Chemotherapy-related risk management toward safe administration of medications: Apply failure mode and effects analysis to reduce the incidence of chemotherapy errors

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Abstract: Chemotherapy is considered a high-risk procedure where system failures are more likely to occur. Failure mode and effects analysis (FMEA) is a systematic, multidisciplinary team-based approach to error prevention. We described our experience of using FMEA as a prospective risk-management technique throughout the chemotherapy process. The occurrence, detectability and severity were assessed. Fifteen potential risk factors associated with 10 failure modes were identified. Improvement measures were proposed according to risk priority number. A computerized physician order entry (CPOE) and complete prescription audit system (CPAS) were introduced to reduce potential risks during chemotherapy. Introduction of this system was associated with a decrease from 2.60% to 0.60%. As a result, FMEA is a useful tool to evaluate potential risk in healthcare processes.

Keywords: failure mode and effects analysis (FMEA), chemotherapy process, risk analysis, computerized physician order entry (CPOE), complete prescription audit system (CPAS)

INTRODUCTION

Medical risks generally refer to uncertainties that may cause damage or disability or unsafe events that could possibly occur in the health care process. Such risks include medical malpractice, medical errors, medical accidents, complications and medical disputes or litigations. Medical risks can cause physical and mental harm to patients and result in varying degrees of financial loss both to the patient and the hospital. This could also affect normal hospital operation and the confidential relationship between doctors and patients. Chemotherapy is regarded as a high-risk process because of multiple drug uses, provision of dangerous compounds, high utilization rate, and complexity processes. These risks associated with the processes of prescription writing, preparation, mixing, dispensing and administration. All these risks may lead to serious consequences, even death (Dizon *et al*. 2005). Little attention has been focused on available proactive methodologies that exist to predict such failures.

Compared with other risk management tools, FMEA was a proactive tool and performs a more detailed analysis, and the primary goal is to avoid error by systematically examining (Chandonnet *et al*. 2013). It uses brainstorming, expert assessment, cause-effect diagrams and other methods to assess potential failure modes. The research team collected and categorized failure data, filled out FMEA forms, and determined potential consequences of each failure mode. The severity, possibility of occurrence and detectability of consequences of the current system were assessed. Risk priority numbers (RPNs) were calculated and key failure points were determined by sorting the different failure modes and their impacts on the system. The goal was to be able to take appropriate measures to prevent failures and reduce the occurrence of risk events in the system (Teoh and Case. 2005). It was introduced to the health care industry in the 1990s in the development of critical systems, pharmaceuticals and the prevention of medication delivery errors in hospitals (Herzer *et al*. 2009). In 2001, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) selected FMEA as the basic method for improving patient safety standards (Duwe, *et al*. 2005). In this way, predictive assessment of medical risks could be performed before adverse events occurred, and corresponding measures could be taken to reduce the occurrence of poor medical outcome effectively. FMEA has been successfully applied across a wide range of healthcare settings including radiology (Thornton *et al*. 2011), trauma (Day *et al*. 2011), blood transfusion (Burgmeier 2002), intravenous drug administration (Shebl *et al*. 2009), drug administration (Chiozza and Ponzetti 2009) and pediatrics (Chandonnet *et al*. 2013).

Only one published studies discussed the application of HFMEA in chemotherapy administration. It found that the CPOE system reduced potential risks in the chemotherapy process (Cheng *et al*. 2012). The present study was conducted at the First Affiliated Hospital, Zhejiang University, a tertiary first-class hospital with 2500 beds that was certified by the Joint Commission International (JCI) in 2013. The hospital has established a complete quality management system that is in accordance with the

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JCI criteria. The Department of chemotherapy was committed to improve patient care and safety through the use of FMEA and to prevent and minimize the risks of errors in chemotherapy process. The purpose of this article was to demonstrate the application of a collaborative process of using FMEA as a prospective risk management technique in the whole complex chemotherapy at a tertiary first-class hospital in China.

