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Application of Failure Mode and Effects Analysis in risk management of drug therapy in an intensive care unit

Aplicación del Análisis Modal de Fallos y Efectos en la gestión de los riesgos de la terapia farmacológica en una unidad de cuidados intensivos

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Resumen

Objetivo: Utilizar el Análisis de Modos de Falla y Efectos (FMEA) para gestionar los riesgos en la terapia farmacológica prescrita dentro de una Unidad de Cuidados Intensivos (UCI).

Metodología: Esta investigación-acción, que integra métodos cualitativos y cuantitativos, evalúa las prescripciones médicas en una UCI Coronaria (CECOR) en Fortaleza, Brasil, utilizando FMEA. El estudio implica definir el proceso, formar un equipo multidisciplinario, realizar un diagnóstico situacional, evaluar los modos de falla (MF) con índices de Severidad (S) y Detección (D), monitorear la Prevalencia de los MF (P) y calcular el Coeficiente de Priorización (PC). Cada MF está acompañado de recomendaciones farmacéuticas. Se diseñan actividades de educación basadas en el PC para los profesionales de CECOR.

Resultados: En el diagnóstico situacional se evaluaron 170 prescripciones y 60 MF, con las categorías principales siendo las interacciones medicamentosas (39,7 %) e incompatibilidades (30,0 %). Las causas asociadas con estos errores fueron multifactoriales. Respecto a la respuesta del equipo ante un FM, se determinó que el 36,7% de los FM serían aceptados con seguimiento. Durante el monitoreo de prevalencia, el 63,3 % de los tipos de MF ocurrieron 837 veces, con alta severidad (50,0 %) y baja detección (55,3 %). Los MF más frecuentes fueron la ausencia de forma farmacéutica (29,4 %) y dosis (8,8 %).

Conclusión: El FMEA facilita identificar, clasificar y priorizar los riesgos en la terapia farmacológica en CECOR, subrayando su efectividad como herramienta de calidad para mejorar la seguridad del paciente.

Palabras-clave: Análisis de Riesgo; Seguridad del paciente; Calidad de los Servicios de Salud; Cuidados críticos.

Abstract

Objective: To utilize Failure Mode and Effects Analysis (FMEA) to manage risks in prescribed drug therapy within an Intensive Care Unit (ICU).

Methodology: This action research, integrating qualitative and quantitative methods, assesses medical prescriptions in a Coronary ICU (CECOR) in Fortaleza, Brazil, using FMEA. This study involves defining the process, forming a multidisciplinary team, conducting a situational diagnosis, evaluating failure modes (FMs) with Severity (S) and Detection (D) indices, monitoring FM Prevalence (P), and calculating the Prioritization Coefficient (PC). Each FM is accompanied by pharmaceutical recommendations (RF). Continuing education activities are designed based on the PC for CECOR professionals.

Results: In the situational diagnosis, 170 prescriptions and 60 FMs were assessed, with primary categories being drug interactions (39.7 %) and incompatibilities (30.0 %). Causes are multifactorial. Regarding the team's response to an FM, it was determined that 36,7 % of the FMs would be accepted with monitoring. During prevalence monitoring, 63.3 % of FM types occurred 837 times, with high severity (50.0 %) and low detection (55.3 %). Most frequent FMs were absence of pharmaceutical form (29.4 %) and dose (8.8 %).

Conclusion: FMEA facilitates identifying, classifying, and prioritizing risks in drug therapy at CECOR, underlining its effectiveness as a quality tool for enhancing patient safety.

Keywords: Risk Assessment; Patient Safety; Quality of Health Care; Critical Care.

Highlights

Quality tools are needed to monitor risks associates with drug therapy in Intensive Care Unit.

Drug interactions and incompatibilities are the major failure modes for risks associated with drug therapy in Intensive Care Unit

FMEA can enhance patient safety within Intensive Care Unit.

Introduction

The complexity of care within an Intensive Care Unit (ICU), which includes taking care of critically ill patients, mastering advanced technologies, and the need for quick decision-making, can make health care very vulnerable to errors.[1] The intricate pharmacological therapies, often composed of a signifi-

cant number of high-alert drugs, increase the risks of medication errors, drug interactions and incompatibilities, adverse reactions, and, consequently, adverse outcomes for the patient.[2,3]

Since the publication of the report "To Err is Human" in 2000, governmental and non-governmental agencies have mobilized to develop strategies for the control and prevention of adverse events arising from healthcare practices. This report estimated that up to 98,000 deaths per year in the United States of America (USA) are caused by adverse events and about half would have been preventable. Since then, terms such as quality of care, patient safety, and medication errors have been increasingly disseminated among health professionals and institutions.[4]

Recent data reveals that one in ten patients hospitalized in US hospitals experiences an adverse event, and a medication error occurs each day during hospitalization.[5,6] In the ICU, the frequency of medication errors among adult patients is variable, with an average of 105.9 per 1,000 patient days.[7] In Brazil, a study conducted in an ICU showed a prescription error rate of 43.5 %, encompassing errors in dose, frequency of administration, diluent, and time of infusion, across seven different therapeutic classes.[8] Given this scenario, the World Health Organization (WHO) acknowledges adverse care events as a significant public health issue, emphasizing the necessity of employing quality tools to prevent them.[9]

Quality tools play a vital role in healthcare by helping to identify, understand, and mitigate risks associated with the medication process.[10] Among the various tools available, the Failure Mode and Effects Analysis (FMEA) stands out for its proactive nature and multidisciplinary approach. FMEA enables the prevention of adverse events before their initial occurrence, thereby promoting the development of best practices.[11] In evaluating the medication process using FMEA, involving pharmacists is recommended due to their ability to contribute significantly to the management of this process, given its direct correlation with medical prescription and drug dispensing.[12]

The utilization of the FMEA tool for analyzing potential risks within the medication process in an intensive care setting offers valuable insights into existing care challenges and enhances teamwork and patient safety practices.[13] Despite its importance, there is a shortage of studies employing this tool for analyzing risks in the medication prescription process in ICU, particularly within the national literature.[14,15] Hence, the aim of the study was to apply the FMEA tool to manage the risks associated with prescribed medication therapy within an ICU setting in Brazil. The implementation of the FMEA was characterized by identifying, classifying and prioritizing risks associated with drug therapy.

