treatment modality may introduce new safety risks into oncology practice. In a survey of 42 US cancer centers, researchers found that most organizations lacked basic features that have long been used for infusion chemotherapy, such as required prescription elements or written informed consent.[2] In another study, investigators described oral chemotherapy errors involving each stage of the medication use process[3] and in home medication administration.[4,5]

To evaluate the risks associated with oral chemotherapy, we conducted failure mode and effects analyses—a type of prospective risk assessment—for six oral chemotherapies.[6] We found that prescription writing was particularly vulnerable to errors, including miscalculations, illegible handwriting, and miscommunication with the pharmacy. To mitigate this risk, we developed a set of enhancements to the existing prescription-writing module in our ambulatory electronic medical record.

This project had two major objectives. First, we sought to offer providers writing oral chemotherapy prescriptions safety features similar to those present in the ordering modules for parenteral chemotherapy. Second, we hoped to provide pharmacists with additional critical information about their patients and the intent of the ordering clinicians, again similar to the modules that govern parenteral chemotherapy orders. The goal of this report is to describe the oral chemotherapy prescription module, examine its performance to date, and identify lessons learned and opportunities for improvement.

Methods

Patients and Practice Setting

Dana-Farber/Partners Cancer Care is an organization composed of Dana-Farber Cancer Institute, Brigham and Women's Hospital, Massachusetts General Hospital, and affiliated community hospitals and practices in eastern Massachusetts and New Hampshire. Dana-Farber/Partners Cancer Care clinicians serve adult and pediatric patients with a wide variety of hematologic malignancies and solid tumors. In the care of adult patients, clinicians use the longitudinal medical record (LMR), a multi-feature electronic medical record shared with clinicians across the affiliated Partners Healthcare system, to document encounters, check laboratory and diagnostic test results, and generate prescriptions that can be printed, faxed, or transmitted electronically to pharmacies.[7]

Intervention

The LMR prescription module offers a set of standard electronic features, including medication choice lists with default doses and frequencies. The system requires complete prescription elements including number of units dispensed. It offers several types of decision support, including drug allergy and interaction checks as well as geriatric and renal dose warnings.[8-10] The LMR can identify different classes of drugs, in this case drugs designated as chemotherapy, and allow for the design of specific functionality to manage that drug class.

With guidance from physician, nurse, pharmacy, and information technology colleagues, we designed several safety-oriented enhancements to the existing module to support safe prescribing of oral chemotherapy. The enhancements included the ability to order oral chemotherapy based on a fixed dose, a weight-based dose, or a dose based on body surface area (BSA). For weight- or BSA-based dosing, the module used the most recent weight recorded in the medical record (if <30 days) and the most recent height (if <1 year) to calculate the BSA, which was in turn used to determine the final dose. If timely data were unavailable in the electronic record, the provider could update this information. These features reduced the risk of calculation errors. A calculator was provided to support toxicity-related dose adjustments.

The module also displayed the patient's primary cancer diagnosis. If the patient had received infusion chemotherapy, the diagnosis was pulled into the oral chemotherapy prescription automatically. The prescriber could also add or modify the diagnosis, adding the cycle number and clinical trial number if he or she chose. However, to honor patient requests for confidentiality, the prescriber could remove the diagnosis from the prescription. Clinicians could specify if the intent of therapy was for a curative or palliative indication, a feature of infusion orders that helped prescribers to select an appropriate regimen. Intent of therapy was not a required field, and it did not print on the prescription.

Like any prescription, oral chemotherapies could generate drug allergy and interaction alerts and trigger geriatric and renal dose warnings. We enhanced these decision support tools by creating, with the assistance of oncologists and oncology pharmacists, daily and weekly dose-limit warnings that would alert the prescriber to potential overdoses. The system generated alerts with new prescriptions as well as renewals.

Given the differences in their clinical use, we excluded hormonal chemotherapies such as tamoxifen and aromatase inhibitors and investigational agents from the first version of this enhanced oral chemotherapy prescription module. Because the LMR displays oral chemotherapies for oncology use separately from the same drug used for nononcology indications (eg, methotrexate for rheumatologic diseases), we excluded oral chemotherapies prescribed by nononcologists.