Method

Failure modes and effects analysis (FMEA)

Failure mode and effects analysis was performed to analyze potential risk factors occurring during a course of chemotherapy and to assess the existing failure modes. The following are the key steps in the FMEA process:

Steps in FMEA

1. Team formation

A multidisciplinary team consisted of nine members specializing in medicine, nursing, information technology, pharmacy, and medical management. The team should include subject matter experts and an advisor to ensure that various perspectives are considered.

2. Defining the topic

The topic should be of high risk or worthy to invest resources in.

3. Defining the process flow

The FMEA team draws a full description of the chemotherapy medication process and constructs a flow diagram. The diagram should identify all sub processes and consecutively enumerate these sub process steps.

4. Failure modes

Next, our team brainstormed to identify failure modes for each of the sub steps. A failure mode is a probable error that could occur at each sub step.

5. Hazard analysis and detection of failure causes

All possible failure modes for each of the sub processes should be listed and numbered consecutively. Various sources and tools can be used for identifying potential failure modes, such as brainstorming, cause-and-effect diagramming, root cause analysis, working experience, and reference to other medical clinics.

Brainstorming consisted of identifying sub-processes where errors might occur, factors associated with failure, and their potential causes and impacts. Brainstorming of potential failure modes that may cause risks during chemotherapy was performed. Risk priority number (RPN) was calculated for each factor. The RPN was calculated using the possibility of occurrence (O: 1 -10 points, from extremely unlikely to occur → extremely likely to occur), detectability (D: possibility of being detected after failure occurs, 1 -10 points, from extremely unlikely to be detected → extremely likely to be detected) and severity (S: potential consequences of failure, 1 -10 points, from not severe → extremely severe). The RPNs (Severity X Occurrence X Detection) calculated by all team members were averaged and the mean RPNs of different sub-processes were sorted. Severities of different sub-processes were also sorted. RPNs and severities were combined for determining which sub-processes and steps needed to be improved.

There were several degrees of tolerance to consequences caused by drug risks: negligible risks, levels 1-3; tolerable risks, levels 4 -6 (low degree); risks that need attention, levels 8-12 and risks that cannot be tolerated, levels 12-20 level (high degree). For risks that need attention, methods of risk management should be applied and timely measures should be taken to eliminate or reduce these risks. For risks that cannot be tolerated, measures should be taken to completely eliminate the risks.

The root cause was identified from previous failures and the extent of their damages during chemotherapy was determined. Analysis of root cause was a systematic problem-solving process, which included confirming and analyzing the source of the problem, finding solutions, and developing preventive measures. Specific process reengineering was conducted and corresponding measures were taken to eliminate or reduce the risk of critical failure modes.

6. Actions and outcome measures

As next steps, for each failure mode, risk reduction strategies were identified. This helped us identify action plans for causes with all levels of hazard scores. In addition, the individuals responsible for implementing and ensuring the completion of each action should be identified.

In this study, FMEA was applied as a first step to form a multidisciplinary team, which consisted of nine members specializing in medicine, nursing, information technology, pharmacy and medical management. The first meeting was held in November 2011 to discuss the FMEA process and time-line. Particular focus was placed on ensuring expert representation from various disciplines to bring out the most relevant perspectives and ideas. Roles and responsibilities were clearly identified. The pharmacy administration and therapeutics committee, nursing department and pharmacy department jointly plotted a process flowchart characterizing the administration of chemotherapy. Information technology specialists collected data and were responsible for technical support and computer use. The medical management staff oversaw the process of conducting the FMEA. The team meticulously followed each step of the FMEA to understand the current processes, identify failure points,

