Performance of the trigger tool methodology in the identification of adverse drug events in intensive care

Desempenho da metodologia trigger tool na identificação de eventos adversos a medicamentos em unidade intensiva

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Arthur Lopes Agrizzi
Mestre em Administração e Gestão da Assistência Farmacêutica pela Universidade Federal Fluminense
Instituição: Maternidade Escola - UFRJ
End Institucional: Rua das Laranjeiras, n 180, Laranjeiras, Rio de Janeiro.
E-mail: arthur_agrizzi@yahoo.com.br

Selma Rodrigues de Castilho
Doutora em Engenharia Biomédica pela COPPE/UFRJ
Instituição: Universidade Federal Fluminense
End. Institucional: Rua Dr Mario Vianna, 523 – Santa Rosa – Niterói – RJ
E-mail: selmarc@id.uff.br

ABSTRACT
Adverse drug events (ADE) may increase the length of hospital stay, cause complications in the patient's clinical condition, contribute to death and increase hospital costs. The aim of this study was to apply the trigger tool methodology based on the method proposed by the Institute for Healthcare Improvement for the detection of adverse drug events in an intensive care unit, assessing the incidence of event and the feasibility of incorporating this practice into the unit. After the development of a trigger list, a retrospective review was carried out on a random sample of 10 patient records / month, among patients over 18 years of age, of both sexes, who were hospitalized in the intensive care unit of the study hospital. The incidence of patients with adverse drug events was 15%, and the rate of ADE was 15.8 ADE / 100 medical records, with most (85%) of the events categorized as temporary damage requiring intervention. The main therapeutic classes involved in adverse events were antibiotics, anticoagulants, sedatives and hypoglycemic agents. The main advantage of the methodology was the ability to detect more adverse drug events than the voluntary notification, methodology present at the institution at that time.

Keywords: Trigger Tool, Adverse Drug Event, Hospital Pharmacy, Intensive Care

RESUMO
Os eventos adversos a medicamentos (EAM) podem aumentar o tempo de internação hospitalar, causar complicações no quadro clínico do paciente, contribuir para o óbito e aumentar os custos hospitalares. O objetivo deste estudo foi aplicar a metodologia da ferramenta de gatilho baseada no método proposto pelo Institute for Healthcare Improvement para a detecção de eventos adversos a medicamentos em uma unidade de terapia intensiva, avaliando a incidência do evento e a viabilidade de incorporação dessa prática na unidade. Após o desenvolvimento de uma lista de gatilhos, foi realizada uma

revisão retrospectiva em uma amostra aleatória de 10 prontuários / mês, entre pacientes maiores de 18 anos, de ambos os sexos, internados na unidade de terapia intensiva do hospital em estudo. A incidência de pacientes com eventos adversos a medicamentos foi de 15%, e a taxa de EAM foi de 15,8 EAM / 100 prontuários, com a maioria (85%) dos eventos categorizados como danos temporários que requerem intervenção. As principais classes terapêuticas envolvidas nos eventos adversos foram antibióticos, anticoagulantes, sedativos e hipoglicemiantes. A principal vantagem da metodologia foi a capacidade de detectar mais eventos adversos a medicamentos do que a notificação voluntária, metodologia presente na instituição à época.

Palavras-chave: Trigger Tool, Evento Adverso a Medicamento, Farmácia Hospitalar, Cuidado Intensivo

1 INTRODUCTION

Adverse drug events (ADE) are defined as drug-related harm resulting from a therapeutic intervention [1]. The ADE can increase the length of hospital stay, generate complications in the patient's clinical condition, contribute to death and increase hospital costs. In 2017, the World Health Organization announced the third global patient safety challenge, which goal is to reduce by 50% the medication –related harm [2-3].

The ADE can be classified as preventable and non-preventable. The preventable ones are characterized as harm caused by an error at any stage of the drug use process and can be avoided when the technology or processes are properly applied [4].

A recent study in public hospitals in Portugal [5], a second one in China [6] and a third one in the ICU of a tertiary public hospital in the Brazilian Midwest [1] showed that more than 60% of in-hospital patients suffered from at least one ADE, many of which are preventable [1]. Molina and colleagues, in a retrospective descriptive study performed in a 12-bed university ICU found that 52,1% of the individuals presented at least one AE, and almost half of them were considered preventable [7].

