

Using an enhanced oral chemotherapy computerized provider order entry system to reduce prescribing errors and improve safety

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Abstract

Objective. To reduce the probability of failure in the oral chemotherapy order, review and administration process and to reduce oral chemotherapy-related prescribing errors intercepted by clinical pharmacists prior to reaching the patient.

Design. A before-and-after cohort study.

Setting. A 719-bed multidisciplinary tertiary care institution with a pediatric division and an outpatient cancer center.

Participants. A multidisciplinary team characterized key elements of the oral chemotherapy process using healthcare failure modes and effects analysis (HFMEA).

Intervention(s). Oral chemotherapy computerized provider order entry (CPOE) was developed and implemented.

Main Outcome Measure(s). Pharmacist-intercepted oral chemotherapy prescribing errors over a 24-month period (before) and over a 6-month period (after) were analyzed according to the error type (errors in clinical decision making, errors in transcription or errors related to prescribing policy). The incidence of prescribing errors prior to and following CPOE implementation was compared by calculating the odds ratio (OR) and the 95% confidence interval (CI).

Results. HFMEA hazard analysis revealed seven potential failure modes, with the highest hazard scores in the prescribing and administration components of the process. CPOE implementation significantly ($P = 0.023$) reduced prescribing error risk by 69% [OR (95% CI) = 0.31 (0.11–0.86)] and eliminated certain types of errors that can lead to significant patient harm.

Conclusions. Prescribing oral chemotherapy is a failure mode with significant risk of inducing patient harm. CPOE is effective in reducing prescribing errors of oral chemotherapy and should be considered part of a fail-safe process to improve safety.

Keywords: healthcare FMEA, oral chemotherapy, patient safety, computerized order entry

Introduction

Oral chemotherapeutic agents are characterized by narrow therapeutic indices and sometimes complicated dosing regimens. In the past 10 years, an increasing number of oral chemotherapy agents have been approved and the proportion of new oral chemotherapeutic agents in the development pipelines is increasing. Combined, this poses growing challenges to patient safety. Over the past decade, the need for multidisciplinary approach and continuous processes to improve

chemotherapy safety and reduce medication errors has been highlighted [1–3]. Despite safety risks, a survey of US comprehensive cancer centers found that fewer safety standards for oral chemotherapy agents have been adopted compared with infusion chemotherapy [4].

The objectives of this study were to assess the severity and probability of failures in the inpatient oral chemotherapy order, review and administration process in a large medical center using the healthcare failure modes and effects analysis (HFMEA) [5] and to investigate the impact of developing

oral chemotherapy computerized provider order entry (CPOE) on oral chemotherapy medication-prescribing errors.

Methods

Setting

This study was conducted at Rhode Island Hospital (RIH), Providence, RI, USA, an academic medical center affiliated with Warren Alpert Medical School at Brown University and a member of the Lifespan Healthcare system, as a part of an ongoing institution-wide quality-improvement program. The hospital is a 719-bed multidisciplinary tertiary care institution that has a pediatric division (The Hasbro Children's Hospital) and an outpatient cancer center. The institution uses a closed-loop medication safety process including CPOE, a pharmacy interface, a clinical decision support system, a bar-code point-of-care electronic nursing administration check and an automated drug-dispensing system [6]. Oral chemotherapy agents are ordered using a chemotherapy paper order form, and prescribing is restricted to oncologists or attending physicians in the area of practice for non-oncology indications. The decision to use oral chemotherapy order forms instead of CPOE was driven by concerns of potential prescribing errors, e.g. inadvertent selection of a sound-a-like oral chemotherapy agent (methotrexate instead of metoclopramide) and erroneous dosing schedule [methotrexate once daily instead of once weekly for treatment of rheumatoid arthritis (RA)]. At that time, customization of the CPOE with advanced functionalities and safeguards was not feasible and oral chemotherapy CPOE was viewed as a compromise to patient safety compared with paper order.