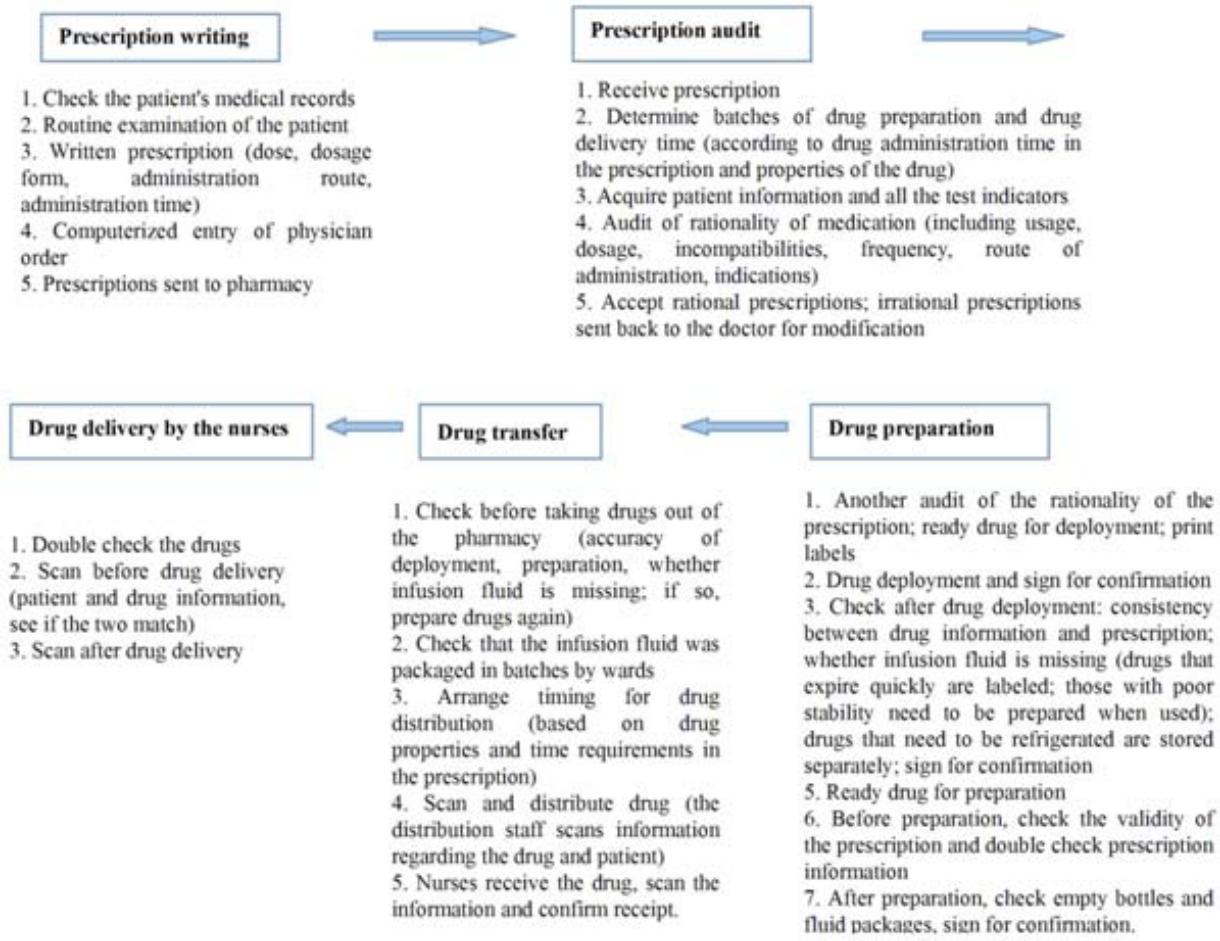

Fig. 1: Flow chart of chemotherapy administration to hospitalized patients.

and prioritize areas of focus. Then, the topic should be of high risk or worthy to invest. The FMEA team drawn a full description of the chemotherapy medication process and constructed a flow diagram. The diagram should identify all sub processes and consecutively enumerate these sub process steps. Next, our team brainstormed to identify failure modes for each of the sub steps. A failure mode was a probable error that could occur at each sub step. All possible failure modes for each of the sub processes should be listed and numbered consecutively. Various sources and tools could be used for identifying potential failure modes, such as brainstorming, cause-and-effect diagramming, root cause analysis, working experience, and reference to other medical clinics. As next steps, for each failure mode, risk reduction strategies were identified. This helped us to identify action plans for causes with all levels of hazard scores. In addition, the individuals responsible for implementing and ensuring the completion of each action should be identified. Preventive measures were taken in the processes of prescription writing, prescription audits, drug preparation, drug transfer and drug administration to reduce the incidence rate of adverse reactions during chemotherapy process.

