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Use of the failure mode and effects analysis tool in the clinical drug process in an intensive care unit

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Abstract

Objective: To describe failure modes and establish contingency measures related to the clinical medication process using medical prescriptions of patients admitted to an Intensive Respiratory Therapy Unit (UTIR), using the Failure Mode and Effects Analysis (FMEA) tool. **Methods:** This is a descriptive and cross-sectional study carried out in an Intensive Care Unit of a public hospital in Fortaleza, Brazil, from November/2015 to March/2016. Study population included adults aging ≥ 18 years in intensive care at the UTIR. The study included the medical prescriptions released on Mondays, Wednesdays, and Fridays. The study was divided in five phases: situational diagnosis, formation of a multiprofessional team, assessment of failure modes (FM), monitoring of FM and calculation of the priority coefficient (PC). In the FM assessment, scoring of the three indicators of the FMEA was used within a range of 1-10, whereas a score of 10 characterized the most concerning situation. Therefore, the indicators gravity (G), prevalence (P) and detection (D) were analyzed. The study was carried out with an active interaction between the subjects of the group and several in-person and virtual sessions were performed. Drugs used in the study were categorized for therapeutic class, according to the Anatomical Therapeutic Chemical Classification System. Data analysis was performed using Microsoft Office Excel® 2013 software. **Results:** 301 prescriptions were analyzed, with the identification of 452 FMs, which related mostly to systemic antibacterials (21.6%, n = 8), psycholeptics (13.5%, n = 5) and antithrombotic agents (10.8%, n = 4). FMs were divided in eleven categories, from which "drug interaction" (36.8%; n = 14), "dose adjustment" (21.1%, n = 8) and "food-drug interaction" (7.9%, n = 3) were the most frequent. The PC of the detected FMs varied between 28 and 294, and 42.1% (n = 16) of them presented PC above 100. Median of the indicators G (6 – min: 3; max: 9), D (7 – min: 3; max 7) and priority coefficient (72 – min: 28; max: 294) indicate that FM had generally moderate gravity, low prevalence and low detection. For the majority of FMs (72.7%, n = 28), the chosen conduct was 'not to accept' and the established contingency measure included a sentinel event notification. **Conclusion:** The use of FMEA enabled the identification, classification, and prioritization of risks of the clinical medication process in the UTIR. This study indicates the need to implement measures that increase safety in the clinical practice of the study Intensive Care Unit.

Keywords: healthcare failure mode and effect analysis; patient safety; quality of health care; intensive care units.

Utilização da ferramenta análise dos modos de falha e seus efeitos no processo medicamentoso clínico em uma unidade de terapia intensiva

Resumo

Objetivo: Descrever os modos de falhas (MF) e estabelecer medidas de contingência relacionados ao processo medicamentoso clínico através das prescrições médicas de pacientes internados em uma Unidade de Terapia Intensiva Respiratória (UTIR), por meio da ferramenta Análise do Modo de falha e seus Efeitos (FMEA). **Métodos:** Trata-se de um estudo descritivo e transversal realizado em uma UTIR de um hospital público em Fortaleza, Brasil, em novembro/2015 a março/2016. A população foi constituída por indivíduos adultos (idade ≥ 18 anos) em cuidados intensivos na UTIR. O estudo incluiu as prescrições médicas liberadas nas segundas-feiras, quartas-feiras e sextas-feiras e foi realizado em cinco fases: diagnóstico situacional, a formação de uma equipe multiprofissional, avaliação dos MF, acompanhamento dos MF e o cálculo do coeficiente de prioridades (CP). Na avaliação dos MF, foram estabelecidos critérios para os três indicadores que constituem o FMEA com pontuação que varia de 1 a 10, onde 10 caracteriza a situação mais preocupante. Assim, pontuaram-se os indicadores de Gravidade (G), Prevalência (P) e Detecção (D). O estudo foi realizado por meio de interação ativa entre os integrantes do grupo e com a realização sessões presenciais e virtuais. Os medicamentos envolvidos foram classificados por classe

terapêutica, de acordo com o *Anatomical Therapeutic Chemical Classification System*. A análise dos dados foi realizada utilizando o software Microsoft Office Excel® 2013. **Resultados:** Foram analisadas 301 prescrições, com a identificação de 452 MF que envolveram principalmente os antibacterianos para uso sistêmico (21,6%, n=8), psicolépticos (13,5%, n=5) e agentes antitrombóticos (10,8%, n=4). Os modos de falha foram classificados ainda em 11 diferentes categorias, sendo as mais frequentes 'interação medicamentosa' (36,8%; n=14), 'ajuste de dose' (21,1%; n=8) e 'interação medicamento-alimento' (7,9%, n=3). Os CP dos MF encontrados variaram entre 28 e 294 e 42,1% (n=16) destes apresentaram CP acima de 100. As medianas dos indicadores de G (6- mín:3; máx:9), P (2 – mín:1; máx:7), D (7 – mín:3; máx:7) e coeficiente de prioridade (72 – mín: 28; máx: 294), indicam que os modos de falha possuíam, em geral, gravidade moderada, baixa prevalência e baixa detecção. Para a maioria dos MF (72,7%, n=28), a conduta definida foi 'não aceitar' e a medida de contingência estabelecida incluiu uma notificação de evento sentinela. **Conclusão:** A utilização da FMEA permitiu a identificação, classificação e priorização dos riscos do processo medicamentoso clínico da UTIR. O estudo indica a necessidade de implementação de medidas que aumentem a segurança da prática clínica na Unidade de Terapia Intensiva em estudo.