Methods

This study adopts an action-research approach utilizing a mixed method (qualitative and quantitative) to evaluate medical prescriptions within the Coronary Intensive Care Unit (CECOR) of a public hospital in Fortaleza, Brazil, using FMEA[11] from July 2017 to January 2018. The researchers actively engaged in constructing the observed reality, monitoring decisions, actions, and proposed activities of the involved professionals while analyzing their knowledge. The study was conducted with respect for human dignity and initiated after receiving approval from the National Research Ethics Committee (Opinion Number: 062804/2017).

The hospital under study is part of the Sistema Único de Saúde (SUS) and is a highly complex reference center for heart and lung diseases, renowned for teaching and research. It is integrated into the Sentinel Network and operates with its own Risk Management, in direct collaboration with the Agência Nacional de Vigilância Sanitária (ANVISA). CECOR comprises eight active beds, predominantly serving cardiac patients, and maintains a multidisciplinary care team consisting of doctors, nurses, physiotherapists, and nutritionists. During the study period, the hospital did not possess an electronic prescription system or electronic medical records.

The study progressed through six phases, as illustrated in Figure 1. The study population across all phases consisted of adult patients (age ≥ 18 years) of both genders, admitted to CECOR any day of the week, with at least one medication prescribed, irrespective of diagnosis and length of stay. Sociodemographic and clinical patient data were excluded from the study, as it solely focused on describing

specific issues identified in the drug prescription process, for which sociodemographic data are not relevant.

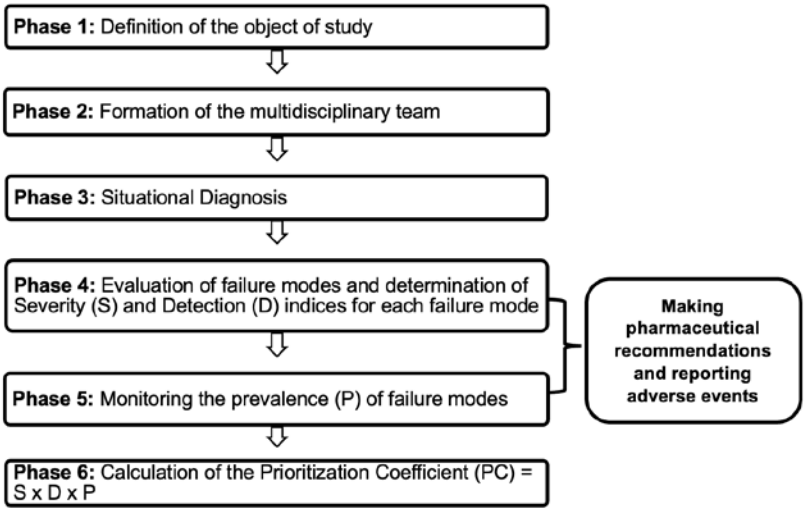

Figure 1. Methodological flow of the study carried out in a Coronary Intensive Care Unit of a public hospital in Fortaleza, Brazil, from July/2017 to January/2018.

The medication process is intricate, involving various health professionals and encompassing prescription, dispensing, preparation, and administration of medications. Each of these stages entails a series of interconnected decisions and actions that can pose clinical risks, directly or indirectly linked to the actions of these professionals. In this study, the medication process is evaluated from a clinical perspective, with the primary object of study being the daily medical prescription.

At CECOR, the medication process initiates with the release of the medical prescription by the attending physician or medical resident. Following its release, the unit nurse schedules the prescribed medications and forwards the duplicate prescription to the pharmacy service for validation by the clinical pharmacist. After validation, the pharmacy technician processes and dispenses the prescribed medications at CECOR, where a nursing technician receives and verifies the medications before administering and monitoring them.

The study followed the recommended methodology of the FMEA tool.[16] Phase 1 entailed defining the process to be analyzed: the potential risks in CECOR's medical prescriptions, along with their causes, effects, and contingency measures. This phase was facilitated by a pharmacist from the institution with expertise and interest in employing the FMEA tool.

Phase 2 involved forming a multidisciplinary team, as advocated by the literature, to ensure diverse perspectives representing all professionals and managers involved. Unfortunately, a representative from the nursing assistant category couldn't participate due to work overload and time incompatibility with the research meetings. The team members were selected based on their proactive engagement in the drug prescription process, comprising a day laborer, a pharmacist, a nurse, and a head nurse.

In Phase 3, a situational diagnosis of risks associated with medical prescriptions was conducted, employing an exploratory and retrospective approach. Medical prescriptions from Monday to Friday in July 2017 were directly analyzed from patient medical records regarding need, effectiveness, and safety. Prescription data were cross-referenced with information from package inserts, scientific articles, and platforms such as Micromedex® and UpToDate®.[17,18] The identified risks were termed Fail-

ure Modes (FMs), representing clinical situations posing a degree of uncertainty regarding established goals and introducing risk.[14]

Phase 4 involved evaluating and categorizing the identified FMs. The FMs were classified into different categories, including drug interactions and incompatibilities, lack of necessary information, absence of dose adjustment in special situations (e.g., renal failure), and lack of essential guidelines for administering a drug. The multidisciplinary team identified potential causes for each category. Furthermore, considering the effects of each FM, the team assigned Severity (S) and Detection (D) scores ranging from 1 to 10, where 10 signifies the most critical situation (Table 1). Additionally, the care team's stance toward each FM was determined: whether to accept the risk and monitor or not accept it and notify risk management as a sentinel event. A sentinel event refers to a severe, undesirable occurrence in a hospital, compromising patient care and involving death, injury, or physical or psychological risk.[8]

Table 1. Criteria for classification of Severity (S) and Detection (D) of the failure modes found in the study carried out in a Coronary Intensive Care Unit of a public hospital in Fortaleza, Brazil, from July/2017 to January/2018.