Recommended computerized physician order entry (CPOE) system

A computer-assisted physician order entry system was launched in August 2012. The functions of this system were divided into four regions on the computer monitor based on the needs of the end-users: (1) upper left panel, patient information region; (2) upper middle panel, latest examination report region; (3) upper right panel, review of physician orders; (4) bottom panel, physician order entry (fig. 2A). Based on end-user requirements, the system had to perform the following: (1) check past medication administration sheets, (2) calculate the dosage of medications based on body surface area, (3) search for laboratory information system in order to provide liver or renal function insufficiency alerts and (4) automatically show medication quantity (vial, ampule, or pill) according to required dosages.

Physicians at our hospital must use the CPOE system to order chemotherapy prescriptions. Handwritten prescriptions were prohibited. In preparation for surgery, the physician entered the patient's height and weight and the system automatically calculated the body surface area.

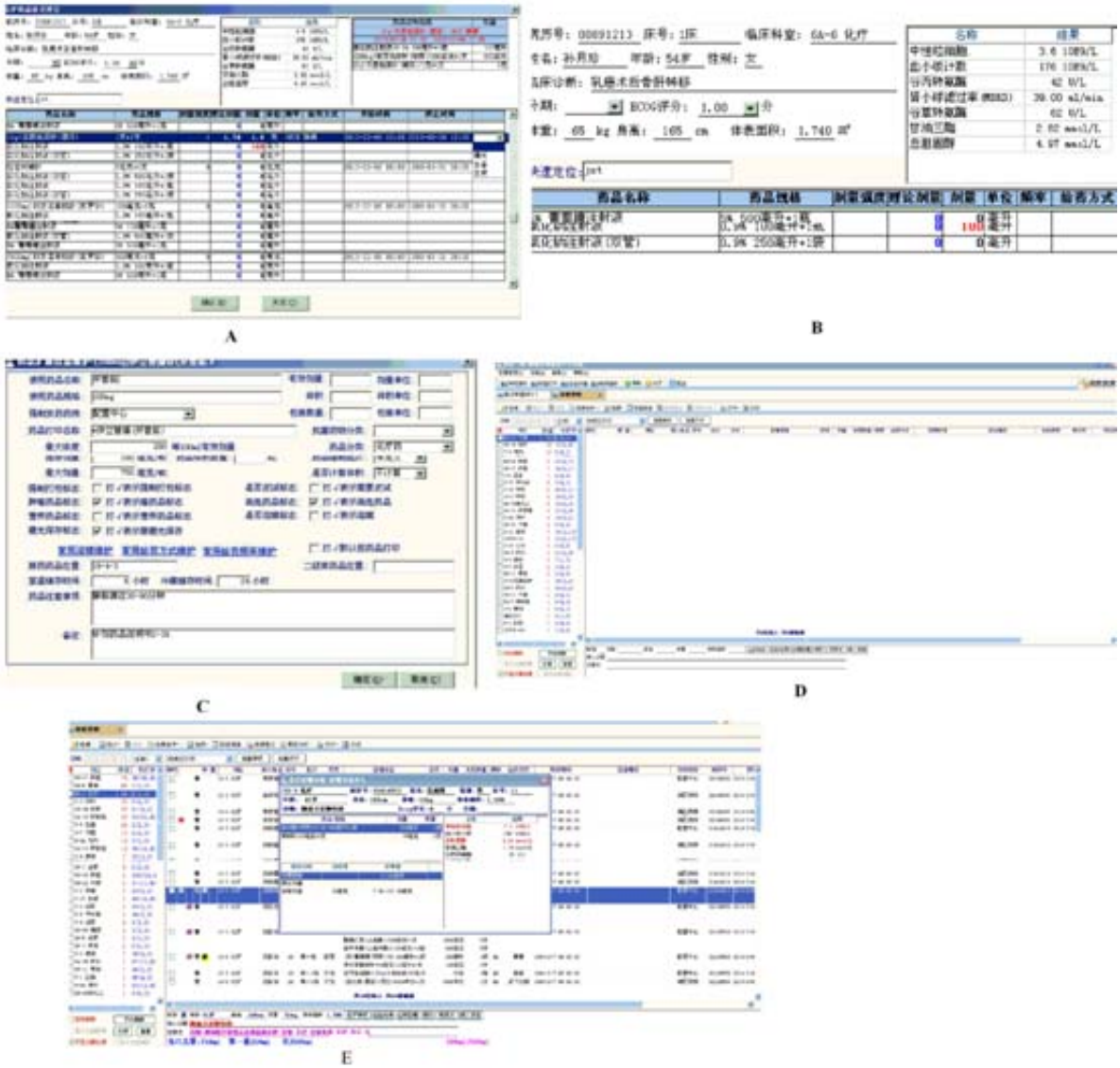

Fig. 2 Computerized physician order entry (CPOE) and complete prescription audit system (CPAS). A, The system read height and weight information and automatically calculated body surface area; B, After entering the dose intensity, the system automatically calculated the dose based on body surface area; C, Background maintenance including drug solvent, frequency of administration, route of administration and safe dose; D, The initial CPAS interface; E, Complete prescription audit of information indicators, chemotherapy plan, dose and other information.

After dose intensity was entered, the system automatically calculated the dose based on body surface area. If the dose intensity or total dose, administration frequency, or the route of administration fallen outside of the default range, an alert window will automatically pop up suggesting a correction. Information regarding drug solvent, administration frequency, administration route and safe dosing was displayed in the background. This information was periodically updated (fig. 2B, 2C).