Palavras-chave: análise do modo e do efeito de falhas na assistência à saúde; segurança do paciente; qualidade da assistência à saúde; unidades de terapia intensiva.

Introduction

Health care practices related to hospital assistance can lead to the occurrence of adverse events (AEs) that are often seen as inefficiency of the health services.[1] According to the Institute of Medicine's *To Err is Human* report, every year nearly 100,000 people die due to AEs in hospital environments in the USA.[2] Since the publication of this report, terms such as patient safety, quality in health and medication errors have gained greater relevance worldwide.[3,4]

Given the above, there is a growing tendency to assess health processes proactively and prospectively, as is the case in the aviation and nuclear energy industries.[5] The most prominent risk assessment method in health care is Failure Mode and Effects Analysis (FMEA). FMEA is a risk assessment tool used to promote patient safety, preventing failures and proactively analyzing the risks of a process.[6] The method is capable of managing failure modes, mapping the care process and identifying how failures occur, being recommended by the Joint Commission for the management of risks in health.[7] It is based on the concept that a risk is not only related to the probability of a failure occurring, but also to the severity of the consequences of that failure and to the ease of detecting and intercepting the failure before it occurs.[8]

According to the Joint Commission Resources (2002), the FMEA tool is useful in any procedure or process that may affect patient safety.[9] A number of studies in the literature indicate the use of the FMEA method in the management of risks in health processes, such as drug administration, opioid stock control, venous thrombosis prophylaxis in critically-ill patients, control of catheter-related bloodstream infection, adherence to drug therapy, and in critical care.[10-15] In Intensive Care Units (ICUs), the complexity of care, procedures and available technologies considerably increases the health risks, as well as the frequency and severity of AEs, suggesting that the application of the FMEA tool in this environment can be of extreme relevance.[16]

In the context of medication use in ICUs, drug prescription, validation and dispensing are considered critical processes for patient safety.[17] However, studies assessing the risks associated with the clinical drug process in ICU environments are scarce in the literature, especially in the national scope. In this sense, the objective of this study was to describe the failure modes and to establish contingency measures related to the clinical drug process through the prescriptions of patients hospitalized in an ICU, using the FMEA tool.

Methods

This is a descriptive and cross-sectional study with a quantitative approach conducted in the respiratory ICU (RICU) of a public hospital in Fortaleza, Brazil, from November 2015 to March 2016. This study was approved by the hospital's Research Ethics Committee (opinion number 1107043) and was conducted observing human dignity.

The drug process can be understood as a complex activity which involves the act of prescribing, dispensing and administering medications, and it encompasses different health professionals. In each of these stages, there is a series of decisions and actions that are intertwined and which can generate clinical risks (those linked to the health professionals' direct or indirect actions).[5] In this study, the drug process is assessed from a more clinical perspective, having the daily medical prescriptions as main study object.

The Hospital, study locus, provides high-complexity health assistance and with a focus on situational diagnosis and treatment of heart and lung diseases, integrated to the Unified Health System (*Sistema Único de Saúde*, SUS). The RICU consists of eight active beds, serves clinical patients with lung diseases, and has an open clinical medical staff. The multidisciplinary team of the ICU under study is composed of on-duty and day-shift physicians, nurses and nursing technicians, physiotherapists and nutritionists. We highlight that, when the study was conducted, the RICU did not have a clinical pharmacist. The unit is also used as a teaching locus for resident professionals and students. The institution lacks an electronic prescription and/or evolution system and has an individualized drug distribution system.[18]

In all the phases, the population consisted in individuals admitted to the RICU any day of the week, regardless of the clinical diagnosis, of both genders and adults (age ≥ 18 years old), as the study locus was a specialized care unit for adults. The data were collected from the medical prescriptions released on Mondays, Wednesdays and Fridays, through the data collection and processing technical capabilities of the authors of the study, and because the RICU presented low patient turnover. The patients' sociodemographic and clinical data were not collected, since the study only describes the specific problems related to the pharmacotherapy identified in medical prescriptions, for which sociodemographic data do not infer.

The study consisted of five phases and followed the methodology recommended by the FMEA tool (Figure 1). The study phases were divided in two stages: 1 – comprised of phases 1, 2 and 3 and conducted in November and December 2015; and 2 – comprised of phases 4 and 5 and conducted between January and March

2016. Phases 1, 2 and 3 represented the situational diagnosis, the assembling of a multidisciplinary team, and the assessment of the failure modes identified by the FMEA tool, respectively. Phases 4 and 5 represented the monitoring of the failure modes in the clinical drug process and the calculation of the priority coefficient (PC), respectively (Figure 1). In this study, the failure mode is treated as a clinical situation that results in a degree of uncertainty in relation to the established goals, causing a risk condition. The tool used was not validated for the Portuguese language.

