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RESEARCH

PREVENTIVE STRATEGIES OF ADVERSE EVENTS WITH POTENTIALLY DANGEROUS MEDICATIONS

ESTRATÉGIAS PREVENTIVAS DE EVENTOS ADVERSOS COM MEDICAMENTOS POTENCIALMENTE PERIGOSOS

ESTRATEGIAS DE PREVENCIÓN DE EVENTOS CON MEDICAMENTOS POTENCIALMENTE PELIGROSOS

Flavia Giron Camerini[1], Lolita Dopico da Silva[2], Taylane Guimarães Gonçalves[3], Fernanda Mello de Lima[4], Marina Lopes Thompson[5], Sabrina Cruz Esteves Pessôa[6], Caroline Campos Santos[7]

ABSTRACT

Objective: To describe the strategies adopted by nurses for safe administration of a potentially dangerous drug in the intensive care unit. **Method:** This is an exploratory study literature which included articles about potentially dangerous drugs and medication errors in intensive care units published in the period 1998 to 2009. **Results:** The study included 16 items that resulted in three categories of potentially dangerous medications (amines, heparin and insulin), which were described the light of error prevention strategies. **Conclusion**: The occurrence of adverse events with potentially dangerous medications is mostly preventable, and that for each class of potentially dangerous medications can be taken specific measures to prevent possible adverse events. **Descriptors**: Nursing care, Intensive care, Medication errors, Adverse drug reaction and security.

RESUMO

Objetivo: Descrever as estratégias adotadas pelo enfermeiro para uma administração segura de um medicamento potencialmente perigoso em unidade de terapia intensiva. **Método**: Trata-se de estudo exploratório bibliográfico onde foram incluídos artigos sobre medicamentos potencialmente perigosos e erros de medicação em unidades de terapia intensiva publicados no período de 1998 a 2009. **Resultado**: Foram analisados 16 artigos que resultaram em três categorias de medicamentos potencialmente perigosos (aminas, heparinas e insulinas), que foram descritas a luz das estratégias preventivas de erros. **Conclusão**: A ocorrência de eventos adversos com medicamentos potencialmente perigosos é na maioria das vezes, evitável, e que para cada classe de medicamentos potencialmente perigosos podem ser adotadas medidas específicas a fim prevenir possíveis eventos adversos. **Descritores**: Assistência de enfermagem, Cuidados intensivos, Erros de medicação, Reação adversa a medicamento e segurança.

RESUMEN

Objetivo: Describir las estrategias adoptadas por las enfermeras para la administración segura de una droga potencialmente peligrosa en la unidad de cuidados intensivos. **Método:** Se trata de una literatura estudio exploratorio que incluyó artículos acerca de las drogas potencialmente peligrosas y los errores de medicación en unidades de cuidados intensivos publicados en el período 1998 a 2009. **Resultados:** El estudio incluyó 16 artículos que dieron lugar a tres categorías de medicamentos potencialmente peligrosos (aminas, la heparina y la insulina), que fueron descritos a la luz de las estrategias de prevención de errores. **Conclusión:** la ocurrencia de eventos adversos con medicamentos potencialmente peligrosos es en su mayoría prevenibles, y que para cada clase de medicamentos potencialmente peligrosos se pueden tomar medidas específicas para prevenir posibles efectos adversos. **Descriptores**: Cuidados de enfermeira, Cuidados intensivos, Los errores de medicación, Reacciones adversas a medicamentos y seguridad.

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INTRODUCTION

The medications administration is one of the most commonly used interventions in the hospital environment, however, some studies have revealed the existence of mistakes during the drug therapy that can cause harm to patients, by ranging from the non-administration of such a drug until injuries and deaths caused by inadequate doses of such a drug, or when a drug is indicated to the wrong patient.[1,2]

The erroneously administered medications are directly linked to the issue of patient safety.

According to the World Health Organization, the term "patient safety" consists in *"reducing the risk of unnecessary harms associated with the healthcare to an acceptable minimum level",* which has motivated discussions, since this care action is performed by human beings, hence, they are liable to make mistakes. [3]

Within this issue linked to the patient safety regarding the medications administration, it is understood by Adverse Event, *"an incident that occurs to a patient and results in harm, arising from the care provided to it and not related to the natural progression of the underlying disease".*[3]

By considering the survey of Harvard Medical Practice Study II, adverse events with the highest incidence are related to medication mistakes, being that most of them are considered avoidable. One can say that between 50% and 60% of adverse events are preventable.[4,5]

It is estimated that, in the United States, the mistakes related to the drug therapy have reached about 1,3 million people per year, by generating a cost that, annually, reaches 76,6 billion dollars related to patients' admission due to adverse events.[6]

Faced with the high incidence of mistakes related to the use of medicinal drugs, one must emphasize the requirement of an extensive technical/scientific knowledge by the nursing professional, as regards to the medications handling, since some medicinal drugs have singular capability of damaging the patient when mistakes are committed during their use. Such medications are called high-alert medications or high risk medications; here, in Brazil, they are called potentially dangerous medications, in compliance with the ANVISA nomenclature.