Oral chemotherapy process flow and HFMEA analysis

A team led by the director of pharmacy services and comprised seven physicians (three adult and pediatric oncologists, a rheumatologist, a dermatologist, a chief medical resident and a medical informatics), seven certified oncology nurses and clinical nurse managers, four pharmacists and one quality specialist was assembled to review and evaluate oral chemotherapy order, review, administration and monitoring process in all settings: inpatient and outpatient, pediatrics and adults. The team identified various ways in which each element of the process might fail. Failure modes were defined, and for each failure mode, values were assigned to two characteristics of each failure mode: severity and probability. A severity index describes the outcomes of failure and can assume one of the four values: minor (score = 1) indicates no injury to the patient, need for increased level of care or length of stay; moderate (score = 2) indicates increased length of stay or increased level of care for 1–2 patients; major (score = 3) indicates permanent lessening of body function for one patient or increased length of stay or increased level of care for three or more patients; and catastrophic (score = 4) indicates death or permanent loss of

function for any patient [5]. A probability index describes the likelihood of occurrence of the failure mode and can assume one of the four values: remote (value = 1) indicates that it is unlikely to occur in the next 5 years; uncommon (value = 2) indicates it is possible to occur in the next 5 years; occasional (value = 3) indicates a probability of occurrence of once or twice a year and frequent (value = 4) indicates that it is likely to occur immediately or at several times a year [5]. Score assignments were reached by consensus from the team participants.

A hazard score for each failure mode was calculated by multiplying the severity and probability indices yielding values ranging between 1 as a minimum value and 16 as a maximum hazard score [5]. A decision tree was used to determine whether further action was needed based on a hazard score ≥ 8 , detectability and presence of existing control measures. Remedial interventions for failure modes with the highest hazard scores were developed and prioritized.

Development of oral chemotherapy CPOE and drug therapy guidelines

The HFMEA team recommended instituting oral chemotherapy CPOE with enhanced safety features and functionalities. The clinical pharmacy team along with information service developed the oral chemotherapy CPOE for 21 formulary oral chemotherapeutic agents. The decision to develop oral chemotherapy CPOE was aided by recent institutional technology enhancements [6] and the ability to institute CPOE safety measures. The institution utilizes Siemens Invision CPOE system (Siemens USA, Malvern, PA, USA). The specialized prescribing pathway for oral chemotherapy required customized programming by the institution's information services. Specialized oral chemotherapy order sets with recommended laboratory orders, and ordering screens were developed to provide the functional requirements necessary to prevent inadvertent prescribing and were implemented at RIH as well as other affiliated hospitals in the healthcare system. Prescribers were notified of the change in prescribing policy from paper orders to CPOE prescribing. Training for prescribers was not required due to the ease of accessibility and intuitiveness of the oral chemotherapy CPOE. Drug-specific guidelines were developed for the oral chemotherapy agents by clinical pharmacy services, reviewed by a focus group that included oncology physicians and nurses and were approved by the institution's Pharmacy and Therapeutics (P&T) Committee.

Assessment of the effect of oral chemotherapy CPOE and guidelines on prevented medication errors

The RIH pharmacist intervention database was utilized to isolate pharmacist-intercepted oral chemotherapy prescribing errors over a 24-month period reflecting pre-oral chemotherapy CPOE error rate and over a 6-month period reflecting post-oral chemotherapy CPOE error rate.

The definition used for prescribing errors in this study has been widely adopted and identifies a prescribing error as an unintentional significant reduction in the probability of treatment being timely and effective *or* an increase in the risk of harm when compared with generally accepted practice [7, 8]. Prescribing errors were categorized as either errors in clinical decision making, or errors in transcription or errors related to prescribing policy. Errors in clinical decision making included prescribing a drug in the wrong dosing schedule/duration with a significant potential for patient harm, prescribing a drug with existing laboratory values that may lead to serum levels above recommended range or increased risk of adverse effects, prescribing a drug in a dose that would lead to sub-therapeutic serum levels and prescribing a drug for which there is no indication. Errors of transcription included lack of clarity in drug name or route of administration as well as drug name omission. Errors related to adherence to prescribing policy included orders by unauthorized prescribers.

Statistical analysis

The incidence of oral chemotherapy prescribing errors prior to and following CPOE implementation was compared by calculating the odds ratio (OR) and the 95% confidence interval (CI). Fisher's exact test was used to calculate the probability of a significant difference, and the significance level was set *a priori* at $\alpha = 0.05$.