Phase 1, performed by a pharmacist, was of the exploratory type and intended to list the problems involving the clinical drug process, herein described as failure modes. The situational diagnosis was performed by analyzing the medical prescriptions of patients hospitalized in the RICU from Monday to Friday during November 2015. The medical prescriptions were collected directly from the patients' records. The potential failure modes such as drug interactions and incompatibilities, prescription errors, overdose due to lack of dose adjustment in special situations, and absence of information on the management of the use of a drug were verified. The problems related to pharmacotherapy, such as identification of overdose, underdose, inappropriate guidelines under special conditions, adverse reactions and inappropriate dilutions or infusion times, were considered failure modes. For example, a prescription of Meropenem 1g every 8h in a patient with CrCl < 50 mL/min was considered a failure mode of the "overdose" type, due to lack of dose adjustment in special situations. This analysis took place retrospectively and was followed by a notification to the institution's risk management area about the failure modes identified. In this phase, a reference list was prepared with the different failure modes found according to the search in the Micromedex® database.[19]

In phase 2, a multidisciplinary group of professionals (two physicians and a pharmacist) was assembled in order to ensure several points of view regarding the study object. Consequently, an invitation was made to a medical coordinator with complementary training in the FMEA methodology, to a day-shift physician from the unit under study and with a specialty in intensive care, and to a resident pharmacist with an interest in the application of the tool. The study was conducted by means of active interactions among the group members and through the conduction of in-person and virtual sessions. Due to the lack of availability and interest of other professionals from the study institution, the multidisciplinary group was reduced to two professions and lacked the valuable presence of a professional nurse.

During phase 3, meetings were held with the multidisciplinary group in order to assess and define the types of failures, their causes, effects, severity, detection methods and contingency measures. The condition was assessed in a standard and reliable manner for all the participants. Criteria were established for the three indicators that constitute FMEA with scores varying from 1 to 10, where 10 characterizes the most concerning situation. Therefore, the Severity (S), Prevalence (P) and Detection (D) indicators were attributed scores (Table 1).

Severity is understood as how severe the failure mode is if it occurs and to what extent it compromises the patient's functionality and/or integrity. Prevalence is the occurrence frequency of this failure mode, whether it is something rare or present. Detection is the probability for the failure mode to be easily recognized; to predict its possibility, we characterized the performance policy of its professionals in relation to the failure mode.[8] In this phase,

Figure 1. Methodological flowchart corresponding to the application of the Failure Mode and Effects Analysis (FMEA) tool to the medication use process in a Respiratory Intensive Care Unit (RICU).