The development of new work processes is essential to increase the patient safety in hospital environments, especially in an environment such as the Intensive Care Unit (ICU), where severe, polymedicated patients are hospitalized and who require numerous invasive procedures [1].

Among the changes in the processes that could be employed to avoid the occurrence of new cases are well-defined protocols for the use of certain drugs, such as antibiotics [8] and high-alert medications [9]; improving the identification of both dispensed medicines and storage locations [10]; the creation of routine health team training [11] and adopting new methods for ADE search [10] and root cause analysis [12].

The identification of ADE contributes to the dimensioning of the problems that occur in the care processes and provides valuable information concerning patient safety and the quality of the care provided [13].

The voluntary or spontaneous reporting is still an important part of pharmacovigilance [14]. The main problem found in the voluntary reporting method is the underreporting of ADE, estimated at around 94%, which reduces the sensitivity of the method. Among the strategies applied to reduce this problem stand out multifaceted educational interventions and motivational ones [14].

In view of the difficulties encountered with voluntary reporting, some methods involving active participation in the detection of ADE have been developed. Using them, health professionals began to meet the events and not just receive the notifications. Among the traditional methods of active surveillance described in the literature are: chart review, direct observation of care and patient monitoring [13]. Electronic healthcare databases have become an important source for active surveillance of drug safety too [15], as well as data mining [12].

The need for more effective way to identify events to the "trigger tool", a method used to detect potential adverse drug events developed by the US Institute The US Institute for Healthcare Improvement (IHI) [16]. According to Pierdevara et al. [13], in order to make the method less expensive and more applicable to the practice, IHI developed IHI Global Trigger Tool (GTT) methodology, in the 2000s.

With this adaptation, there is no longer a need for computer programs, and the form of detection has been made through retrospective review of medical records. The methodology aim the identification of triggers, which can be characterized as the abrupt prescription or stop of a certain medication, alteration in laboratory tests or other events related to the period of hospitalization. They act as alerts that will guide a more detailed case assessment for confirmation of ADE [17]. The review uses the GTT tool triggers, and the search for these trackers in each chart should not exceed 20 minutes [13]. This study applied the IHI GTT trigger tool methodology for the detection of adverse drug events in an intensive care unit, evaluating the incidence of the events and the feasibility of incorporating this practice into the unit.

2 MATERIAL AND METHODS

The study took place at the intensive care unit of general hospital located in the city of Rio de Janeiro, with 502 beds for adults, of which 16 are for ICU. The unit has an

electronic medical record system that allows access to the clinical evolution of the multiprofessional team, medical prescription, imaging exams and laboratory tests.

LITERATURE REVIEW AND TRIGGER LIST CREATION

Initially, a review of the literature was carried out using the Virtual Health Library (VHL), whose search limits were the original scientific articles or reviews published between 2000 and 2016 in English, Portuguese and Spanish.

The keywords and descriptors employed were: trigger tool, drug, adverse event, trackers, adverse drug events, adverse effects (MeSH), monitoring (MeSH).

The papers retrieved were initially evaluated based on the analysis of titles and abstracts available. The papers developed in oncology, outpatient and pediatric patients, as well as those developed outside the hospital environment and those involving only description of medication errors, were discarded. Those that were selected for full reading had descriptions of triggers tested in the identification of adverse drug events in intensive care patients. To obtain greater sensitivity in the detection of ADE, the triggers were confronted with the characteristics of the study environment.

The adapted trigger list to the intensive care unit was composed of 18 triggers, 5 of which were drug related, 5 laboratory tests and 8 related to the clinical evolution of the patients.

STUDY POPULATION AND DATA COLLECTION

A clinical pharmacist who carries out follow-up of the patients undergoing intensive therapy selected a random sample of 10 patient records / month of patients over 18 years old, of both sexes, hospitalized in the ICU in the period of a year. The stay for less than 24 hours at the ICU was the exclusion criteria adopted.

The review of electronic medical records was performed retrospectively, without contact with patients, as proposed by the IHI. This technique was chosen because it represents a methodology that is easy to apply and does not require specific programs for the detection of triggers [17].