The intensive care units are extremely vulnerable sites to adverse events occurrences, due to a higher probability of invasive procedures occurrence, multiple medications administration, severity of pathologies and the need for fast decision-making. One study reports that the prevalence of adverse event with potentially dangerous medications is settled in several sectors in the hospital environment, but there was a higher concentration in intensive care units.[7]

Based on these considerations, we have drawn as the study object the establishment of some strategies for a safe administration of a potentially dangerous medication in intensive care unit environment and with the aim at describing the strategies adopted by the nursing professional for a safe administration of a potentially dangerous medication in intensive care unit scope.

METHODOLOGY

To meet the objective proposed in this study, we have performed an exploratory literature research with the following steps: research question, descriptors selection, selection criteria definition, bibliographic material survey, categories organization and data analysis. The study was grounded on the following guiding question: what strategies should be adopted by

the nursing professional for a safe administration of a potentially dangerous medication in the intensive care unit scope?

The study object definition was conducted by including all papers on potentially dangerous medications and medication mistakes in intensive care units published in the period from 1998 to 2009 and which were indexed in the following databases: *Agência Nacional de Vigilância Sanitária* (ANVISA), Virtual Health Library (VHL), Latin American and Caribbean Health Sciences (LILACS), World Health Organization (WHO), PUBMED, Scientific Electronic Library Online (SciELO) and the Inter-American Society of Pharmacovigilance (ISPhar), with a view to meeting the literature recommendation of seeking in different sources when performing a publications survey. The selection criteria were: articles in Portuguese and English with texts available in their full version in the established period, indexed by the following descriptor expressions: "Nursing care"; "Intensive care"; "Medication mistakes"; "Adverse reaction to medication" and "Safety"; besides making reference to the admitted adult population. For data collection, we have developed a tool based on literature review protocols, being that we replaced items originally written in English "citation" and "intervention" by *"título"* and *"procedimentos metodológicos"*.

The 16 selected papers were divided into three categories (amines, heparins and insulins) that supported the analysis of the data obtained in this study.

RESULTS AND DISCUSSION

The survey was resulted of 54 different papers arranged in the selected databases, by adding review studies or original data presentation.

The results emerged from selection of 16 papers, relevant to the issue and the study object, which were analyzed and, subsequently, grouped into three medication categories: amines[7,11,14], anticoagulants[17,20,22,23] and insulins[24,25,26,27,28,29,30], being that such a grouping guided the study discussion. The aforementioned categories were created from the reading of papers.

It should be highlighted that the publication period of the articles analyzed in this research, which has formed an updating paper, was specifically established as a result of the availability of the scientific material that was found, by showing a gap between the technological and practical advances of the nursing staff in intensive care units and the publication thereof, by this same professional category, which hindered the development of our labor.

Most of papers have highlighted legal and ethical issues inherent in the nursing profession, as well as the civil accountability of the nursing professional before of the potentially dangerous medications administration in the intensive care unit and its repercussions arising from avoidable adverse events, i.e., medication mistakes.

Given the alarming statistics about the incidence of adverse events with potentially dangerous medications in the intensive care units, studies of Toffoleto and Padilha reveal that every eight patients/day, one patient suffers an adverse event. Another study also highlights that every 300 patients/day, one fatal adverse event occurs; being that every 750 patients/day might be represented as one avoidable death for every 68 weeks.[8,9,10]

Before these discussions, the three medication classes covered in this study will be presented below by means of categories, in order to subsidize a technical and scientific foundation for the proposal of describing safe administration

strategies for potentially dangerous medications in intensive care unit scope.

Category I: vasoactive medications (amines)[7,11,14]

Amines are drugs that have their actions focused on the cardiac output regulation, which is the end product of the systolic volume versus the cardiac rate, where the systolic volume is related to the ventricular filling volume and pressures, also called pre-load, as well as the resistance to the myocardial emptying and contractility, called after-load. These are medications that, in small doses, produce fast responses, which can generate a dose-dependence effect.[11.]