Index	Severity (S)[1]	Detection (D)[2]
1	Minimum. The patient does not realize that the exposure occurs.	Very tall. It will certainly be detected. The protocol is well designed, has good adherence, and can prevent FM[3] from proceeding.
2	Small. Slight change in the patient's clinical picture, a symptom or sign, with laboratory alteration.	Alta. Provavelmente será detectado. O protocolo existe com tripla checagem em locais diferentes, porém com baixa adesão.
3	Small. Slight change in the patient's clinical condition, a symptom or sign, with clinical alteration.	High. It will likely be detected. The protocol exists with double checking, but with low adherence.
4	Moderate. Significant deterioration of the patient's clinical condition, more than one symptom or sign, with discontinuation of therapy.	Moderate. It probably won't be detected, although there is a double check in place. Need for active search.
5	Moderate. Significant deterioration of the patient's clinical condition, more than one symptom or sign, with the addition of a therapy.	Moderate. It probably won't be detected despite on-site checking. Need for active search.
6	Moderate. Significant deterioration of the patient's clinical condition, more than one symptom or sign, with addition of more than two or more therapies.	Moderate. It will probably not be detected, because although there is a check, there is an overload of work. Need for active search.
7	High. Significant deterioration of the patient's clinical condition with intervention to maintain the patient's life with a low risk of death/sequelae.	Low. High probability of not being detected. Absence of protocol, verification, and no active search. The FM[3] can be identified by all professionals in the sector.
8	High. Significant deterioration of the patient's clinical condition with intervention to maintain the life of the patient with medium risk of death/sequelae.	Low. High probability of not being detected. Absence of protocol, verification, and no active search. FM[3] can be identified by some industry professionals.
9	High. Significant deterioration in the patient's clinical condition. Intervention to maintain the life of the patient at high risk of death/sequelae.	Low. High probability of not being detected. Absence of protocol, verification, and no active search. FM[3] cannot be identified by industry professionals.
10	Very tall. Significant deterioration of the patient's clinical condition with permanent functional damage (motor, sensory, psychological) alteration of two systems, very high risk of death.	Minimum. It certainly won't be detected. Absence of protocol, verification, and no active search and difficult to recognize. Only an expert would check and recognize.

[1]Severity: considers how much the occurrence of FM can compromise the functionality and/or completeness of the patient and applies only to the effect. [2]Detection: is an assessment of the ability or chance of the current controls to identify the FM, before the component causes damage; to predict its possibility, we characterized the policy of action of its professionals in relation to a failure mode. [3]FM: Failure Mode. Table was based on Duwe B et al.,[13].

In phases 3 and 4, active interaction among group members took place during five face-to-face meetings, totaling 12 hours, held in August and September 2017. The technique employed was Brainstorming, allowing the participants to freely explore ideas and insights, leveraging their knowledge and hierarchical positions within the care team.[19] All meetings were conducted in one of the hospital's auditoriums, with the participation of all members. Due to other institutional demands and time constraints for the team members, organizing additional meetings was not feasible.

Phase 5 involved monitoring the occurrence of identified FMs using a checklist-type form, examining prescriptions released on Mondays, Wednesdays, and Fridays from October 2017 to January 2018. This phase was managed by a pharmacist within the multidisciplinary team, possessing experience in utilizing FMEA and leading the study. In this phase, the monthly Occurrence (O) of FMs was determined by tallying the number of times each FM appeared in medical prescriptions.

In Phase 6, the Prioritization Coefficient (PC) was calculated—an absolute number aiding in ranking the identified FMs and guiding prioritization of corrective interventions. The PC was computed by multiplying the Severity indices (S) x Occurrence (O) x Detection (D), thus PC= SxPxD. The PCs were classified as low if up to 50, medium if within the range of 51 to 100, and high if above 101.

To facilitate visualization and identification of the most critical FMs, data were analyzed using the Pareto diagram. This diagram, based on the Pareto principle, presents occurrences in descending order combined with the calculation of cumulative frequency. The principle asserts that 80 % of consequences stem from 20 % of causes, aiding in focusing efforts on the most significant issues to enhance service quality.[20]

All identified FMs were promptly communicated to the care team through Pharmaceutical Recommendations (PRs) at the time of identification to minimize the prevalence of these risks. PRs were categorized based on their significance, classified as appropriate, indifferent, or inappropriate according to Farré *et al*.(2000).[21] Appropriate PRs were further rated as extremely significant, very significant, or significant. Conversely, inappropriate PRs were rated as simply inappropriate, very inappropriate, or extremely inappropriate.[21] Each PR was also assessed for acceptability, considering PRs followed by prescription adjustments as accepted. Unacceptable FMs were accompanied by adverse event notifications to the institution's risk management.

Leveraging the PC, periodic continuing educational activities were devised and implemented with CECOR professionals. These initiatives occurred from November 2017 to January 2018, concurrently with the evaluation of FM occurrence. They involved distributing lists highlighting prevalent drug interactions and incompatibilities, alongside monthly meetings with the team of medical residents, focusing on best practices in drug prescriptions.