The time limit of 20 minutes for the analysis of each chart was determined with the aim of identifying the triggers in the evolution of health professionals, medical prescriptions and laboratory tests, as recommended by IHI [13,18]. After the trigger detection, it was recorded in a data collection form along with the relevant variables about the patient. The categorical variables were: hospitalization (post-operative, septic shock,

polytraumatic, other) and sex (female and male). Numerical variables included: time of hospitalization (in days), age (in years of life) and number of medicines used (+ or - 5 drugs).

From the identification of the trigger, the occurrence of an ADE was confirmed when there was some report of damage to the patient in the medical record or when there was no other alternative cause to justify the injury [19]. The time required to carry out this detailed analysis of the cases was recorded in order to evaluate the feasibility of incorporating this methodology in the routine of the service.

The ADE found was evaluated by a clinical pharmacist concerning the following criteria: the severity of the damage; the causality of the event; the predictability of the event using a six-point scale [20]; the stage of the drug use process that originated the preventable events (prescription, dispensation and administration). The distribution of the damage occurred according to the NCC MERP classification [21] and the causality of the events was also performed by Naranjo algorithm [22].

In the previously reported six-point scale, the ADE is considered preventable when it has a value equal to or greater than 4. To consider a preventable event it was assessed whether the drug was used at the dose, administration interval and route of administration correct; if there was any contraindication for use due to underlying disease or clinical condition; and whether the indication was in accordance with institutional protocols and / or the scientific literature. For preventable ADE, corrective measures were proposed in the work process to reduce the occurrence of future events.

DATA ANALYSIS

The Microsoft Excel program was used to analyze the data regarding the characteristics of the study participants and the frequency indicators of the ADE. The general characteristics of the patients were presented through the most prevalent gender and the mean, median and standard deviation of the age and time of hospitalization. The subgroups of patients without and with ADE were compared and the differences were submitted to tests of statistical significance (Chi-square and Student's t). The differences that presented $p < 0.05$ were considered significant.

The ADE were represented by frequency indicators such as: incidence of patients with adverse drug events (number of patients with at least one ADE / total number of inpatients); rate of ADE per 100 patients (ADE number / total number of inpatients). The

distribution of the damage occurred according to the NCC MERP classification and the causality of the events was also performed.

To evaluate possible risk factors for adverse drug events, comparisons were made through the ANOVA table. The variables selected were the use of more than 5 medications per patient, length of hospital stay and gender.

The positive predictive value (PPV) of the triggers was analyzed in three components. The first one was calculated by dividing the number of records of each trigger by the total of medical records, multiplied by 100 (1); The second, by dividing the number of ADE identified by the total number of medical records, multiplied by 100 (2); The third, was calculated by dividing (2) by (1), multiplied by 100. The latter is a ratio that defines the performance of the trigger and expresses, in relative values, the potential of each of them to identify ADE [23].

ETHICAL ASPECTS

The present study was approved by the Research Ethics Committee of the institution where the research was carried out with protocol number CAAE 54908616.7.0000.5256.

3 RESULTS

The study sample consisted of 120 patients. It was verified that the largest proportion was male subjects (55%), mean age was 65.1 years (sd 18.8) and median was 69 years. Regarding the hospitalization time, on average the patients were hospitalized for 15.6 days (sd 21.5) and median of 8 days. Subgroups of patients with and without ADE did not show significant differences when compared (TABLE I).

TABLE I. Characteristics of patients hospitalized in the intensive care unit according to the occurrence of adverse drug events.

Variable	**WithADE**		**Without ADE**		**Total**		**P**
	n	%	N	%	n	%	
Average Age	64 (18,3)	-	65,4 (18,9)	-	65,1	-	0,771
Sex							
Male	10	55,5	56	54,9	66	55	0,959
Female	8	44,5	46	45,1	54	45	
Number of medicines							0,549
More than 5 medicines	18	100	100	98	118	98,3	
Less than 5 medicines	0	0	2	2	2	1,7	
Average Length of Stay (days)	24 (29,3)	-	14,1 (19,5)	-	15,6 (21,5)	-	0,070

The surgical procedures and the infectious complications were the main causes of hospitalization. It was observed that the immediate postoperative period was the most prevalent reason and it took 38 patients (31.6%) to the ICU, followed by sepsis and septic shock, which corresponded respectively to 10.8% and 9.2 % of hospitalizations.