Measurements

We collected all oral chemotherapy prescriptions generated in the LMR from the introduction of the enhanced module on May 1, 2010, to October 1, 2011. We extracted information electronically, including patient characteristics (age, sex, race/ethnicity, height, weight, and BSA), prescriber information (name, oncology clinician [or not], and professional degree), and prescription information (prescription date, drug name, strength, form, instructions, frequency, number of refills, cancer diagnosis, and curative or palliative intent of treatment). We also extracted any medication safety alerts that the system generated, including drug allergy and interaction alerts and dose warnings. Prescriber response to the alert was recorded as well, including the decision to abort the prescription attempt or to continue the prescription, effectively overriding the alert.

Analyses

We collected information about all oral chemotherapy prescriptions generated during the study period. We included oral chemotherapy prescriptions entered by nonphysician oncology clinicians, including nurse practitioners and physician assistants. Clinicians may enter partial prescription information into the medical record to update the electronic medication list (eg, omitting the dose or number dispensed); we excluded these entries from the analyses, because the system requires a complete prescription to generate a paper or electronic prescription. To avoid double counting in cases when the prescriber generated multiple prescriptions for the same drug for a single patient on a given day, we selected the final prescription for an individual patient and drug per day.

We analyzed the characteristics of the patient cohort, including age, sex, race/ethnicity, age, and the number of different oral chemotherapies prescribed for each individual. We tabulated the number of completed oral chemotherapy prescriptions generated during the study period by drug. To understand whether clinicians used the safety features of the module, we analyzed their use of the optional fields for diagnosis and intent of therapy. We also studied clinicians' responses to medication safety alerts, tabulated by the number, rate, and type of oral chemotherapy alerts that were generated, and examined the prescribers' decisions to abort prescription attempts. Analyses were performed using Stata 9.0 (StataCorp, College Station, TX).

Results

Patients

We studied oral chemotherapy prescriptions for 2,043 patients. Forty-three percent were male; 88% identified themselves as white, and 2% as Latino. The average age was 59 years. This profile reflects the general composition of the patient population served by Dana-Farber/Partners Cancer Care clinicians.

Oral Chemotherapy Prescriptions

Table 1 shows the oral chemotherapy prescriptions that providers generated during the first 17 months after the enhancements were introduced. From May 1, 2010, to October 1, 2011, 600 oncology prescribers entered 6,673 prescriptions into the electronic medical record for 18 different oral chemotherapies. The number of prescriptions varied from 1,585 for temozolomide to

Table 1. Oral Chemotherapy Prescriptions by Drug Name, Specification of Diagnosis, and Intent of Therapy*

	Prescriptions		Diagnosis Specified		Intent Specified	
Drug	No.	%†	No.	%	No.	%
Capecitabine	1,168	17.5	765	65.5	236	20.2
Dasatinib	78	1.2	18	23.1	4	5.1
Erlotinib	349	5.2	166	47.6	20	5.7
Hydroxyurea	657	9.9	137	20.9	33	5.0
Imatinib	694	10.4	234	33.7	112	16.1
Lapatinib	128	1.9	90	70.3	26	20.3
Lenalidomide	1,059	15.9	342	32.3	17	1.6
Mercaptopurine	151	2.3	92	60.9	6	4.0
Methotrexate	145	2.2	51	35.2	4	2.8
Sorafenib	149	2.2	94	63.1	22	14.8
Sirolimus	244	3.7	60	24.6	9	3.7
Sunitinib	227	3.4	129	56.8	51	22.5
Temozolomide	1,585	23.8	887	56.0	310	19.6
Vorinostat	24	0.4	4	16.7	2	8.3
Other‡	15	0.2	13	86.7	0	0.0
Total	6,673	100.0	3,082	46.2	852	12.8

* Total of 6,673 prescriptions.
† Totals do not add to 100% because of rounding.
‡ Other prescriptions included altremtamine (n = 4), gefitinib (n = 1), lomustine (n = 9), and thioguanine (n = 1).

one each for gefitinib and thioguanine. Six drugs—temozolomide, capecitabine, lenalidomide, hydroxyurea, imatinib, and erlotinib—accounted for 5,512 of all oral chemotherapy prescriptions (83%).

The enhanced oral chemotherapy prescribing module offered clinicians the opportunity to specify the intent of therapy (curative or palliative) and display the diagnosis, replicating safety features required for infusion therapy. Table 1 shows that prescribers indicated the intent of therapy infrequently, specifying this field 13% of the time. Curative, adjuvant, or neoadjuvant intent was specified in 344 cases, and palliative or metastatic care in 508. In contrast, prescribers listed the patient's cancer diagnosis 46% of the time. Diagnoses were recorded more than half the time for patients receiving prescriptions for capecitabine, lapatinib, mercaptopurine, sorafenib, sunitinib, and temozolomide. The most commonly listed diagnoses were breast cancer (n = 618), CNS gliomas (n = 578), sarcomas (n = 296), multiple myeloma (n = 246), lung cancer (n = 164), and colorectal cancer (n = 153).