Medications were evaluated according to the High Vigilance Medication (HVM) categorization established by the Institute for Safe Medication Practice (ISMP)—a non-governmental, independent, non-profit organization dedicated to promoting safe practices in medication use and health products in Brazil.[22] The study results were initially recorded using a specific tool and then compiled and analyzed using Microsoft Office Excel® 2013 software. Continuous variables were presented as median (central tendency) and range (dispersion) due to data non-normality, while categorical variables were expressed as absolute numbers and percentages.

Results

Situational diagnosis

In the situational diagnosis, a total of 170 prescriptions were evaluated, resulting in the identification of 63 potential FMs. Three types of drug-drug interactions were excluded from the list of FMs as they presented no risk of harm to the patients; in fact, these interactions were beneficial for patients with heart disease: carvedilol and amiodarone (n=1), carvedilol and dobutamine (n=1), and furosemide and vasopressin (n=1). Consequently, 60 FMs remained, encompassing at least 40 different drugs, with 27.5 % (n=11) classified as high-alert drugs.

The primary categories of FMs identified during the situational diagnosis were drug interactions (39.7 %; n=22), drug incompatibilities (30.0 %; n=18), and the necessity for dose adjustment based on renal function (15.0 %; n=9). Qualitative analysis of the FMs revealed their causes to be multifactorial, often involving similar circumstances across various error categories. Major causes included lack of knowledge about medications, slips, and memory lapses, limited therapeutic alternatives, risk-benefit ratio consideration favoring benefits, inadequate patient monitoring, transcription errors, attempts to summarize prescriptions, addiction to prescription practices, disregard for good prescription standards, and inexperience of resident physicians (Table 2).

Table 2. Categories of failure modes and their possible causes identified in the study carried out in a Coronary Intensive Care Unit of a public hospital in Fortaleza, Brazil, from July/2017 to January/2018.

Categories (n=60)	n (%)	Possible causes
Drug interactions	22 (36.7 %)	Lack of knowledge about medications; Memory slips and lapses; Absence of therapeutic alternatives; Consider that the benefits outweigh the risks; Incipient safety culture;
Drug incompatibilities	18 (30.0 %)	Lack of knowledge about medications; Memory slips and lapses; Absence of therapeutic alternatives; Consider that the benefits outweigh the risks; Incipient safety culture;
No dose adjustment for renal function	9 (15.0 %)	Lack of knowledge about medications; Memory slips and lapses; Inadequate patient monitoring; Incipient safety culture; Work overload;
Lack of necessary information	8 (13.3 %)	Transcription errors; Attempt to summarize the prescription; Prescription addictions; Inexperience of resident physicians; Absence of an electronic prescription system; Safety culture of the incipient medication process; Work overload;
Inadequate reconstitution	2 (3.33 %)	Lack of knowledge about medications; Memory slips and lapses; Incipient safety culture;
Presence of non-standard acronyms in the institution	1 (1.7 %)	Transcription errors; Attempt to summarize the prescription; prescription addictions; Ignores good prescription rules; Inexperience of resident physicians; Incipient safety culture;

Considering the effects of the 60 identified FMs, the majority were categorized as having very high severity (53.3 %; n=32), moderate severity (8.3 %; n=5), and minimal severity (48.3 %; n=29) and high (30.0 %, n=18) detection. The mean severity and detection indexes were calculated as 7.6 ± 2.9 and 6.1 ± 4.2, respectively. Concerning the response of the care team to an FM, it was determined that a certain percentage (36,7 %, n=22) of the FMs would be accepted with monitoring. necessitating adverse event notifications. Individual contingency measures were established for each FM, considering the recommendations available on the Micromedex® platform.

Occurrence monitoring

In the phase of monitoring the occurrence of FM, it was observed that 63.3 % (n=38) of the FM types identified in the situational diagnosis occurred a total of 837 times. Regarding the categories, drug interactions were the most prevalent (34.2 %; n=13), followed by lack of information (21.1 %; n=8), lack of dose adjustment for renal function (21.1 %; n=8), drug incompatibilities (21.1 %; n=8), and inadequate reconstitution (2.6 %, n=1) (Table 3).

Table 3. Characterization of the failure modes that occurred in the monitoring phase (n=38) in relation to their effects, conducts, contingency measures and in terms of Severity (S), Detection (D), monthly average of Occurrence (O) and Prioritization Coefficient (PC), in the study carried out in a Coronary Intensive Care Unit of a public hospital in Fortaleza, Brazil, from July/2017 to January/2018.