During the study, a total of 289 triggers were detected in 108 patients. An average time of approximately 9 minutes was required to carry out the detailed analysis of the chart where each trigger was found in order to confirm the occurrence of ADE. After the detailed analysis, a total of 19 ADE presented by 18 patients were identified (BOX 1). The incidence of patients with adverse drug events was 15%, and the ADE rate was 15.8 ADE / 100 medical records.

When analyzing the hospital pharmacovigilance database to compare the ADE detection capacity between the trigger tool methodology and voluntary reporting, it was found that the ICU did not report any ADE through voluntary reporting during the study period.

BOX 1 – Description of adverse drug events identified during intensive care unit hospitalization.

Characteristic of Patient	Triggers Identified	Description of the ADE	Medicines Suspects	Characteristic of ADE
85 years old, male,120 days of hospitalization	Oversedation/Hypotension	Severe hypotension	Fentanyl and Midazolam	Not Preventable
85 years old, male, 120 days of hospitalization	Antiallergic Administration	Erythematous rash on upper limbs	Vancomycin	Not Preventable
50 years old, female, 2 days of hospitalization	Oversedation/Hypotension	Drug Interaction between tramadol and codeine	Tramadol and Codeine	Preventable
43 years old, female, 21 days of hospitalization	Oversedation/Hypotension	Severe hypotension	Midazolam	Preventable
77 years old, female, 24 days of hospitalization	Oversedation/Hypotension	Hypotension	Midazolam	Preventable
88 years old, male, 55 days of hospitalization	INR > 6 PTT > 100 s Transfusion of Blood or Use of Blood Products	Bleeding due to concomitant use of Enoxaparin and warfarin after target INR between 2 and 3.	Enoxaparin and Warfarin	Preventable
73 years old, male, 7 days of hospitalization	Cardiorespiratory Arrest	Hypovolemic shock caused by bleeding	Enoxaparin	Preventable
78 years old, male, 3 days of hospitalization	Oversedation/Hypotension	Hypotension	Captopril and Carvedilol	Not Preventable
71 years old, female, 8 days of hospitalization	Abrupt medication stop	Tachycardia	Fenoterol e Formoterol	Preventable

38 years old, male, 55 days of hospitalization	Decrease in Hemoglobin or Hematocrit of 25% or Greater	Hematuria	Enoxaparin	Not Preventable
63 years old, male, 7 days of hospitalization	Transfusion of Blood or Use of Blood Products Vitamin K Administration INR > 6	Bleeding	Warfarin	Not Preventable
36 years old, male, 8 days of hospitalization	Serum glucose <50 mg/dl	Hypoglycemia	Insulin Regular	Preventable
75 years old, male, 8 days of hospitalization	Antiallergic Administration	Rash cutâneo	Vancomycin	Not Preventable
84 years old, female, 18 days of hospitalization	Serum glucose <50 mg/dl	Hypoglycemia	Insulin Regular and Insulin NPH	Not Preventable
62 years old, female, 5 days of hospitalization	Transfusion of Blood or Use of Blood Products PTT > 100 s Decrease in Hemoglobin or Hematocrit of 25% or Greater	Bleeding	Dabigatran	Not Preventable
68 years old, male, 14 days of hospitalization	Anti-emetic Administration	Nausea, vomiting and sweating	Hydralazine	Not Preventable
25 years old, male, 41 days of hospitalization	Antiallergic Administration	Erythematous rash	Vancomycin	Not Preventable
64 years old, female, 31 days of hospitalization	Oversedation/Hypotension	Hypotension	Fentanyl	Not Preventable
71 years old, female, 6 days of hospitalization	Serum glucose <50 mg/dl	Hypoglycemia	Insulin Regular and Insulin NPH	Preventable

Adverse drug events identified were primarily caused by high-alert medications. Regarding the possible risk factors for the development of ADE in the intensive care unit, the variables age over 65 years, length of stay greater than 15 days, and male gender were used in this analysis. Among these factors only the length of stay greater than 15 days was shown to be related to a higher occurrence of ADE (OR= 2,89). (TABLE II)

TABLE II – Evaluation of risk factors for the development of ADE in an intensive care unit.