Results

Process flow and HFMEA analysis

An overview of the oral chemotherapy order, review and administration process is presented in Fig. 1. The process was divided into seven major steps: prescription, transmission, validation, order entry, order review, administration and monitoring. The inpatient hazard analysis revealed 72 potential failure modes with varying levels of frequency of occurrences and severity of outcomes. A total of seven failure modes had the highest possible hazard score of 16, indicating the combined potential for frequent occurrences (likely to occur immediately and in the short term) and a catastrophic outcome (death or permanent loss of function). Table 1 displays the failure modes with the highest hazard scores and corresponding team recommendations. Prescription, order review, administration and monitoring steps of the overall process were associated with the failure modes of the highest combined severity and probabilities. Handwritten orders, orders written and signed by unauthorized prescribers, orders reviewed and administered by non-certified nurses were associated with the potential of causing severe outcomes. The team recommended implementing oral chemotherapy CPOE with appropriate safeguards, a process of order review by certified nursing staff, providing education to nurses about the importance of improving oral chemotherapy safety and educating patients about adverse effects associated with oral chemotherapy drugs.

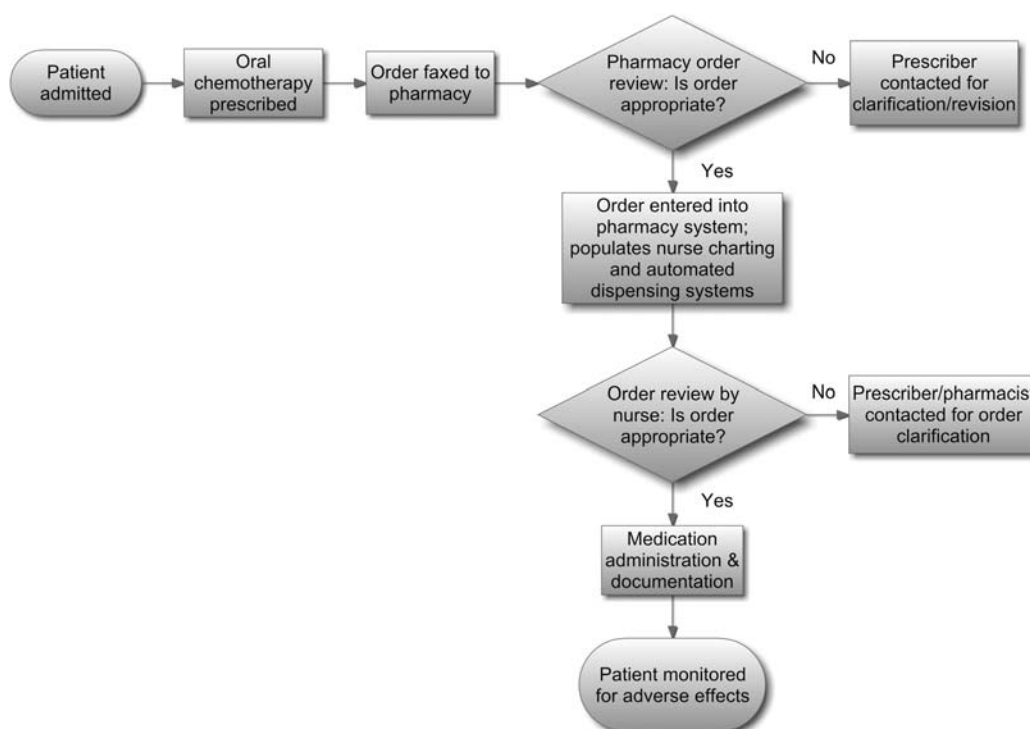


Figure 1 Inpatient oral chemotherapy process flow diagram prior to CPOE implementation. Steps in the process include prescription, transmission, validation, nursing review, medication administration and documentation and patient monitoring.