Category	Failure modes	Possible effect	Conduct	Contingency measure	S[12]	O[13]	D[14]	CP[15]	Classification
Missing information	CIP[1] Heparin Guidance	Heparin sedimentation and loss of effectiveness.	Accept with monitoring	Move the solution every 4 hours and replace it every 24 hours.	10	7.25	10	725	High
Missing information	Infusion speed	Dispensing error, ineffectiveness, ADR[2] and increased costs.	Do not accept	Do not accept. Risk of ADR[2].	10	6.5	10	650	High
Missing information	Pharmaceutical form (PF)	Wrong dispensing and dangerous administration.	Do not accept	Request inclusion of information.	1	61.5	10	615	High
Drug Interaction	Amiodarone + Atorvastatin	Increased concentration of atorvastatin, increasing adverse effects (myopathy, rhabdomyolysis).	Accept with monitoring	Monitor for CK[3] and muscle pain symptoms. If CK[3] increases, replace with pravastatin.	6	9.75	10	585	High
Drug Interaction	Amiodarone + Fentanyl	Inhibition of fentanyl metabolism, with an increase in its plasma concentration, and hemodynamic alteration, may enhance the bradycardic effect.	Do not accept	Avoid concomitant use. Consider replacing fentanyl with propofol or dexmedetomidine. Monitor for signs of respiratory depression, hypotension, bradycardia, and decreased cardiac output.	7	7	10	490	High
Dose Adjustment for Renal Function	Metoclopramide	Increased risk extrapyramidal syndrome.	Do not accept	If CrCl[4]<40 mL/min, administer 50 % of the recommended dose.	5	8.25	10	412.5	High
Dose Adjustment for Renal Function	Ranitidine	Increased risk of thrombocytopenia.	Do not accept	Use 1 tablet or 1 ampoule a day or replace with omeprazole.	5	5.5	10	275	High
Inadequate reconstitution	Hydrocortisone	Loss of stability and therapeutic ineffectiveness if diluted in distilled water.	Do not accept	Reconstitute the medicinal product in a diluent sent by the manufacturer, in PS[5] or GS[6].	10	2	10	200	High
Missing information	Dose	Dispensing the wrong dose and dangerous administration.	Do not accept	Request inclusion of information.	1	18.5	10	185	High
Non-standard acronym	Prescription drug with acronym	Misinterpretations and mismanagement.	Do not accept	Request the use of institutional acronyms only.	10	15.5	1	155	High
Drug incompatibility	Dobutamine + Furosemide	Therapeutic ineffectiveness, risk of lumen obstruction.	Accept with monitoring	Accept up to concentrations of dobutamine - 4mg/ml in PS[5] and furosemide - 1mg/ml PS[5]	10	6.5	2	130	High
Drug incompatibility	Ranitidine + Amiodarone	Therapeutic ineffectiveness, risk of lumen obstruction.	Do not accept	Administer the drugs in double or triple lumen catheters to avoid contact and precipitate formation.	10	6.5	2	130	High

Category	Failure modes	Possible effect	Conduct	Contingency measure	S[12]	O[13]	D[14]	CP[15]	Classification
Drug incompatibility	Amiodarone + Furosemide	Therapeutic ineffectiveness, risk of lumen obstruction.	Do not accept	Administer the drugs in double or triple lumen catheters to avoid contact and precipitate formation.	10	4.25	2	85	Medium
Missing information	Dilution	Ineffectiveness, if use of incompatible diluent and increased costs.	Do not accept	Request inclusion of information.	10	0.75	10	75	Medium
Drug Interaction	Amiodarone + Clonazepam	Inhibition of clonazepam metabolism, with an increase in its plasma concentration.	Accept with monitoring	Reduce the clonazepam dose by half and monitor for signs of benzodiazepine toxicity.	9	6	1	54	Medium
Drug Interaction	Phenytoin + Food	Decrease in the plasma concentration of phenytoin, due to interaction with dietary calcium and protein, reducing effectiveness.	Do not accept	Space out administration as much as possible and/or pause the diet one hour before or after administration. If a patient with nasoenteral feeding-tube, consider administering phenytoin via intravenous.	8	0.75	9	54	Medium
Drug Interaction	Amiodarone + Amlodipine	Reduced amlodipine metabolism may enhance the hypotensive effect.	Accept with monitoring	Monitor heart function.	10	0.5	10	50	Low
Missing information	BIC[7] Furosemide Guideline	Loss of stability (when in high concentration, diluted in PS[5] and exposed to light) and effectiveness.	Accept with monitoring	Photoprotect the solution when using a double dose: 20 ampoules + 60 ml PS[5].	10	0.5	10	50	Low
Dose Adjustment for Renal Function	Midazolam	Increased risk prolonged sedation, even after discontinuation.	Do not accept	Reduce dose by 50 %.	5	1	10	50	Low
Drug Interaction	Clopidogrel + Omeprazole	Reduction in the formation of the active metabolite of clopidrogrel, reducing effectiveness.	Do not accept	Avoid concomitant use. Replace omeprazole with another PPIs[7] (e.g. rabeprazole, lansoprazole, pantoprazole) or ranitidine.	5	9	1	45	Low
Dose Adjustment for Renal Function	Meropenem	Increased risk of neurotoxicity and diarrhea.	Do not accept	Adjust dose after 48h of treatment, according to ClCr[4].	5	0.75	10	37.5	Low
Drug Interaction	Captopril + Food	Decreased absorption of captopril, reducing effectiveness.	Do not accept	Administer captopril 1 hour before or 2 hours after meals. If dieting with nasoenteral feeding-tube, administer captopril during breaks.	2	16.5	1	33	Low
Drug incompatibility	Dobutamine + Pipe/tazo[8]	Therapeutic ineffectiveness, risk of lumen obstruction.	Do not accept	Administer medications through double or triple lumen catheters to avoid contact and precipitate formation.	10	1.25	2	25	Low
Dose Adjustment for Renal Function	Pipe/tazo[8]	Increased risk of diarrhea, hypernatremia, and hypokalemia.	Do not accept	Adjust dose after 48h of treatment, according to ClCr[4].	5	0.5	10	25	Low
Dose Adjustment for Renal Function	Gabapentin	Increased risk of peripheral edema, nausea, vomiting, drowsiness.	Do not accept	Adjust dose according to ClCr[4], If ClCr[4] < 30ml/min.	5	0.5	10	25	Low
Missing information	Route of administration	Dangerous administration or therapeutic ineffectiveness.	Do not accept	Request inclusion of information.	1	2.5	10	25	Low
Drug Interaction	Furosemida + Food	Reduced absorption of orally administered furosemide, reducing effectiveness.	Accept with monitoring	Administration of furosemide 1 hour before or 2 hours after meals.	1	1.75	10	17.5	Low