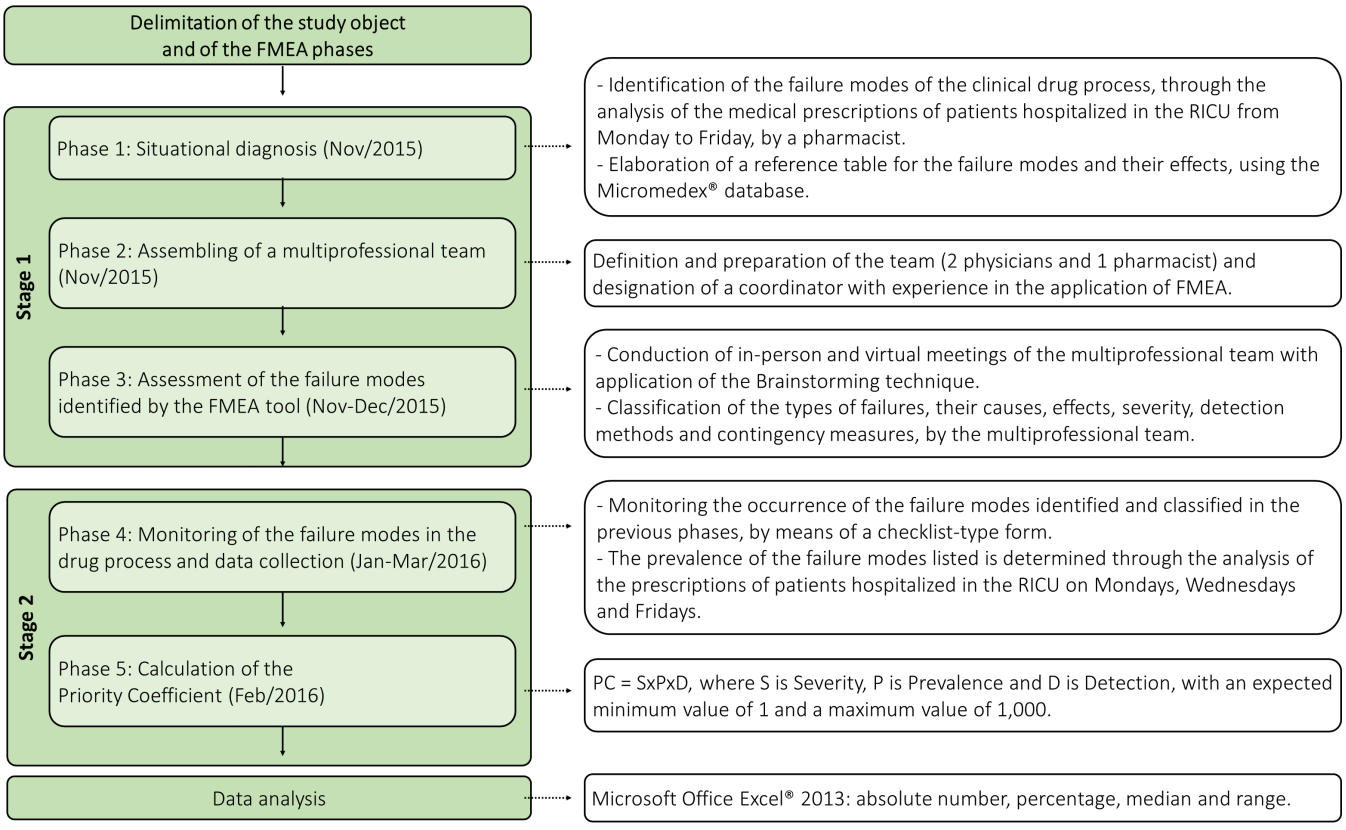

Table 1 – Classification of the study vulnerabilities according to severity, detection and prevalence.

Index	Severity		Prevalence	Detection	
1	Minimum	The patient barely perceives that exposure occurs.	Remote or nonexistent: almost impossible to occur (0.1%).	Very high	It will certainly be detected. The process/ protocol is well-designed, not allowing continuity.
2 3	Low	Slight change in the patient's clinical condition. One symptom or sign.	Low: in general, this type of failure is not present (0.1% > p < 2.1%).	High	It will probably be detected. The process/ protocol exists, although with low adherence.
4 5 6	Moderate	Significant deterioration in the patient's clinical condition. More than one symptom or sign. It changes the therapeutic plan.	Moderate: in general, they occasionally present this type of failure (2.1% > p < 13.6%).	Moderate	It will probably not be detected. Active search for a specialist.
7 8 9	High	Important deterioration in the patient's clinical condition. It considerably changes the therapeutic plan. It changes risk classification.	High or frequent: in general, they frequently present this type of failure (13.6% > p < 34.1%).	Low	Significant probability of not being detected. No protocol. No active search.
10	Very high	Important deterioration in the patient's clinical condition. It considerably changes the therapeutic plan. It changes risk classification. Significant increase in predicted mortality.	Very high or almost unavoidable: in general, they always present this type of failure (p > 34.1%).	Minimum	It will certainly not be detected. No protocol. No active search. Difficult to recognize.

the position that the assistance team would adopt in relation to the failure modes was also determined: 1) accepting the risk and monitoring, 2) not accepting the risk and notifying the risk management area as a sentinel event, and 3) seeking to reduce the risk. To stimulate issuance of opinions and considerations by the participants, the Brainstorming technique was used, in which there is exploration of the participants' knowledge, experience and creativity[20]. The "unaccepted" failure modes presented high probability of associated harm risk and alternative courses of action well established in the scientific literature.

In phase 4, the occurrence of the failure modes identified and explored in the previous phases was monitored using a checklist-type form, through the clinical assessment of the medical prescriptions by a pharmacist. In this phase, the prevalence of the failure modes listed was determined through the analysis of the prescriptions of patients hospitalized in the RICU on Mondays, Wednesdays and Fridays in the period from January to March 2016. All the failure modes identified during the research were informed to the care team and adjustments were recommended as described in the failure modes matrix.

After phase 4, in which the prevalence of the failure modes was monitored, calculation of the Priority Coefficient (PC) of each failure mode was performed using the Severity (S), Prevalence (P) and Detection (D) indicators. The PC was obtained from the product of the three indexes, according to the following formula: PC = SxPxD; each PC is determined by multiplying the indicators, where the expected minimum value is 1 and the maximum value is 1,000, since the detection with the lowest index is considered. Failure modes with a PC above 100 were classified as of high risk.

The medications were classified as per their therapeutic class, according to level two of the Anatomical Therapeutic Chemical Classification System.[21]

The information was collected through an instrument exclusive to the study and it was subsequently compiled and analyzed in Microsoft Office Excel® 2013. The continuous variables were expressed as median (central tendency) and range (dispersion), as the data did not present normal distribution; and the categorical variables were expressed as absolute and percentage figures.

Results

During the first phase of the study, 301 medical prescriptions were evaluated and the different failure modes were present 452 times, with failures often repeating. When performing the overall consolidation, 38 failure modes were identified in the period and they were more frequently associated with antibacterials for systemic use (21.6%, n = 8/38), psycholeptics (13.5%, n = 5/38) and antithrombotic agents (10.8%, n = 4/38).