Prescribers used the free-text "sig" field frequently, in 4,242 (63.6%) of 6,673 prescriptions. This field allowed prescribers to customize their prescriptions, adding information about treatment dates, cycle number, dose calculation, and recommendations about whether to take the medication with food (eg, "take daily days 1 through 21 of a 28-day cycle"). Prescribers also clarified the number of tablets of different strength that should be taken together (eg, "adjuvant temozolomide cycle 2: dose 200 mg/m^2 × BSA 2.38 = 470 mg [250-mg tablet + 180-mg tablet + two 20-mg tablets").

Table 2. Oral Chemotherapy Alerts by Type of Alert and Drug Name*

Alert	No. of Alerts	No. of Prescriptions†	Alerts per 100 Prescriptions†
Dose-limit warning	395	6,673	5.9
Drug generating alert			
Capecitabine	10	1,168	0.9
Dasatinib	1	78	1.3
Erlotinib	2	349	0.6
Hydroxyurea	6	657	0.9
Mercaptopurine	1	151	0.7
Methotrexate	1	145	0.7
Temozolomide	374	1,585	23.6

* Total of 6,673 prescriptions.
† Totals do not add to 100% because of rounding.

Medication Safety Alerts

Clinicians' 6,673 prescription attempts triggered a total of 395 alerts, a rate of 5.9% (Table 2). Although the system was capable of issuing drug allergy and interaction alerts, dose-limit warnings constituted the only type of alert generated during this period.

Prescriptions for seven drugs generated all 395 alerts, and temozolomide alone accounted for 374 (95%). All of the temozolomide alerts indicated that the prescription exceeded a daily dose limit of 200 mg or weekly limit of 1,000 mg. Similarly, the capecitabine alerts indicated that the prescription exceeded a daily maximum of 2,500 mg or weekly maximum of 17,500 mg. The scenario was replicated for the other alerted medications. Almost one quarter (24%) of the 1,585 temozolomide prescriptions triggered an alert; in contrast, only approximately 1% of prescriptions for the other chemotherapies triggered an alert.

A clinician whose prescription generated an alert had the option of aborting the prescription attempt or completing the prescription as planned. As shown in Table 3, prescribers aborted only 17 (4%) of the 395 prescriptions that generated an alert, mostly involving temozolomide. Clinicians aborted a higher percentage of nontemozolomide prescription attempts (three of 21; 14%) than temozolomide attempts (14 of 374; 4%; $P = .054$). Physicians terminated an alerted prescription attempt slightly more often than their nonphysician colleagues (97% *v* 93%; $P = .067$), perhaps because physicians were required to generate initial oral chemotherapy prescriptions rather than periodic renewals. In retrospect, it is surprising that clinicians aborted any prescriptions. Current dosing recommendations exceeded the dose-limit warnings for the alerted medications in every case, thus generating a significant number of inappropriate alerts.

Discussion

In this evaluation of an electronic oral chemotherapy prescription module, we found that a small number of medications accounted for the majority of prescriptions. The frequent use of drugs such as temozolomide, capecitabine, and lenalidomide

Table 3. Prescriber Actions in Response to Oral Chemotherapy Alerts by Drug and Type of Prescriber*

Drug/Prescriber	Prescriber Action After Alert: Abort Prescription (No.)	Continue Prescription (No.)	Continuation Rate (%)	P†
Drug generating alert				< .001
Capecitabine	2	8	80	
Dasatinib	1	0	0	
Erlotinib	0	2	100	
Hydroxyurea	0	6	100	
Mercaptopurine	0	1	100	
Methotrexate	0	1	100	
Temozolomide	14	360	96	
Type of prescriber				.07
Physician	10	139	93	
Nonphysician	7	239	97	

* Total of 395 alerts.
† χ^2 test.

reflects the patient population served by the study hospitals and practices. Clinicians made variable use of the new safe prescribing features that allowed them to enter information such as diagnosis and therapeutic intent. Medication safety alerts triggered dose-limit warnings that were set too low. Alerts fired infrequently, and most were dismissed by the ordering clinician.