Table 1 Failure modes associated with the highest hazard scores as identified by HFMEA and corresponding team recommendations

Process	Failure modes with hazard score = 16	Team recommendations
Oral chemotherapy prescribed	Order handwritten Order written by unauthorized prescriber	Implement oral chemotherapy computerized prescriber order entry with appropriate safeguards
Oral chemotherapy order reviewed by nurse	Order reviewed by non-certified nurses for policy compliance and appropriateness Errors in dosing or frequency not detected	Implement a process to provide order review by a chemotherapy-certified nurse for new and revised orders prior to administration Develop medication guidelines containing dosing information, adjustments, precautions and contraindications
Medication administered and documented	Barcode identification is bypassed	Educate nurses about the importance of barcode identification to oral chemotherapy safety
Patient monitored for adverse effects	Patient does not understand or retain instructions	Develop patient information pamphlets

Table 2 Overview of oral chemotherapy CPOE multifaceted safety enhancements and safeguards

Oral chemotherapy CPOE safety enhancements and safeguards			
Prescribers Order entry is restricted to attending physicians within scope of practice	Clinical Programmed drug-specific maximum dose alerts and frequency options	Monitoring Field entries to indicate protocol number when appropriate	Pharmacy and nursing review Chemotherapy description is built into drug name; enhancing pharmacy and nursing review
Residents are restricted from accessing ordering screen and given guidance on subsequent action CPOE displays alert that the selected drug is a chemotherapeutic agent	Clinical decision support (e.g. drug interactions, conflicting laboratory values and allergy history) Programmed dose default to standard minimum dose, default frequencies and duration Entry fields for treatment cycle day and links to drug therapy guidelines	Drug-specific guidance is provided on appropriate laboratory monitoring Laboratory orders built into order set	Specific alerts regarding critical laboratory values and dosing regimens appear during order review Eliminates the need for order transcription

Oral chemotherapy CPOE and drug guidelines development

Features and safeguards of the oral chemotherapy CPOE are presented in Table 2. A representative oral chemotherapy, methotrexate, order set and specialized ordering screens are presented in Fig. 2. A representative drug guideline for methotrexate is presented in Table 3. The CPOE prescribing safeguards include exclusion of unauthorized prescribers, e.g. residents and physician assistants, and system alerts that indicate that the selected drug is a chemotherapeutic agent. Clinical safeguards include instituting drug-specific defaults to standardized minimum dosing, frequency and duration, drug-specific maximum dose alerts and entry fields for cycle number and day in cycle. Monitoring safeguards include

prompting orders for appropriate laboratory indicators for review. Pharmacy and nursing review safeguards include labeling the drug as chemotherapy agents, and specific critical laboratory values, drug interactions and dosing regimen appear during review. Drug therapy guidelines are directly linked to the order set and provide clinical guidance regarding dosing in different indications, as well as recommended monitoring.

The impact of oral chemotherapy CPOE on prescribing errors

Oral chemotherapy prescribing errors prior to and following CPOE implementation are presented in Table 4. There was approximately a 69% reduction in the risk of prescribing errors as result of CPOE as determined by an OR of 0.31

Medication

☐ Methotrexate CHEMO SS **Chemotherapy label in drug name**

Pick All that Apply

☐ Methotrexate Sodium (Methotrexate) 0.5 Milligram By Mouth*
Enter Cycle day and Protocol number in designated fields

☐ Methotrexate Sodium (Methotrexate) 2.5 Milligram By Mouth
Enter Cycle day and Protocol number in designated fields

Laboratory

Pick all that apply

☐ BUN

☐ CBC w Diff and Plt

☐ Liver Panel

☐ Creat Level

Recommended lab monitoring

Links to drug guidelines

*** Orderset Cautions ***

This medication is chemotherapy. Chemotherapy may only be ordered by authorized prescribers. For example hematology and oncology Attendings and other Attendings within the scope of their specialty. For home medications please review with original prescriber, continuing treatment orders must be placed in POM by an authorized prescriber.

*** Links to Clinical Information ***

Methotrexate oncology guidelines
Methotrexate RA and Psoriasis Indications

Write New Order : Pharmacy Medication (Formulary)

METHOTREXATE CHEMO

*Dose: 2.5 *Units: MG Dose info: 3053

*Route: BY MOUTH Entry fields for cycle, day and protocol { Cycle Day Protocol }

*How often? Once See Dir

? q 1XD every QMON QTUES QWED QTHU QFRI QSAT QSUN

*Start: Next Routine Schedule Time Dose Now/ Then Routine Schedule Times STAT

on: 10/26/2010 after 1546

*Priority: *Reason or Indication

*Ordering Party: BP#:

Figure 2 Methotrexate CPOE order set and prescribing screen. Recommended laboratory monitoring, links to oncology, RA and psoriasis drug therapy guidelines are among the features included in the order set. 'Methotrexate Chemo' and the once-weekly default frequency are among the clinical safety features in the ordering screen along with entry fields for cycle, day and protocol number, if applicable.

and a 95% CI between 0.11 and 0.89. CPOE implementation has resulted in a significant reduction ($P = 0.023$) in total prescribing errors. The most prevalent type of prescribing errors was lack of adherence to prescribing policy and accounted for 38% of total errors. Following CPOE implementation, lack of adherence to prescribing policy was still documented and was attributed to the use of paper order forms in lieu of CPOE. Prior to CPOE, errors of drug dose and/or schedule that can lead to patient harm comprised 33% of total prescribing errors. Examples of this type of error include once-daily methotrexate dosing instead of once-weekly dosing for RA treatment and temozolomide orders that deviated from the standard 5 days every 28 days regimen. CPOE implementation eliminated this type of prescribing errors over a 6-month period. When adjusted for the number of oral chemotherapy orders in the preimplementation ($n = 412$) and postimplementation ($n = 126$) study periods, prescribing errors were documented for approximately 9 orders per 100 orders in the preimplementation phase compared with approximately 3 orders per 100 orders in the postimplementation phase. Prior to CPOE, hydroxyurea was associated with the most prescribing errors

(26%), followed by methotrexate and mercaptopurine (associated with 24% of prescribing errors, each). Among the drugs associated with errors of drug dose and/or schedule that can lead to patient harm, methotrexate accounted for 46% of these errors. Following CPOE implementation, no prescribing errors involving methotrexate were documented.

Discussion

Oral chemotherapy medication safety practices and awareness continue to be suboptimal. In a survey to the US oncology pharmacists, ~32.4% of responders did not consider oral chemotherapy as requiring the same safety concerns as parenteral therapy [9]. While several guidelines have addressed the safe handling and administration of antineoplastic agents [10–12], few have proposed standards to reduce oral chemotherapy prescribing errors. This is reflected in the fact that majority of institutions did not have special requirements for oral chemotherapy prescriptions [4]. Quality-improvement programs are designed to fulfill the 'above all-do no harm' axiom [13]. In our institution, and in

Table 3 Oral methotrexate guidelines including restrictions, dosing and monitoring recommendations

	Oral methotrexate guidelines	
	RA and psoriasis	Oncology
Restrictions and approved prescribers	Must be ordered by a rheumatology or dermatology attending physician using the electronic physician's order management system	Must be ordered by an oncology attending physician using the electronic physician's order management system
Dosing: adults	<p>Prior to initiating therapy, pharmacists and nurses must verify indication and dosing frequency</p> <p>RA: 7.5 mg once weekly or 2.5 mg every 12 h for three doses/week; recommend not to exceed 25 mg/week</p> <p>Psoriasis: 2.5–5 mg/dose every 12 h for three doses given weekly or 10–25 mg given once weekly</p>	<p>Head and neck cancer: 25–50 mg/m² once weekly</p> <p>Trophoblastic neoplasms: 15–30 mg/day for 5 days; repeat in 7 days for three to five cycles</p> <p>Mycosis fungoides (cutaneous T-cell lymphoma): 5–50 mg once weekly or 15–37.5 mg twice weekly</p>
Dosing: pediatrics	Juvenile RA: 5–15 mg/m ² given once weekly as a single dose or three divided doses given 12 h apart	Acute lymphoblastic leukemia (remission maintenance): 20–30 mg/m ² twice weekly
Renal dosing adjustment	Estimated CrCl <50 ml/min: dose reduction should be considered	
Hepatic dosing adjustment	Estimated CrCl <10 ml/min: drug should be avoided	
	Bilirubin: 1–5 mg/dl or ALT/AST >3 ULN: administer 75% of dose	
Monitoring	<p>Bilirubin >5 mg/dl: avoid use</p> <p>Prior to administering initial hospital dose, analysis of WBC, serum creatinine, platelets and LFTs should be obtained from the laboratory.</p> <p>Methotrexate dose should not be administered and prescriber should be contacted to withhold treatment/adjust dosage if any of the following is present:</p> <ul style="list-style-type: none"> • platelets <150 000 • WBC <4 • ALT/AST >3-fold from ULN or bilirubin >3 mg/dl • significant deterioration in renal function 	

response to increased awareness about the safety risks associated with oral chemotherapy, we have proactively examined the oral chemotherapy process with a special focus on prescribing and administration using HFMEA.