The assessment of the failure modes was based on the associated risk, the course of action to be taken, the preventive measures and the contingency measures. For most of the failure modes (72.7%, n = 28/38), the course of action defined was 'Do not accept' and the established contingency measure included a sentinel event notification. A sentinel event is an undesirable serious event that occurs in a sealed hospital and results in compromised patient care, involving death, injury or physical or psychological risk.[1] The failure modes were further classified into 11 different categories, the most frequent ones being 'drug interaction' (36.8%; n = 14/38), 'dose adjustment' (21.1%; n = 8/38) and 'drug-food interaction' (7.9%, n = 3/38) (Figure 2).

The prevalence, severity and detection scores were established through consensus among the three members of the multiprofessional group in an in-person meeting. The PC of the failure modes found varied between 28 and 294, where 42.1% (n = 16) of the failure modes presented a PC above 100, being considered the most critical ones. The most prevalent failure modes were 'concomitant prescription of midazolam and fentanyl' (PC: 294), 'prescription of simvastatin and enteral diet' (PC: 245) and 'prescription of midazolam in patients with dialytic ARF' (PC: 196) The medians of the Severity (6 – min: 3; max: 9), Prevalence (2 – min: 1; max:), Detection (7 – min: 3; max: 7) and priority coefficient (72 – min: 28; max: 294) indicate that, in general, the failure modes presented moderate severity, low prevalence and low detection (Figure 2).

Figure 2. Matrix of the failure modes identified in the exploratory phase of the research. (continued)

Failure mode	S[1]	P[2]	D[3]	PC[4]	Potential risks	Course of action	Prevention	Contingency measures
Dose adjustment								
Midazolam without adjustment in ARF[5]	7	4	7	196	Prolonged sedation	Monitor[6]	Reduce dose by 50%, if CrCl[7] < 10 mL/min	Reduce doses, suspend the medication and/or administer flumazenil
Meropenem without adjustment in ARF[5]	6	2	6	144	Exacerbation of the adverse effects, due to overdose	Do not accept	Adjust dose, if CrCl[7] ≤ 50 ml/min	Sentinel e.,[8] adjust doses and/or substitute ATM[9] and monitor
Enoxaparin in patients with ARF[5]	6	3	6	108	Thrombocytopenia and/or bleeding	Monitor[6]	Substitute with NF[10] heparin, if CrCl[7] < 30 mL/min	Suspend treatment, if platelets below 100,000 x 109/L If necessary, administer 10 units of platelet concentrate
Amikacin without adjustment in ARF[5]	6	2	6	72	Exacerbation of the adverse effects, due to overdose	Do not accept	Adjust dose, if CrCl[7] ≤ 30ml/min	Sentinel e.,[8] adjust doses and/or substitute ATM[9] and monitor
Fondaparinux in patients with ARF[5]	6	2	6	72	Thrombocytopenia and/or bleeding	Monitor[6]	Substitute with NF[10] heparin, if CrCl[7] > 30 ml/min	Suspend treatment, if platelets below 100,000 x 109/L If necessary, administer 10 units of platelet concentrate
PIPE/TZO[11] without adjustment in ARF[5]	6	2	6	72	Exacerbation of the adverse effects, due to overdose	Do not accept	Adjust dose, if CrCl[7] ≤ 40ml/min	Sentinel e.,[8] adjust doses and/or substitute ATM[9] and monitor
SMT/TMP[12] without adjustment in ARF[5]	6	2	6	72	Exacerbation of the adverse effects, due to overdose	Do not accept	Adjust dose, if CrCl[7] ≤ 30ml/min	Sentinel e.,[8] adjust doses and/or substitute ATM[9] and monitor
Acyclovir without adjustment in ARF[5]	6	1	6	36	Exacerbation of the adverse effects, due to overdose	Do not accept	Adjust dose, if CrCl[7] ≤ 50 ml/min	Sentinel e.,[8] adjust doses and/or substitute ATM[9] and monitor
Concentration of the infusion solution								
Noradrenaline 32 cmg/ml in PS[13]	5	5	6	150	Therapeutic ineffectiveness due to loss of the active ingredient.	Do not accept	Dilute in GS[14]	Sentinel e.,[8] increase the dose and perform VR[15]
Hydrocortisone in CIP[16] with concent.[17] > 1 mg/ml	5	2	7	70	Therapeutic ineffectiveness, due to loss of Ph-Ch stability[18]	Do not accept	Prescribe concentration of up to 1 mg/ml	Sentinel e.,[8] monitor the need for increased doses of vasopressors and treat adrenal insufficiency
Diluent of the solution								
SMT/TMP[19] IV[20] diluted with PS[13]	6	2	6	72	Therapeutic ineffectiveness, due to Ph-Ch instability[18]	Do not accept	Dilute in GS[14]. If the patient is diabetic, dilute in fructose	Sentinel e.,[8] adjust dilution and/or substitute ATB and monitor
Dilution								
Methylprednisolone 500 mg diluted in DW[21]	5	5	7	175	Therapeutic ineffectiveness, Ph-Ch instability[18]	Do not accept	Dilute in PS[13] or in GS[14]	Sentinel e.[8] and monitor
Hydrocortisone 500 mg diluted in DW[21]	5	1	7	35	Therapeutic ineffectiveness, Ph-Ch instability[18]	Do not accept	Dilute in PS[13] or in GS[14]	Sentinel e.[8] and monitor
Drug-food interaction								
Simvastatin and enteral diet	5	7	7	245	Therapeutic ineffectiveness due to drug hydrolysis	Do not accept	Substitute simvastatin with atorvastatin	Sentinel e.[8] and monitor
Captopril and enteral diet or through a tube	5	4	7	140	Hypertensive crisis, due to reduced absorption	Do not accept	Administer captopril 1 hour before or 2 hours after meals or substitute it with another ACEI[22] or ARB[23] inhibitor that does not interact with the diet	Sentinel e.,[8] monitor and increase the dose or substitute or apply associations of antihypertensive drugs
Phenytoin and enteral diet or through a tube	6	1	7	42	Therapeutic ineffectiveness, due to reduction of the plasma concent[17]	Do not accept	Administer IV[20] phenytoin or substitute the anticonvulsant	Sentinel e.,[8] monitor, dosage of the serum level. If patient on MV[24], perform VEEG[25]