Given these findings, what can one conclude about the use and performance of electronic prescribing enhancements for oral chemotherapy? First, clinicians used the enhanced oral chemotherapy prescription module extensively. Oncologists accepted the changes without resistance or complaint. Second, the optional fields for diagnosis and therapeutic intent were used inconsistently, reflecting variation in clinical practice and perhaps patient preference. The feature offers clinicians a tool that some seemed to find helpful. It is likely that the more common use of diagnosis compared with therapeutic intent resulted in part from the ability of the module to pull this information from the medical record as a default value, reducing the prescriber's work.

Third, oral chemotherapy prescription must be further modified to offer prescribers an easy way to incorporate information that they currently provide in free-text fields, such as cycle number, days per cycle, nontreatment days, and instructions for combining different pill strengths. Offering a streamlined way to include this information in the prescription may permit quicker prescription writing, facilitate complete prescriptions, and offer more comprehensive data capture.[3,4,6] Some free-text comments replicated information that could have been entered elsewhere, suggesting that providers were either unfamiliar with the application or simply found it to be an easier way to customize the prescription. We believe that the dosing tools that allowed weight- and BSA-based prescription improved the ease and accuracy of dose calculations, but the current data storage structure did not allow us to assess that assumption directly.

Finally, oral chemotherapy dose-limit warnings must be updated regularly to reflect current clinical practice.[9,11] Because dose-limit warnings were inconsistent with current practice, clinicians ignored them routinely. In fact, low-value alerts may contribute to alert fatigue, a condition in which clinicians learn to ignore useful as well as low-value alerts. To prevent alert fatigue, the capacity to generate an alert must be linked to effective knowledge management—a function that keeps clinical decision support in line with evolving clinical practice. Clinicians must be engaged in developing and refining the format of the alert as well as the clinical content that the alert transmits. The alert and its content may need to be monitored and modified separately.

This project is limited in its focus on chemotoxic and targeted agents, rather than hormonal therapies. The latter pose particular challenges related to long-term use, including prescribers' need to monitor and support adherence. The project also has limited generalizability, because the evaluation was completed at a single cancer center with a homegrown electronic order entry system. Its applicability to other centers and systems requires further study. However, an increasing number of oncology practices have introduced electronic prescription.[12,13] A recent study at a 719-bed teaching hospital demonstrated a 69% reduced risk of oral chemotherapy prescription errors with the introduction of oral chemotherapy order sets in a computerized physician order–entry system.[14] The analysis reported here builds on previous work by demonstrating the opportunities and barriers to enhancing an existing, generic electronic order-entry system for prescribing oral chemotherapy safely.

This project also suggests improvement opportunities for practices that rely exclusively on paper-based prescriptions. Practices should consider developing prescription templates for oral chemotherapies that incorporate safety features, such as space for explicit weight- or BSA-based dose calculations, diagnoses, cycle numbers, and perhaps cosignatures. Paper-based prescriptions could include calendar icons that signify irregular dosing intervals. Prescription forms could display drug-specific dose limits as a ready reference, although the full benefit of allergy, drug interaction, and dose-limit alerts requires an electronic order-entry system. A list of selected oral chemotherapy prescription enhancements is included in Appendix Table A1 (online only).

Given the increasingly widespread use and potential toxicities of oral chemotherapies, we recommend that oncology practitioners revisit their prescription practices. Although paper-based prescription offers opportunities for enhancing the safety of oral chemotherapies, we believe that health care organizations and commercial vendors should develop and deploy improvements in electronic prescription systems to ensure that the safeguards for infusion therapies exist for oral agents as well.[15,16] The present report demonstrates the feasibility of this approach and clinicians' willingness to use electronic prescription safety features. We also sound a cautionary note about the importance

of ensuring that clinical decision support in fact supports clinical decisions.

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Authors' Disclosures of Potential Conflicts of Interest

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Appendix

Table A1. Safe Prescribing Features for Oral Chemotherapies

Features
General
Drug name, dose form (ie, pill strength), no. to be taken at one time (eg, two tablets per dose)
Route
Frequency
No. dispensed
No. of refills
Sig (ie, free text)
Special instructions (eg, take with food)
Explicit dose calculations and cycle notation
Dosing rule (fixed dose, weight based, body surface area based)
Dose calculation along with height and weight (if appropriate)
Cycle number
Diagnosis and goal of therapy
Diagnosis
Goal of therapy (curative/adjuvant *v* palliative/metastatic)
Research protocol number (if appropriate)
Additional patient instructions, including safe handling and irregular dosing patterns
Decision support and safety features
Drug allergy checks
Drug interaction checks
Dose-limit warnings (daily, weekly, cumulative)
Geriatric and renal dose warnings
Second physician double check