		CI (95%)		
Risk Factors	**OR**	**Inferior**	**Superior**	**p**
Age over 65 years	0,73	0,27	1,96	0,538
Length of Stay greater than 15 days	2,89	1,05	7,93	0,035
Male Gender	1,03	0,37	2,81	0,959

According to the NCC MERP severity rating [21], most events were allocated to Category E, which are events characterized by temporary damage and requiring

intervention. Nearly 50% of the ADEs were classified as possible according to the Naranjo algorithm used to impute the causality of the events. Pandya et al [16], analyzing a database of an emergency department, through the World Health Organization (WHO)-Uppsala Monitoring Centre (UMC) causality scale, found that only 24,2% of the ADE got this classification. This difference may be explained by the fact that medical records in ICU usually have better quality.

Using the six-point scale, eight preventable ADE were identified due to inadequate doses for the patient's weight, drug interactions already described in the literature, contraindication to use due to clinical condition, and lack of adherence to institutional protocols and scientific literature. Among the preventable events it was verified that all were originated from the medical prescription and managed to reach the patient (TABLE III).

Some improvements in work routines to increase patient safety were proposed based on the identification of preventable ADE. Among the proposals for improvement is the development of drug use protocols, educational measures and changes in the way of work (BOX 2). These suggestions will be forwarded to the pharmacy and therapeutic committee for discussion and later incorporation into the routine of the ICU.

TABLE III - Distribution of adverse drug events according to criteria of severity, avoidability, causality and the stages that gave rise to the events.

ADVERSE DRUG EVENTS		
	Classification	Frequency
NCC MERP Severity	E	16
	F	1
	H	1
	I	1
Avoidability	Not Preventable	11
	Preventable	8
Step that originated the preventable ADE	Prescription	8
	Dispensation	0
	Administration	0
Causality	Definite	2
	Probable	7
	Possible	10

BOX 2 – Description of the proposals of improvement in the work routine from the identification of preventable ADE

Description of the ADE	Medicines Suspects	Number of ADE	Proposals for Improvement
Drug Interaction	Tramadol e Codeine	1	Educational measure on management of pain proposed by WHO and on the adverse effects of analgesics and adjuvants
Hypotension	Midazolam	2	Development of clinical protocol for the use of sedatives with description of maximum recommended doses
Bleeding due to concomitant use of Enoxaparin and warfarin after target INR between 2 and 3.	Enoxaparin and Warfarin	1	Educational measure on the use of the institutional protocol for prophylaxis and treatment and venous thromboembolism
Hypovolemic shock caused by bleeding	Enoxaparin	1	
Tachycardia	Fenoterol and Formoterol	1	Protocol development of chronic obstructive pulmonary disease
Hypoglycemia	Insulin Regular	2	Educational Measure on Continuous Insulin Infusion Protocol

A more detailed analysis of the study triggers found that the most frequent were: Oversedation/Hypotension (63/289), Transfusion of Blood or Use of Blood Products (54/289), Cardiorespiratory Arrest (40/289), Anti-emetic Administration (32/289) and Intubation (23/289).

The positive predictive value of the trigger, ie, the ability to detect an adverse drug event was calculated and the triggers with the highest values were the "Abrupt medication stop", "INR > 6", "Serum glucose <50 mg/dl" and "Antiallergic Administration" (TABLE IV). For the "Naloxone Administration" trigger, PPV was not calculated because this trigger was not detected during medical records review.

TABLE IV – Frequency of triggers found, adverse drug events identified and positive predictive value.

Trigger	Occurrence rate Trigger	Occurrence rate ADE	PPV
Abrupt medication stop	0,8	0,8	100,00%
INR> 6	1,7	1,7	100,00%
Serum glucose <50 mg/dl	5,0	2,5	50,00%
Antiallergic Administration	5,8	2,5	42,86%
PTT> 100 s	4,2	1,7	40,00%
Decrease in Hemoglobin or Hematocrit of 25% or Greater	8,3	1,7	20,00%
Vitamin K Administration	5,0	0,8	16,67%
Oversedation/Hypotension	52,5	5,0	9,52%
Transfusion of Blood or Use of Blood Products	45,0	2,5	5,56%
Anti-emetic Administration	26,7	0,8	3,13%
Cardiorespiratory Arrest	33,3	0,8	2,50%
Intubation	19,2	0,0	0,00%
Serum Creatinine Two Times (2x) over Baseline	17,5	0,0	0,00%

Restraint Use	6,7	0,0	0,00%
Acute Dialysis	5,8	0,0	0,00%
Flumazenil Administration	1,7	0,0	0,00%
Readmission to the UCI	1,7	0,0	0,00%

4 DISCUSSION

Using the trigger adapted for intensive therapy was found a rate of 15.8 ADE/100 medical records, mainly caused by high-alert medications. MacFie et al. found that the incidence of ADE in ICU ranged widely, from 1.3 to 21.1 [24]. High-alert medications are named because of the increased risk of causing significant harm to patients as a result of a failure to use them [10].