Category	Failure modes	Possible effect	Conduct	Contingency measure	S[12]	O[13]	D[14]	CP[15]	Classification
Drug incompatibility	Pipe/tazo[8] + Amiodarone	Therapeutic ineffectiveness, risk of lumen obstruction.	Do not accept	Administer the drugs in double or triple lumen catheters to avoid contact and precipitate formation.	10	0.75	2	15	Low
Drug incompatibility	Amiodarone + Impenem	Therapeutic ineffectiveness, risk of lumen obstruction.	Do not accept	Administer the drugs in double or triple lumen catheters to avoid contact and precipitate formation.	10	0.75	2	15	Low
Drug Interaction	Atorvastatin + Clopidogrel	Reduction of formation of the active metabolite of clopidrogrel, reducing effectiveness.	Accept with monitoring	Administer the drugs in double or triple lumen catheters to avoid contact and precipitate formation.	5	3	1	15	Low
Dose Adjustment for Renal Function	Teicoplanin	Increased risk of adverse reactions.	Do not accept	Adjust dose after 48 hours of treatment, according to ClCr[4].	5	0.25	10	12.5	Low
Dose Adjustment for Renal Function	Enoxaparin	Increased risk of thrombocytopenia	Do not accept	Replace with sodium heparin if CrCl[4] < 30ml/min.	5	0.25	10	12.5	Low
Drug Interaction	Amlodipine + Clopidogrel	Reduction of formation of the active metabolite of clopidrogrel, reducing effectiveness.	Accept with monitoring	Use with caution. Monitor the effectiveness of clopidogrel and consider adding cilostazol to therapy to reduce this effect.	10	1	1	10	Low
Drug incompatibility	Furosemide + Milrinone	Therapeutic ineffectiveness, risk of lumen obstruction.	Do not accept	Administer medications through double or triple lumen catheters to avoid contact and precipitate formation.	10	0.5	2	10	Low
Drug Interaction	Fluconazole + Midazolam	Increased plasma concentration of midazolam, increasing the risk of adverse reactions.	Accept with monitoring	Use with caution. Special attention for patients on hemodialysis. Consider reducing the midazolam dose and monitoring for signs of benzodiazepine toxicity.	3	0.25	10	7.5	Low
Drug incompatibility	Furosemide + Vancomicin	Therapeutic ineffectiveness, risk of lumen obstruction.	Do not accept	Administer medications through double or triple lumen catheters to avoid contact and precipitate formation.	10	0.25	2	5	Low
Drug Interaction	Fluconazole + Omeprazole	Increased plasma concentration of omeprazole, increasing the risk of adverse reactions.	Accept with monitoring	Use with caution. Adjust the dose of omeprazole if it is used in very high doses (e.g.: 240 mg/day). Monitor liver enzymes, headache, diarrhea, and abdominal pain.	2	0.75	1	1.5	Low
Drug Interaction	Metamizol + Captopril	Reduction of renal prostaglandin synthesis, diminish the antihypertensive effect and enhance the adverse/toxic effect of Nonsteroidal Anti-Inflammatory Agents.	Accept with monitoring	Monitor blood pressure, diuresis, and renal function.	5	0.25	1	1.3	Low

[1]CIP: Continuous Infusion pumps, [2]ADR: adverse drug reaction, [3]CK: creatinine kinase, [4]CrCl: Creatinine clearance, [5]PS: Physiological saline solution, [6]GS: glucose solution, [7]PPIs: Proton pump inhibitors, [8]Pipe/tazo: Piperacillin/Tazobactam, [9]Smx/tmt: Sulfamethoxazole and trimethoprim, [10]Amp/sulb: Ampicillin and sulbactam, [11]CNS: central nervous system, [12]S: Severity, [13]O: Occurrence, [14]D: Detection, [15]CP: Coefficient Priorization.

High-alert drugs were involved in 14.7 % (n=123) of the cases, with unfractionated heparin (23.6 %; n=29) and fentanyl (22.7 %; n=28) being the most frequent. The most common occurrences were lack of pharmaceutical form (29.4 %; n=246), lack of dose (8.8 %; n=74), interaction between captopril and

food (7.9 %; n=66), substitution of a drug name with an acronym (7.4 %; n=62), and interaction between amiodarone and atorvastatin (4.6 %; n=39). A majority of these detected FMs were categorized as having very high severity (50.0 %; n=19) and moderate severity (28.9 %; n=11), with minimal detection (55.3 %; n=21) (Table 4).

The PCs ranged from 1.3 to 725, with a mean of 88.5 ± 177.2. Notably, most occurrences had a medium PC (36.7 %; n=22). FMs with the highest PC included absence of guidance on the preparation of a Continuous Infusion Pump of heparin (PC=725), absence of infusion speed (PC=650), and absence of pharmaceutical form (PC=615). Conversely, FMs with the lowest PC encompassed drug interactions between metamizol and captopril (PC=1.3) and between fluconazole and omeprazole (PC=1.5), as well as drug incompatibility between furosemide and vancomycin (PC=5). Correlation analyses between occurrence and PCs revealed that fentanyl + amiodarone had a high PC but a low occurrence rate, whereas the interaction between captopril and food had a low PC despite its frequent occurrence (Table 4).

Table 4. Classification of severity, detection and prioritization coefficient of the failure modes identified in the study carried out in a Coronary Intensive Care Unit of a public hospital in Fortaleza, Brazil, from July/2017 to January/2018.