Figure 2. Matrix of the failure modes identified in the exploratory phase of the research. (continued)

Failure mode	S[1]	P[2]	D[3]	PC[4]	Potential risks	Course of action	Prevention	Contingency measures
Drug-drug interaction								
Midazolam and fentanyl	7	6	7	294	Respiratory depression, hypotension, deep sedation and potential coma or death	Accept, if patient on mechanical ventilation, and monitor	Limit doses and length of treatment of each drug to the minimum possible and use scales to assess sedation and pain	Reduce doses and length of treatment, suspend the medications and/or administer benzodiazepine (flumazenil) and/or opioid (naloxone) antagonists. Manage hypotension through VR[15] and vasoconstrictor medications (noradrenaline)
Fluconazole and methadone	[9]	3	7	189	QT interval prolongation, due to decreased methadone metabolism	Do not accept	Reduce the methadone dose and substitute it with tramadol	Sentinel e.,[8] suspend methadone, perform routine ECG[26], administer antiarrhythmics and monitor SpO2.[27] Consider that the effect continues for 4 to 5 days after discontinuation of fluconazole (half-life: 20-50 hours)
Haloperidol and quetiapine	[9]	3	7	189	Increase in the QT interval	Do not accept	Substitute quetiapine with risperidone	Sentinel e.[8] Monitor via ECG.[26] Proceed with the administration of antiarrhythmics
SSRI[28] and heparin	6	4	7	168	Bleeding (epistaxis, ecchymosis, bruises)	Monitor	Monitor APTT,[29] platelets and signs of bleeding	If necessary, administer 10 units of platelet concentrate
Clopidogrel and omeprazole	8	3	7	168	Loss of the antiplatelet effect of clopidogrel and increased risk of cardiac events	Do not accept	Substitute omeprazole with ranitidine, pantoprazole or rabeprazole	Sentinel e.,[8] monitor platelet levels and, if necessary, proceed with the AMI protocol[30]
Metoclopramide and linezolid	[9]	2	7	126	Hypertensive crisis, due to release of catecholamines	Do not accept	Substitute metoclopramide with bromopride	Sentinel e.[8] and treat serotonergic syndrome
Carbapenems and valproic acid	6	2	7	84	Convulsive crises, due to a reduction of the valproic acid plasma concent[17]	Do not accept	Substitute valproic acid with phenytoin and phenobarbital or include some supplementary anticonvulsant	Sentinel e.[8] and treat the convulsive crisis. If patient on MV[24], perform VEEG[25]
Metoclopramide and haloperidol	5	2	7	70	Extrapyramidal Syndrome and/or Neuroleptic Malignant Syndrome	Do not accept	Substitute metoclopramide with bromopride, ondansetron or domperidone and monitor (fever, sweating, confusion, muscle stiffness)	Sentinel e.,8 discontinue metoclopramide and the antipsychotic agent, prescribe promethazine or diphenhydramine. In more severe cases that evolve to bradycardia and seizure status, administer atropine and benzodiazepine, respectively
Fluconazole and haloperidol	9	1	7	63	Ventricular tachyarrhythmia and QT interval prolongation, due to decreased haloperidol metabolism	Monitor	Reduce the dose or suspend haloperidol or administer haloperidol through oral route	Monitor HR,[31] correct symptoms with an antiarrhythmic (e.g., amiodarone). Consider that the effect can continue for 4 to 5 days after its discontinuation after suspension of fluconazole (half-life: 20-50 hours)
Fluoxetine and linezolid	9	1	7	63	Serotonergic syndrome (hypertension, tachycardia, hyperthermia, myoclonus)	Do not accept	Suspend fluoxetine and resume it 24 hours after the end of linezolid	Sentinel e.[8] and treat serotonergic syndrome (suspend medication, sedation, cooling) with short-acting antihypertensives (esmolol or nitroprusside) and, if necessary, administration of serotonergic action antagonists
Cisatracurium and polymyxin	8	1	7	56	Prolonged NMB[32]	Accept if on MV[24] and monitor	Monitor the prolonged effect of NMB[32]	Administer antidotes such as prostigmine and atropine
Quetiapine and phenytoin	6	1	7	42	Epileptic crises, due to reduction of quetiapine serum concentration	Monitor	Increase quetiapine dose up to 5x and/or reduce/suspend phenytoin. Resume quetiapine dose 7-14 days after suspension of phenytoin	Monitor new psychotic crises