Recommended complete prescription audit (CPAS) system

Its main function of CPAS is to perform a second review of the patient's condition and drug delivery plan, including pharmacist recommendations if requested. The CPAS provides an automatic alert for abnormal liver and kidney function indices and abnormal changes in hemogram.

The chemotherapy audit key in the CPAS allows easy access to patient information, imaging data and progress notes. Drug dose is automatically calculated based on the height and weight of the patient and the theoretical dosage intensity of the chemotherapy drug. This calculated dose

is compared to the physician order. Drug delivery frequency, drug solvent and administration route are automatically calculated.

Table 1: Failure modes, causes, effects with hazard scores

Process	Failure Modes	Causes	Effects	S	P	HS	D
Prescription	Prescription error	Errors in dose calculation	Error medication	6	2	12	N
		Errors in entering the prescription	Error medication	6	2	12	N
	Computerized prescribing errors	Patient information missing	Error prescription	4	3	12	N
		Information systems lack reminder	Error prescription	3	2	6	N
Prescription audit	Physician prescription error	Lack prescription audit	Error prescription	4	3	12	N
	Important information not verified	Patients with incomplete information	Delay prescription	4	3	12	N
		Incomplete information systems alert settings	Error prescription	3	2	6	N

Table 2: Failure Modes, Causes, Effects With Hazard Scores (Continued)

Process	Failure Modes	Causes	Effects	S	P	HS	D
Dispensing	Dispensing error	missing warning signs in label	Error administration	2	3	6	N
		No responsibility to the people in dispensing	Error dispensing	4	3	12	N
	Formulated dosage errors	Incomplete information systems alert settings	Error dispensing	2	3	3	N
		Drug signs blur	Error adminstration	4	3	12	N
Transportation	Delivered to the wrong ward	Transportion delays in the wrong place	Error transportion	2	3	6	N
	Infusion leakage	Overflow in the way	Error transportion	2	2	4	N
Administration	unnoticed	Chemotherapy extravasation	Error adminstration	3	2	6	N
	Time errors	Administration order is unreasonable	Error adminstration	2	2	4	N