Thus, the main avoidable adverse events related to the amines are: cardiac arrhythmias, arterial hypotension/hypertension, bradycardia/tachycardia and urinary tract changing.[12,13]

Faced with the severity of changes provoked in the body by the improper use of these medications, the incidence rates of 31% and the avoidable adverse events related to the administration thereof, which have already been mentioned in this paper, we suggest some extreme important strategies for the safe administration of this class of potentially dangerous medications, which will be hereinafter described.[7]

According to the Norepinephrine label, the amines administration should strictly occur in continuous infusion pump and their dosage should be monitored through daily weight assessment, since it will enable the infusion of the correct dose in function of the patient's needs, by avoiding an overdosage and consequent tachycardia/ arterial hypertension. [12]

The amines administration should exclusively occur in deep venous catheter, in order to avoid disorders caused by accidental leakage of these medicinal drugs[13], such as tissue necrosis adjacent to the catheter, due to the vesicant hydrogenionic potential (pH) of this medications class, i.e., pH below the normal plasma pH (7:35 -7:45). Given these considerations, one must be careful about the pHs of some medications, such as: Dobutamine (pH 2.5 – 5.5) Epinephrine (pH - 2.2), Dopamine (pH = 2.5) and Norepinephrine (pH=4.5).[14,15]

With regard once more to the vasoactive medications administration, it was observed that there is a convention in clinical practice regarding the use of deep venous catheters, where we should give preference to always insert these medicinal drugs through the proximal route (which should be identified to provide exclusivity) since this has a “prime” (gauge), gravitational flow and infusion rate (ml/hr) lower than the other lumen (distal and medial), with a view to avoiding “flushes” of these medications and, consequently, their overdosage.

During amines infusion, there should be a frequent assessment of the peripheral tissue perfusion, through the verification of the peripheral pulses, since they might be associated to the risk of developing pressure ulcers by decreased peripheral perfusion in dosages from 2 to 15 mcg/kg/min. Moreover, we should promote body warming (especially of the extremities) with quilts and/or blankets, bear in the mind the peripheral vasoconstriction caused by these medications.[16]

Due to the increased systemic arterial resistance (in dosages from 2 to 15 mcg /kg/min) and considering the arrhythmogenic potential of amines, it should be installed the continuous cardiac monitoring, pulse oximetry and invasive method (or minimally invasive) for monitoring the blood pressure, with sights to accurately control the patient’s hemodynamic parameters in use of vasoactive medications.[16]

According to the Norepinephrine label, in relation to the hemodynamic monitoring, the

measurement of vital signs should occur every 5 minutes throughout the infusion, since the amines have dependent doses and that the endogenous release might alter the route of exogenous absorption. Nonetheless, it was practically observed that the vital signs can be hourly measured, without incurring in damages to the hemodynamic monitoring and the care itself, as well as the patient's condition.[12]

In the hemodynamic monitoring, for performing a precise control of the urinary output, one should perform a permanent vesical catheterization and establishing a rigorous hydric balance, because these medications have peculiar action over the regulatory parameters of the cardiac output and the reduction of organ perfusion, given that some amines make use of the renal system like excretory route, which might interfere with the diuresis, being that it should be leveled between 0.5 and 1 ml/kg/h.[13]

Through the above mentioned strategies, it can be inferred that the safe administration of amines should be performed in a systematic and extremely careful manner by the whole nursing staff, so that it contributes to the reduction of avoidable adverse events rates due to this medication class.

Category II: anti-thrombotic (heparins)[17, 20, 22, 23]

The antithrombotic drugs are widely used in several treatments in intensive care units, both in preventive and in therapeutic way. They encompass various medication types. But, we have decided to address only those most commonly used in intensive care units throughout this study, i.e., intravenous and subcutaneous heparins, which will be discussed in this category.[17]

The intravenous heparin (also known as non-fractionated heparin) acts through two anticoagulant mechanisms: direct inhibition of thrombin and factor Xa inhibition, thus interfering in the coagulation cascade. The drug therapy with intravenous heparinization is known as Raschke Scheme, which aims at maintaining serum levels of heparin between 0.35 and 0.70 U/ml, according to the patient's body weight. This scheme provides for the initial heparin administration in bolus, by giving continuity to the therapy with permanent infusion under rigorous analysis of APTT (activated partial thromboplastin time) and PTT (partial thromboplastin time).[17,18]