Figure 2. Matrix of the failure modes identified in the exploratory phase of the research. (conclusion)

Failure mode	S[1]	P[2]	D[3]	PC[4]	Potential risks	Course of action	Prevention	Contingency measures
Drug-drug interaction								
Metoclopramide and chlorpromazine	5	1	7	35	Extrapyramidal Syndrome and/or Neuroleptic Malignant Syndrome	Do not accept	Substitute metoclopramide with bromopride, ondansetron or domperidone, and monitor (fever, sweating, confusion, muscle stiffness)	Sentinel e.,[8] discontinue metoclopramide and the antipsychotic agent, prescribe promethazine or diphenhydramine. If necessary, administer atropine and benzodiazepine
Methadone and risperidone	4	1	7	28	Precipitation of opioid withdrawal symptoms in opioid-dependent patients and QT interval prolongation	Monitor	Reduce risperidone dose or substitute it and monitor (opioid withdrawal, arrhythmias)	Increase methadone dose. If necessary, prescribe clonidine. Long-acting benzodiazepines (clonazepam, diazepam) can be added to control insomnia and muscle cramps
Guidance for the team								
NF[10] heparin in CIP[17] without homogenization	8	1	7	56	Thromboembolism, due to loss of heparin effectiveness	Do not accept.	Homogenize heparin every 4h and change equipment every 24h	Sentinel e.[8] and prescribe chemical and/or physical anticoagulants
Regular insulin in CIP[17] without changing equipment	6	1	7	42	Hyperglycemia, due to insulin loss resulting from the adsorption process	Do not accept	Change the equipment every 24h, wash it with the solution and monitor blood glucose every hour	Sentinel e.,[8] increase insulin dose and monitor glycaemia every hour
Dosage								
Polymyxin every 8h	6	4	6	144	Intensification of nephrotoxicity	Do not accept	Adjust dosage every 12h	Sentinel e.,[8] monitor KF[33] and, if necessary, initiate renal replacement therapy
Amlodipine every 12h	3	4	7	84	Lack of scientific evidence (half-life: 30 to 60 hours)	Do not accept	Adjust dosage every 24h	Sentinel e.,[8] adjust dosage and monitor signs of adverse reaction
Adverse reaction								
Amphotericin without pre-infusion hydration	6	4	6	144	Intensification of nephrotoxicity	Do not accept	Include hydration with 500 ml of PS[13] before and after administration of amphotericin. If ARF5, nephrologist opinion	Sentinel e.,8 monitor KF[33] and, if necessary, initiate renal replacement therapy
Polymyxin infusion ≥ 120 minutes.	6	4	6	144	Therapeutic ineffectiveness, due to loss of solution stability	Do not accept	Adjust infusion time up to 120 minutes	Sentinel e.,[8] monitor antibiotic effectiveness and consider scaling and/or expanding the antimicrobial therapy, if therapeutic ineffectiveness
Cisatracurium for a long period of time	9	1	7	63	Reduction in CF[34], RF[35] and extended NMB[32]	Accept if patient on MV and monitor	Monitor RF[35] and CF[34]	Proceed with the administration of antidotes, such as prostigmine and atropine, and monitor RF[35] and CF[34]
IMP/CLT[36] infusion > 60 minutes.	6	1	7	42	Loss of drug stability	Do not accept	Adjust infusion time up to 60 minutes	Sentinel e.[8] and administer intravenous phenytoin, in the absence of contraindications

[1]S: Severity. [2]P: Prevalence. [3]D: Detection. [4]PC: Priority Coefficient. [5]ARF: Acute Renal Failure. [6]Monitor: Accept with monitoring of the adverse effects/effectiveness. [7]CrCl: Creatinine Clearance. [8]Sentinel e.: Notify as a sentinel event. [9]ATM: Antimicrobial agent. [10]NF: Non-fractioned. [11]PIPE/TZO: Piperacillin/Tazobactam. [12]SMT/TMP: Sulfamethoxazole/Trimethoprim. [13]PS: Physiological Serum. [14]GS: Glucose Serum. [15]VR: Volume Replacement. [16]CIP: Continuous Infusion Pump. [17]Concent.: Concentration(s). [18]Ph-Ch: Physical-Chemical. [19]SMT/TMP: Sulfamethoxazole/Trimethoprim. [20]IV: Intravenous. [21]DW: Distilled Water. [22]ACEI: Angiotensin-Converting Enzyme Inhibitors. [23]ARB: Angiotensin Receptor Blockers. [24]MV: Mechanical Ventilation. [25]VEEG: Videoeletroencephalogram. [26]ECG: Eletrocardiogram. [27]SpO2: Peripheral Oxygen Saturation. [28]SSRI: Selective Serotonin Reuptake Inhibitor. [29]APTT: Activated Partial Thromboplastin Time. [30]AMI: Acute Myocardial Infarction. [31]HR: Heart Rate. [32]NMB: Neuromuscular Block. [33]KF: Kidney Function. [34]CF: Cardiac Function. [35]RF:Respiratory Function. [36]IMP/CLT: Imipenem/Cilastatin.