Variable (Average ± SD[a])	Classification	n (%)
Severity (7.1 ± 3.2)	Very high	29 (48.3)
	High	5 (8.3)
	Moderate	15 (25)
	Low	7 (11.7)
	Minimum	4 (6.7)
Detection (6.1 ± 4.2)	Very high	10 (16.7)
	High	18 (30.0)
	Low	3 (5.0)
	Minimum	29 (48.3)
Prioritization coefficient (PC) (88.5 ± 177.2)	High	12 (20.0)
	Medium	22 (36.7)
	Low	4 (6.7)
	Null[b]	22 (36.7)

[a]: Standar desviation. [b:]The null PC referred to the FM that did not occur in the monitoring phase.

Pareto analysis

Based on the Pareto diagram analysis of occurrence, the accumulated percentage indicated that the prioritized FMs should include absence of pharmaceutical form, lack of dose, interaction between captopril and food, use of non-standard acronyms, interaction between amiodarone and atorvastatin, interaction between clopidogrel and omeprazole, lack of dose adjustment for metoclopramide, and absence of guidance on Continuous Infusion Pump usage for heparin. Conversely, the Pareto analysis of Probability of Occurrence (PC) categorized as high and medium (n=17) highlighted the following prioritized FMs: absence of pharmaceutical form and dose, interaction between amiodarone and atorvastatin, interaction between fentanyl and amiodarone, lack of dose adjustment for metoclopramide and ranitidine, and inadequate reconstitution of hydrocortisone (Figure 2).

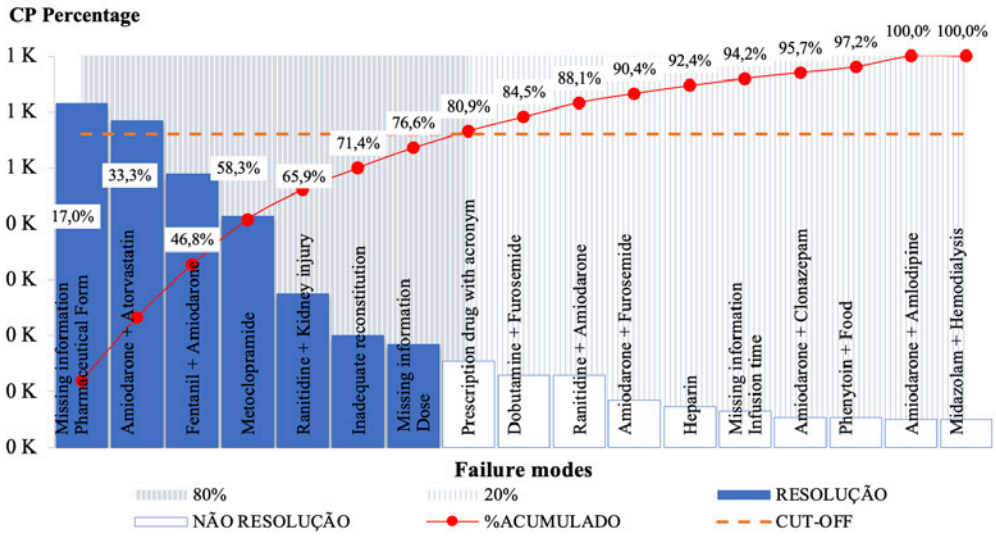

Figure 2. Pareto diagram of the high and average prioritization coefficients (PC) of the failure modes identified in the study carried out in a Coronary Intensive Care Unit of a public hospital in Fortaleza, Brazil, from July/2017 to January/2018.

Pharmaceutical recommendations (PR) and educational actions

During the study, 287 PRs were generated, most of which were accepted (70.0 %; n=201). The most frequent PRs were for the FMs absence of pharmaceutical form (56.1 %, n=161), absence of dose (10.8 %, n=31), use of abbreviations (7.3 %, n=21), adjustment of metoclopramide dose for renal function (3.8 %, n=11) and absence of infusion time (3.5 %, n=10). Communication of PRs predominantly occurred with the medical team (93.4 %; n=268), while involving the nursing team in 6.6 % (n=19) of the instances. Regarding the significance levels, it was noted that 63 % (n=182) of the RF were deemed appropriate and significant, 26 % (n=75) were classified as appropriate and very significant, and 11 % (n=30) were considered appropriate and extremely significant.

Discussion

Based on our research, this study stands as one of the pioneering investigations in Brazil to assess failure modes of drug prescriptions within an adult ICU utilizing the FMEA tool. Notably, it incorporates an additional analysis through the application of the Pareto diagram.[14] The utilization of this combined approach enabled the identification of the root causes and effects of failure modes, ultimately aiding in the prevention of minimization of potential risks. Consequently, this study underscores the efficacy and applicability of the FMEA tool in evaluating drug processes within the ICU.

The results of this work reveal a high frequency of FM (n=60) in prescriptions and a broad range of error categories. Additionally, the study demonstrates the usefulness of the Pareto diagram; however, it emphasizes that it can suggest varying failure modes for prioritization. In the existing literature, various studies have consistently reported prescription errors as the most prevalent type of error within the medication process, thus underscoring the criticality of their analysis.[23-25] Notably, other studies employing FMEA in the evaluation of medication use processes have reported varying numbers of FM, ranging from 40 to 90.[26-29] These discrepancies may be attributed to differences in the medication processes evaluated, the patient profiles included, and the safety culture within each institution.

The data presented suggest that a combination of strategies should be implemented in the ICU under study to enhance the safety of drug prescriptions. Additionally, these findings indicate a potential inadequacy in the safety culture and a notable absence of a pharmacist within the CECOR care team. Extensive literature emphasizes that the inclusion of intensive-care pharmacists significantly mitigates adverse events, reduces medication errors, and lowers mortality rates. This integration ultimately improves the overall quality and safety of healthcare in the ICU.[30]

In terms of error categories, drug interactions related to FM were found to be prevalent, both during the diagnosis phase (39.7 %) and in the monitoring of incidents (34.2 %). Comparable results have been reported by other researchers.[31-33] In clinical practice, potential drug interactions are often overlooked during the medical prescription process, posing a risk to patient safety, diminishing therapeutic effectiveness, causing toxicity, and prolonging hospitalization time.[25,34] These findings underscore the significance of vigilant monitoring for drug interactions and ensuring the training of the care team to effectively identify them.