Thus, the main avoidable adverse events associated to the intravenous heparin are: bleeding /hemorrhages and thromboembolism (in case of insufficient doses). Before the risks and changes in the body caused by the improper use of this medicinal drug, as well as the incidence of avoidable adverse events related to the administration thereof, as previously mentioned, we suggest some crucial strategies for the safe administration of this class of potentially dangerous medications, which will be hereinafter mentioned.[19]

According to the heparin protocol from the Albert Einstein Israelite Hospital, the non-fractionated heparin administration should strictly occur in continuous infusion pump and its dosage should be adjusted by daily weight assessment, since it will enable the infusion of the correct dose in function of the patient's needs, in order to avoid an overdosage and consequent and, consequently, hemorrhagic events.[17]

With regard once more to the non-fractionated heparin administration, it was observed that there is a convention in the clinical practice with regard to the use of deep venous catheters, where one should give preference to always install this medication in the proximal route (which should be identified to provide exclusivity) since this has a “prime” (gauge),

gravitational flow and infusion rate (ml/hr) lower than the other lumen (distal and medial), with a iew to avoiding "flushes" of such a medication and, consequently, its overdosage.

Another strategy to assure the safe administration is setting the therapeutic dose, which requires a rigorous collection and assessment of the activated partial thromboplastin time (APTT), initially every 6 hours, by increasing the time interval to control to every 12/12 hours, when the healthcare professional achieves two consecutive controls within the ideal range (61-85 seconds).[20]

Concerning the subcutaneous heparin (or low molecular weight heparin), also frequently used in intensive care, it is primarily metabolized in the liver, by causing depolymerization and/or desulfation, when forming molecules of lower weight, with extremely reduced biological potency, which results in a safe medication in its administration, with less risk of hemorrhages and thrombocytopenia. The drug therapy recommends the subcutaneous heparin administration at 1mg/kg-2x/day and prophylactic subcutaneous heparin at 40mg 1x/day or, furthermore, intravenous heparin 5.000 IU through subcutaneous route for every 8/8 hours. It is worth mentioning that, according to the Food and Drug Administration (FDA), the use of subcutaneous heparin is not recommended for patients under hemodialysis treatment, since the primary excretion route is the renal one.[17,21,22.]

Thus, the main avoidable adverse events related to the subcutaneous heparin are: bleeding/hemorrhage and necrosis of the subcutaneous tissue. According to the risks caused in the body by the inappropriate use of this medication, as well as the incidence of avoidable adverse events associated to the administration thereof, as previously mentioned, we suggest some crucial strategies for the safe administration of this class of potentially dangerous medications, which will be reported below.[17]

It is worth mentioning that there is a small inert gas bubble into the syringe of subcutaneous heparin, which should not be removed, because its function is to avoid the medication leakage.[23]

In line with the suggested strategies, one can say that the safe administration of heparins, both venous and subcutaneous should be performed in a standardized way, according to institutional protocols, in order to contribute to the preventable adverse events prevention in this medication category.

Category III: insulin[24-30]

It is an anabolic hormone that holds regulatory action of the glucose homeostasis in several levels, by reducing the hepatic glucose production (gluconeogenesis and glycogenolysis) and increasing the peripheral glucose uptake, especially, in muscle and adipose tissues. Moreover, it stimulates the lipogenesis in the liver and adipocytes and reduces the lipolysis, as well as increases the synthesis and inhibits the protein degradation.[24]

Given the above, it worth mentioning that among patients admitted to the intensive care unit is common the existence of changes in the endocrine and metabolic system, whether with or without a previous diagnosis of diabetes mellitus. The elevated glucose levels are strongly associated with increased morbidity and mortality indexes in patients under intensive care. This is corroborated by a study conducted by Van den Berghe (2001) addressing critical patients in an intensive care unit, which showed that intensive control of blood glucose levels with continuous intravenous insulin therapy drastically reduced morbidity and mortality when compared to the subcutaneous therapy. [25]

The hyperglycemia in the intensive care patient is a constant factor related to the

response to the organic stress, where there is increased release of counterregulatory hormones secretion, by decreasing the insulin secretion and action and favoring the hyperglycemia and the peripheral insulin resistance. Added to this situation, one can see the common interventions in intensive care units, such as corticotherapy, therapy with vasoactive amines and nutritional supports, which culminates in the worsening of the patient's hyperglycemic state. [26]