Most of the damages were considered temporary and required intervention. It is in accordance with the results of other studies [16,25]. The positive predictive value showed that the "Abrupt medication stop", "INR > 6" and "Serum glucose <50 mg/dl" had a greater ability to detect an adverse drug event when they were identified in medical records of patients. Pandya et al pointed out that “Abrupt medication stop” was the most common trigger and showed a significant statistical result for the ADE identification [16].

An intensive care unit serves patients who are critically ill and need interventional techniques and medications to achieve positive results. Because of the critical nature of the diseases, patients are usually receiving multi-drug regimens, many of which are classified as potentially dangerous, and therefore have a higher risk of presenting ADE [10,24]. Besides the intensive use of high-alert and intravenous medications [10,26], the characteristics of the diseases, the potential for drug interactions and the large number of drugs administered are also considered risk factor to the development of ADE [10].

It is noteworthy that 3 of the drugs involved in the observed ADE, warfarin, insulin and midazolam, are among the 10 drugs that accounted for 60% of the ADR identified by Winterstein et al. [27]. Other studies also identified those drugs in medicines related problems [28,29]. McFie et al., in a integrative review of drug errors in critical care, found that the drug groups more commonly implicated in ADE in the literature were cardiovascular, gastrointestinal, antimicrobial and hypoglycaemic agents [24]. Though, anticoagulants, opiates and insulin were identified in many papers analyzed by the authors.

Marsilio et al. [29], studying intravenous drug incompatibilities in the ICU prescriptions of a Brazilian hospital, reported that midazolam was the drug most commonly involved in drug incompatibilities and vancomycin was the third one. A similar situation was observed by Teixeira et al, analyzing the pIM in the ICU[30].

Otero and colleagues [9], studying 12 Spanish hospitals, found that the majority of ADE were mild with corticosteroids, loop diuretics, opioid analgesics and oral anticoagulants been the main drugs involved on those events.

The Institute for Safe Medication Practices in Brazil classifies high-alert medications as "those that present an increased risk of causing significant harm to patients as a result of a failure to use" [31]. This feature emphasizes the importance of implementing measures of rational use of drugs in intensive care patients in order to avoid harm reduction [10].

The rate of ADE identified in the study was lower than other previous studies performed in intensive care. A study using the same methodology to evaluate the incidence of ADE in the ICU of Antwerp University Hospital, in Belgium, detected a rate of 230 ADE/79 records using a total of 14 triggers [32].

A retrospective chart review conducted without computerized systems for the detection of the triggers was capable of detecting a rate of 32 adverse events / 100 medical records in a total of 128 patients included in the study [33]. Other methodologies used for the evaluation of adverse events in intensive care also demonstrated higher rates of ADE. In the study carried out through an observational cohort study that analyzed the admissions in the ICU, a total of 1126 adverse events were identified in 202 admissions studied, of this total 25.8% were related to the use of drugs [34].

Regarding risk factors, some studies have related age, gender and race with a greater chance of developing ADE. Age, due to pharmacokinetic and pharmacodynamic changes, comorbidities and polypharmacy; the female gender, due to hormonal changes and because they present more health problems, making them use more health services, conducting frequent consultations and examinations, obtaining more diagnoses and medical prescriptions and consequently consume more medication; and racial differences, due to genetic variations that may alter the receptors and the metabolism of drugs [35]. In this study, no relation was found between gender and age and a higher occurrence of ADE. Only length of stay greater than 15 day has been shown to be a risk factor for adverse events. This result probably must be related to a greater consumption of medicines and the realization of more frequent interventionist techniques.

The study performed by Otero et al. [9] in hospitals in Spain found a proportion of preventable ADE of 59,5%. In this study using only the ICU of a hospital a proportion of approximately 42% of preventable events was found. This difference may be related to the characteristic of the hospital that frequently has professionals with low clinical

experience, due to the teaching actions such as medical residency and a temporary hiring process of professionals.