RESULTS

A chemotherapy flowchart was constructed by the FMEA research team. The chart included detailed steps of each sub-process including prescription writing, prescription audits, drug preparation, drug transfer and drug administration. The complete process of drug administration during chemotherapy was illustrated in fig. 1. Our FMEA team characterized the detailed chemotherapy process for hospitalized patients and used brainstorming to identify potential failure modes. The possibility of the actual occurrence of each failure mode (O) and the severity of the consequence associated with each failure (S) were assessed by all team members independently. A total of 15 potential risk factors that could lead to 10 failure modes were identified during prescription writing, prescription audit, drug preparation, drug transfer, and drug delivery (See tables 1-6). Preventative measures were taken based on the corresponding risk priority number. As illustrated in table 7, the incidence rate of adverse drug events during chemotherapy among hospitalized patients was reduced from 2.60% to 0.60%. These measures effectively reduced the incidence of adverse events during chemotherapy.

There were three potential high-risk factors associated with the process of prescription writing, dose calculation errors, physician order entry errors and missing patient information. As shown in table 7, the error rate in prescription writing was 1.47%. The FMEA team proposed that the medical, pharmacy, nursing and information departments should jointly take two measures, which were approved by the hospital management. First, a computerized physician order entry system (CPOE) was developed where chemotherapeutic drugs could be ordered (fig. 2). Second, a complete prescription audit system (CPAS) was developed as illustrated in fig. 2. This system automatically evaluated the suitability of prescriptions ordered. The system included the patient's basic information, drug selection, drug dose, dosage form and administration frequency. Nearly 85% of clinical prescriptions for chemotherapy were entered using the CPOE system in our hospital. A satisfaction survey evaluated its accuracy, reliability,

Table 3: Failure modes, causes, person responsible and control measures

Process	Failure Modes	Causes	Person Responsible	Action
Prescription	Prescription error	Errors in dose calculation	Information department	Adopt CPOE
		Errors in entering the prescription	Information department	Adopt CPOE and enhance training
	Computerized prescribing errors	Patient information missing	Information department	Adopt CPOE and improve patient information
		Information systems lack reminder	Information department	Chemotherapeutic medicine with red "danger" in doctor interface

Note: CPOE: Computerized physician order entry.

Table 4: Failure modes, causes, person responsible and control measures (continued)

Process	Failure Modes	Causes	Person Responsible	Action
Prescription audit	Physician prescription error	Lack prescription audit	Pharmacy department	Adopt (CPAS)
	Important information not verified	Patients with incomplete information	Information department	Adopt CPOE and supply and improve patient-related information, such as imaging and biochemical markers
		Incomplete information systems alert settings	Information department	Pop chemotherapeutic prescription audit tools in red in the interface

Note: CPOE: computerized physician order entry; CPAS: complete prescription audit system.

Table 5: Failure modes, causes, person responsible and control measures (continued)

Process	Failure Modes	Causes	Person Responsible	Action
Dispensing	Dispensing error	Missing warning signs in label	Pharmacy department	Add the chemotherapeutic warning markers
		No responsibility to the people in dispensing	Pharmacy department	Set clear job, use the entire barcode traceability, automated dispensing systems
	Formulated dosage errors	Incomplete information systems alert settings	Information department	Chemotherapeutic medicine prescription in red italics in swap interface
		Drug signs blur	Information department	Improved visual management of chemotherapeutic medicine

maintainability, and efficiency showed that satisfaction rate was 84.6%.

After the CPOE system was used for half a year, failure modes and their potential causes in the process of prescription writing were re-evaluated. It was concluded that the use of the CPOE system was an effective measure for eliminating or reducing the risks of critical failure. The error rate decreased significantly from 1.47% before CPOE system use to 0.20% with the system (Chi square test, $p<0.001$, table 8).

DISCUSSION

Drug administration is a complex process and there are large individual variations. CPOE is only a tool that helps standardize physician orders. It cannot prevent incorrect or erroneous physician orders. The CPAS is an auxiliary tool for the CPOE system that is used for automatic auditing of chemotherapy drugs. This system had corrected about 90% of physician prescription errors.