HFMEA is a tool that aims to systematically evaluate, either prospectively or retrospectively, a complex process, identify elements in such process with the risk of causing harm and prioritizing remedial interventions. The Joint Commission on Accreditation of Healthcare Organizations recommends the use of HFMEA as a proactive risk assessment tool [14, 15]. However, few reports are found in the literature describing successful applications of HFMEA in medicine [16–20], and more specifically in improving chemotherapy safety [21–23]. In one report, pediatric chemotherapy errors were significantly reduced following implementation of a CPOE as a result of HFMEA recommendations [21]. In another report, HFMEA was applied prospectively to successfully improve chemotherapy safety

[22]. HFMEA should not be relied upon as the only tool for quality improvement by healthcare institutions, as the ability to identify and evaluate failure modes in any process significantly depends on the team reviewing the process [24]. In our institution, HFMEA was employed, as a component of an overall systematic approach, to analyze the failure modes in the oral chemotherapy process flow, and interventions were implemented to mitigate risk and improve patient safety. The failure modes with the greatest hazard scores included prescribing and administration. Our findings are in agreement with another published HFMEA analysis conducted in a pediatric oncology ward where prescribing and administration had the highest hazard scores and were the focus of the interventions [25].

Using an oral chemotherapy CPOE, we were able to demonstrate the ability to reduce total prescribing errors and potentially eliminate certain error types that can cause patient harm. CPOE technology has been shown to reduce

Table 4 Effect of oral chemotherapy CPOE implementation on prescribing errors

Error type	Number of prescribing errors (percentage)		Prescribing error rate (per 100 orders)	
	Preimplementation (24 months)	Postimplementation (6 months)	Preimplementation	Postimplementation
Prescribing a drug in a wrong dosing schedule/duration that can significantly lead to patient harm	13 (33)	0 (0)	3.16	0
Prescribing a drug in a dose where clinical laboratory values indicates likelihood that it would lead to serum levels above recommended range or increase risk of adverse effects	3 (8)	1 (25)	0.72	0.79
Prescribing a drug in a dose with the correct frequency, but is predicted to give serum levels below the desired therapeutic range	2 (5)	1 (25)	0.48	0.79
Prescribing a drug in a dose with the correct frequency, but exceeds the maximum recommended range for the indication	2 (5)	0 (0)	0.48	0
Prescribing a drug for which there is no indication	1 (3)	0 (0)	0.24	0
Omission of drug name, unclear drug name or route of administration	3 (8)	0 (0)	0.73	0
Prescribing policy not followed	15 (38)	2 (50)	3.64	1.59
Total ^a	39 (100)	4 (100) ^b	9.47	3.17

^aThe results were based on total oral chemotherapy orders of 412 during the preimplementation period and on total oral chemotherapy orders of 126 during the postimplementation period.

^bCalculated OR (95% CI) = 0.31 (0.11–0.86), $P = 0.023$ using Fisher's exact test.

medication errors, including chemotherapy medication errors [26], as well as adverse drug events rate [27]. The extent of CPOE effectiveness in improving patient safety is highly variable and depends on study design and quality as well as the implemented functionality [28, 29], and can be limited by methodological flaws [30]. The safeguards incorporated in our CPOE design are unique, address different failure scenarios and are a significant improvement compared with the paper-based process previously implemented in our institution. The CPOE design and implementation should not be considered in isolation of other approaches, e.g. improving training and competency of prescribers and improving communication among healthcare providers, as no single intervention creates a 'fail-safe' process needed to improve oral chemotherapy safety.

This study is limited by the lack of a repeat HFMEA analysis following CPOE implementation to demonstrate a reduction in prescribing failure risk. Furthermore, our analysis focussed on inpatient oral chemotherapy process and did not extend to the outpatient ambulatory setting. To our knowledge, no published description of the use of HFMEA to improve oral chemotherapy safety exists. The process of design and implementation of an oral chemotherapy CPOE

can serve as a model for adoption by other healthcare institutions to improve oral chemotherapy safety.

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