Discussion

To our knowledge, this is the first study to determine and analyze the problems related to the clinical drug process using the FMEA tool in an ICU in Brazil, since the existing national studies are focused on the drug administration process.[22] The use of the FMEA methodology is increasingly frequent in health systems, specifically in specialties or more vulnerable areas, such as pediatrics and intensive care.[8]

During the first phase of the study, the high number of failure modes identified in a short period of time can reflect a deficient patient safety culture, in addition to the absence of an active and cohesive multidisciplinary team. Of the 38 potential failure modes identified, more than 40% obtained a PC above 100, representing the priority failure modes in the implementation of improvement actions. In fact, the application of the FMEA tool assists in determining the failure modes to be prioritized, based not only on the probability of a failure occurring, but also on its severity and ease of detection.[15]

In the case of an ICU with a profile of respiratory tract diseases such as pneumonia, pulmonary sepsis and acute respiratory failure, antibacterials are considered one of the main drug classes used in this population.[23] Henceforth, psycholeptics are used in intensive care because there are patients on mechanical ventilation, in addition to the pharmacological attempt at managing delirium.[24]

The most frequently found categories of failure modes were drug interaction, need for dose adjustment, and drug-food interaction. This prevalence can reflect the absence of an electronic prescription system. Other studies indicate that electronic prescription systems minimize the number of errors in drug prescriptions when compared to the traditional manual prescription.[25] Additionally, this result suggests that the daily participation of a clinical pharmacist can contribute to reducing the frequency of these failure modes, since it is up to this professional to analyze potential failure modes arising from pharmacotherapy and to offer therapeutic recommendations.[26,27]

The pharmacist's activities in intensive care range from guidance of the constant monitoring of the therapeutic plan, evaluating the presence of drug/drug or drug/nutrient interactions, the prescribed dose and the occurrence of adverse effects, to the optimization of the pharmacological therapy, offering pharmaceutical recommendations.[28,29,30] In fact, the Joint Commission requires that "*in cases of non-urgent situations, all the medical prescriptions and/or drug requests must be reviewed by a professional pharmacist*".[31] However, it is important to emphasize that the management of failure modes, as well as their recognition, must permeate all actors involved in patient care, since many of the failures result from practices rooted in the daily routine of each professional.[8]

When analyzing the means of the Severity, Prevalence and Detection indicators, it was verified that the highest median found was related to the Detection indicator (7), revealing a deficit in the identification of problems involving medications by the care team. In addition to that, such result can be a probable reflex of the absence of risk management protocols inherent to the clinical drug process. A number of studies suggest that prescriptions based on clinical protocols contribute more patient safety by reducing the frequency of errors.[32] In addition, these data indicate the need to train and sensitize the health professionals working in the RICU through a training plan. The development of a good training plan can be an important strategy in establishing a safety culture and in risk management in health centers, both for seasoned and novice professionals.[33,34]

This study enabled the identification of important failure modes in the clinical drug process in the ICU through the FMEA tool. However, it does have some limitations. In the first place, the study sample was limited to the prescriptions made on three days of the week, which represents an important source of bias in data interpretation. Secondly, the reduced number of professionals and the absence of a professional nurse in the evaluation team may have limited the identification of failure modes. There is also the possibility of overestimating the failure modes found, as the results depend on the opinion and subjectivity of the participating group members. In addition to that, this was a single-center study carried out in a short period of time that was intended only to identify and assess the failure modes, not evaluating the impact of applying FMEA on the reduction of the priority coefficients. Nevertheless, despite the limitations, we believe that the results of this study may assist other professionals in detecting and preventing the risks associated with this same process.

Conclusion

In this study, several failure modes in the clinical drug process were identified in the ICU under study, with a ratio of 1.5 errors per prescription. They were mainly related to drug interactions, need for dose adjustments and drug-food interactions. It was possible to determine which failure modes must be prioritized and to identify that more than half of the failure modes present a high priority coefficient. These data can reveal the need to establish a continuous quality process in the institution and, perhaps, to incorporate a pharmacist in the ICU clinical staff. Additionally, this study supports the use of the FMEA tool to proactively identify and reduce the risks associated with the clinical drug process and to enhance patient safety.

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Collaborators

Project conception: KSM, HMC, GAR. Data collection: KSM, HMC. Data analysis and interpretation: KSM, HMC. Writing of the article and responsibility for all the information presented in the paper, ensuring accuracy and integrity of any of its parts: KSM, HMC, EFC, GAR, MFF. Relevant critical review of the intellectual content and final approval of the version to be published: GAR, MFF.

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Declaração de conflito de interesse

Os autores declaram inexistência de conflitos de interesses em relação a este artigo.

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