The lack of notifications of ADE through the voluntary reporting methodology enforces the underreporting problem, already pointed out in the literature [13,14]. From the analysis of the medical records was verified that most events are reported in the clinical evolutions of the health professionals who attend the patient, but this information do not generate notifications. Educational interventions seem to be an important strategy to promote a change in attitude. But is worth noting that the literature suggest that multiple interventions have a greater potential to promote increase in ADR reporting rates than single ones [14].

Regarding the severity of ADE, in 2003, the IHI verified that approximately 80% of the ADE were included in Category E as temporary harm requiring intervention. The second most prevalent, corresponding to 12.4%, were those events that caused temporary harm to the patient and necessitated initial or prolonged hospitalization [17]. The severity of the events observed by the IHI presented a similar proportion to that found in the intensive care unit of this study. In the ICU, the ADE classified in Category E of the NCC MERP corresponded to 85%, while the other events were classified in the categories F, H and I with a frequency of 5% for each category.

Seynaeve et al [32] did not find ADE of sufficient severity to be classified in categories G, H and I. The proportion of events that were classified as category E was 96% and the other 4% were classified as category F.

Assessing the ability of triggers to detect adverse drug events, a study performed at a tertiary teaching hospital found similar positive predictive values using the "INR> 6" and "Over-Sedation/Hypotension" triggers while the "Antiallergic Administration" and "Abrupt medication stop" triggers had lower PPV, being 25 % and 43%, respectively [36]. Another study found that only fifteen triggers had PPV ≥20% and six of them (serum glucose >110 mg/dL, abrupt cessation of medication, oversedation/lethargy, hypotension, adverse reaction recorded and constipation) were involved in 69.8% of the ADE identified [9].

Using only the "Vitamin K Administration" trigger for the detection of bleeding adverse events in a hospital specialized in cardiology, a study presented a performance of this trigger of 30.4% in event detection [37]. This result differs from ours. This difference could be related to drug use objective. In the cardiology hospital [37] the drug was used as an antidote for cases of bleeding caused by warfarin, while in the ICU the drug was used

with a higher frequency by patients who needed to perform invasive procedures and had altered INR values.

Hu and colleagues, analyzing the occurrence of the AE in a tertiary hospital, using the Global Trigger Tool, found 610 AE in total in 480 medical records reviewed, corresponding to 127 injuries per 100 admissions. The authors suggest that GTT should be applied into routine screening of AE [6].

However, Silva and colleagues, in a prospective and longitudinal study, in a university hospital in the state of Minas Gerais, considered that the IHI Trigger Tool did not show good accuracy in detecting ADE. The authors suggest the adoption of combined strategies to enhance effectiveness in safety flaws detection [38].

The main advantage of the present study was the ability to detect adverse drug events, since the voluntary reporting at the institution does not receive data from the hospitalization units and therefore does not generate concrete data regarding the incidence of ADE. The data obtained will serve to elaborate new protocols and institutional routines that will be used to increase patient safety. It is noteworthy that similar clinical pharmacists actions to prevent adverse drug events in ICU have been reported at the literature [25, 30, 39, 40].

As a pilot study was conducted, the absence of previous studies in the institution using this active surveillance methodology becomes a limitation, because it is not possible to perform a comparison between different units and/or periods. The creation of a list of triggers for each patient profile and the low availability of intensive care studies also made it difficult to compare the results obtained with other works present in the scientific literature.

Another limitation was the use of only one professional category for the retrospective review of medical records. The presence of nurses, physicians and other health professionals in the review process could complement the analysis, bringing to the study different concepts and professional experiences.

5 CONCLUSION

The present study emphasized the importance of using an active surveillance methodology to detect adverse drug events. Because it can be applied in a short period of time and able to present good results from a representative sample of patients, it was possible to confirm that the trigger tool methodology can be incorporated into the work routine of the unit.

With the information obtained, it was possible to elaborate a profile of this intensive care unit to later propose educational and operational measures aimed at reducing the number of new cases of preventable adverse drug events. From these results the professionals who provide care in the unit will be qualified to make the environment increasingly safe for patients who need intensive care.

New studies should be carried out to evaluate the effectiveness of the proposed measures and to improve the use of the trigger tool methodology.

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