Drug incompatibilities also exhibited a high prevalence in both the situational diagnosis (30 %) and the occurrence monitoring phase (21.1 %). Notably, drug incompatibilities are frequently observed in ICU settings, given that patients often necessitate simultaneous intravenous administration of multiple drugs, while the number of available venous accesses is limited.[35] Moreover, the situational diagnosis demonstrated that nearly 28 % of the drugs administered to patients within the FM category were classified as high vigilance, implying a heightened risk of causing severe harm if used incorrectly.[22] This aligns with findings by Miarons *et al*. (2021), who reported a similar rate of approximately 22 % of drugs within their patient registry being classified as high-alert.[36]

The occurrence monitoring phase and Pareto analysis highlighted that a significant issue lies in the absence of critical information in prescriptions, particularly concerning pharmaceutical form and dose, with a prevalence of 21.1 %. Addressing this issue in medication prescriptions should be a priority. A comparable study conducted in Italy reported a concerning 29.9 % of incomplete antimicrobial prescriptions, a rate deemed unacceptably high by the authors.[37] Likewise, Cho *et al*. (2014) found that over half of the prescriptions analyzed in their study contained at least one medication error, with 94 % attributed to inadequate information, such as the route of administration or the diluent.[38] The recurrent absence of necessary information in prescriptions underscores the imperative to enhance the safety culture within the institution and to raise awareness among professionals regarding the ramifications of not adhering to proper medical prescription guidelines.

Concerning potential causes, it was observed that they are multifaceted and that a single cause could be linked to various types of medication-related issues. The most prevalent causes were lack of knowledge about medications and occurrences of slips and memory lapses, aligning with findings from other studies and indicating the necessity for ongoing education.[26,39] Additionally, given that the institution under study is a teaching hospital, the observation of these types of causes is anticipated. The literature highlights that newly graduated physicians often grapple with insecurity and insufficient knowledge regarding medications.[40] Furthermore, factors such as work overload, an emerging safety culture, and the absence of an electronic prescription system are indicative of organizational environment-related causes, underscoring the necessity of integrating computerized technologies, notably the implementation of electronic prescriptions.[34]

The FMs exhibited a severity index categorized as very high or high in over 50 % of the cases, and a moderate index in 25 % of them, highlighting a substantial frequency of issues that could potentially cause significant harm to patients. Furthermore, it was observed that more than 40 % of the failure modes had minimal or low detection, underscoring the necessity to devise protocols that facilitate their timely identification and monitoring. Regarding the PC, a broad range of scores was noted in this study. In contrast, Kunac *et al*. (2005) observed a narrower range for PC (33 to 273) in their study.[26]

The FM that presented higher PC as determined by Failure Mode and Effects Analysis (FMEA), was linked to the absence of relevant information. In a separate study conducted in a pediatric ICU, different results were obtained, where the prioritized failure mode was the calculation of the drug dose for administration via a Continuous Infusion Pump.[41] In a prior study by the same authors, conducted in a

respiratory ICU, the highest PC was associated with the lack of dose adjustment based on the patient's renal function.[14] These variations may be attributed to differing patient profiles, prescription formats (whether electronic or manual), and, chiefly, the practices of local prescribers and the established safety culture within the unit.

In this study, most of the PR made were accepted (70.0 %) and directed towards physicians (93.4 %). A similar outcome was reported in a study by Fideles *et al*. (2015), where over 80 % of the PRs were directed to the medical team.[42] The acceptance rate of PRs in this study aligns with rates reported in other studies, ranging from 71 % to 97 % for accepted recommendations.[31,43,44] The most prevalent PRs in this study involved incorporating information and removing acronyms from prescriptions, likely due to the absence of an electronic prescription system and the presence of resident physicians in the institution.

Alongside implementation of the FMEA tool, training and education of prescribers were performed to attenuate prescription errors. These initiatives aimed to standardize prescription practices, discourage the use of unauthorized abbreviations, and emphasize the importance of including doses and pharmaceutical forms. Research by Shaughnessy and D'Amico (1994) has demonstrated that physicians benefiting from training on drug prescriptions can enhance the quality of their prescriptions and reduce errors.[45] In addition, educational efforts were directed towards the nursing team to enable them to identify prescription errors and intervene before potential harm reaches the patients. The information and guidance conveyed verbally were made accessible within the unit through protocols and operational flows, serving as reference materials. However, no specific tool was employed to evaluate these educational endeavors. Future studies are needed to evaluate the impact of these activities.

As explained above, our study presents valuable information about the use of the FMEA tool in a highly complex health care setting. However, it has some limitations, such as the small sample size, as some medical prescriptions were only for three days of the week; it is not a multicenter study; the monthly turnover of medical residents may have influenced the PR analysis, as well as continuing education activities. Furthermore, the study did not assess the impact of FMEA application on reducing priority coefficients. Thus, these data cannot be extrapolated to other centers, although they can be used as an initial standpoint. Despite these limitations, we believe the results generated in this study can help other professionals detect and prevent risks associated with the medication prescription process.

Conclusion

In this study, the FMEA tool was utilized for evaluating the medication prescription process in a cardiac ICU, identifying and prioritizing risks based on a defined coefficient. Critical FMs and error categories were described and potential causes/consequences were investigated. These findings should reinforce the usefulness of FMEA for patient safety in ICUs, as well as corroborating further measures for process of quality improvement.

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