Medical risk management has become an important part of patient safety programs and hospital management. FMEA was used to identify risk related factors and the most critical steps requiring modification in order to improve patient safety.

Risks factors including drug administration violations, lack of double-checking of drugs being administered and lack of confirmation of patient identity were improved using FMEA. Another study of the application of FMEA in the management of drug administration (Voeffray *et al*. 2006; Markert *et al*. 2009) found that the error rate of

Table 6: Failure modes, causes, person responsible and control measures (continued)

Process	Failure Modes	Causes	Person Responsible	Action
Transportion	Delivered to the wrong ward	Transportion delays in the wrong place	Logistics sector	Pre-job training and performance appraisal
	Infusion leakage	Overflow in the way	Logistics sector	Implement overflow management and prevention measures
Adminstration	Unnoticed	Chemotherapy extra vasation	Nursing department	Warning system
	Time errors	Administration order is unreasonable	Nursing department	Doctor define each batch of administration; Centralized preparation in PIVAS; Nurse strictly enforced; Cooperation in various sectors

Note: CPOE: computerized physician order entry; CPAS: complete prescription audit system; PIVAS: pharmacy intravenous admixture services.

Table 7: Reduction in chemotherapy prescription errors (2012.1-2112.11)

Procedure	Before FMEA (2012.1-6)			After CPOE (2012.10.22-11.21)			P Value
	Prescription	Error	Error Rate (%)	Prescription	Error	Error Rate (%)	
Prescription	21589	318	1.473	5950	12	0.202	P<0.001 63.674
Dispensing	21589	179	0.829	5950	8	0.134	P<0.001 33.375
Transportion	21589	33	0.153	5950	8	0.134	P=0.744 0.106
Adminstration	21589	32	0.148	5950	6	0.131	P=0.383 0.760
Total			2.603			0.601	

Table 8: Comparisons of chemotherapy prescription error

	Before CPOE			After CPOE			
	Prescription	Error	Error Rate (%)	Prescription	Error	Error Rate (%)	P value
Total	21589	318	1.473	5950	12	0.202	P<0.001, 63.674
Division Chemotherapy Med.	1174	335	2.98	464	3	0.65	P=0.005, 7.999
Hematology	3775	37	0.98	127	24	0.31	P=0.022, 5.232
Liver Center	665	13	1.95	423	2	0.47	P=0.041, 4.177
Gastroenterology	328	7	2.13	252	1	0.39	P=0.075, 3.162

chemotherapy was 0.45%-15% (mean 3.34%) before the use of CPOE and decreased from 15% to 5% after its implementation. Previous studied the use of healthcare FMEA in preventing errors in chemotherapy administration and found that the CPOE system reduced potential risks in the chemotherapy process, significantly reducing errors in chemotherapy prescriptions from 3.34% to 0.40% (Cheng *et al*. 2012)

The chemotherapy process includes prescription writing, prescription audit, drug preparation, drug transfer and drug administration by nurses. There are risks for errors in each of these steps, which are dangerous to the patients. Some errors may cause substantial harm, and some may even be lethal. We identified 15 potential risk factors that contributed to 10 failure modes during chemotherapy drug administration. In the sub-process of writing physician order, errors in dose Calculation, errors in entering prescription and item missing in patient information are three potential high-risk factors. The introduction of CPOE and CPAS decreased the error rate in physician orders from 1.47% to 0.20%. CPAS is an auxiliary tool in the CPOE system. Its use was found to prevent over 95% of errors in physician orders. Eliminating potential risks in prescription writing, prescription audits, drug preparation, drug transfer and drug administration resulted in a decrease in the incidence rate of adverse reactions to chemotherapeutic drugs among hospitalized patients from 2.60% to 0.60%.

CONCLUSION

In conclusion, chemotherapy is vulnerable to human error owing to its complexity nature. Guided by FMEA, our

experiences show that CPOE and CPAS could effectively improve patient safety by fundamentally re-engineering the chemotherapy medication processes. Evidently, FMEA is a useful tool to evaluate potential risks in healthcare processes, and CPOE and CPAS is an effective technology to prevent human errors.

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