Concerning the hypoglycemia, associated with the intravenous insulin therapy, occurs in about 4 to 7% of patients, by reflecting the result of the excessive insulin administration; insulin infusion maintenance without concomitant replacement of dextrose solution at 5%, after obtaining glucose ≤ 250 mg/dl; inability to interpret institutional protocols and difficulties of administering the dosage. [27]

Hence, to maintain the blood glucose in an acceptable range, it is recommended to implement an insulin therapy protocol with defined strategies, thus preventing complications such as hypoglycemia. That said, we recommend some strategies necessary for a safe administration of the single insulin type that can be intravenously administered (regular insulin), which will be hereinafter considered. [28]

The intravenous regular insulin administration should strictly occur in continuous infusion pump and its dosage should strictly be controlled, with sights to avoid hypoglycemia. [28]

According to Van den Berghe et al., during the whole time of regular intravenous insulin infusion, there should be an intensive monitoring of the glycemic control (hourly) and of the hypoglycemia signs such as: cold and clammy sweating, mucocutaneous paleness and altered awareness level, which are anticipated to this event that can harm the central nervous system, if it is not immediately identified and corrected.[25]

Another important measure of monitoring consists in daily contrast the results of the capillary blood glucose with the results of the serum glucose, in order to detect very different values in the event of failure of the glucometer available at the healthcare unit, thus avoiding hypo or hyperglycemia intercurrences arising from wrong dosages. [28]

With regard to the glycemic monitoring, it is recommended to collect, preferably in a closed system of deep access, a minimal blood volume necessary for performing the capillary blood glucose, in order to avoid discomfort, pain resulting from multiple digit-punctures, infection risk linked to numerous invasive procedures, as well as contribute to the eradication of anemia caused by excessive collections of laboratory examinations.[28]

To prevent severe hypoglycemia and its irreversible effects on the central nervous system, one should administer/ offer diet or some glucose intake (according to the route by clinical indication) immediately before the beginning of the intravenously regular insulin infusion. The same author states that one should suspend the administration concomitant with the interruption of enteral or parenteral infusion, before the hemodialysis time, (considering the hypoglycemic effects inherent in the therapeutic time), since it can trigger a severe hypoglycemia and its irreversible effects over the central nervous system, in case of non-interruption of the medicinal drug stream.[29]

Concerning the leading preventable adverse events related to the regular insulins by subcutaneous administration route, they are hypoglycemia and necrosis of subcutaneous tissue, which characterize avoidable adverse events during the administration of these drugs, due to the misuse or ineffective monitoring throughout the therapy. Before the presented risks, we

propose some important strategies for the safe administration of this class of potentially dangerous medications, which will be hereinafter publicized.[30]

According to Clayton, to prevent abscess and/or necrosis of subcutaneous tissue, pain at the injection site and promote a quick absorption of insulin by means of subcutaneous route, according to the application site, depending on the need of the absorption speed thereof in the body, one should implement and maintain the rotation of sites for applying thereof.[16]

Furthermore, according to the aforementioned scholar, it should be performed a skinfold thickness by using only two fingers, in order to avoid the lifting of the muscular fascia, as well as the pain arising from this maneuver. Moreover, according to the already cited protocol, to avoid the lifting of the tissue trauma and changes in the drug absorption, after the insulins administration by means of subcutaneous route, it is recommended to apply a soft pressure on the administration site and do not rub it.[16,17]

According to Van den Berghe, for anticipating in relation to the hypoglycemia, which can bring about harms to the central nervous system, if it is not immediately identified and corrected, it is recommended to coordinate the meal times with the use of subcutaneous insulin, besides monitoring the capillary glucose levels (pre-prandial ones) and the hypoglycemia signs such as: cold and clammy sweating, mucocutaneous paleness, as well as altered awareness level, during the administration of these medicinal drugs. [25]

Given the need for insulin therapy, it is a task of the nursing professional to show ability towards the protocol adopted in its institution, holding pathophysiological knowledge of hypo/hyperglycemia and establishing preventive strategies to deal with adverse events, in order to maintain adequate glycemic control and success in therapy, as the proposals of this study.

CONCLUSION

This study highlights how the avoidable adverse events are common in the hospital environment, especially in intensive care units, due to the complexity of pathologies, technological advancement, as well as greater likelihood of invasive procedures, and that such incidents can occur in several times throughout the admission. It also emphasizes that the most frequent preventable adverse events are related to medications, especially, to the potentially dangerous medications, which can be fatal.

We have confirmed that the nursing care provided in the intensive care unit is dedicated in a complex scope, composed of critical ill patients and modern technological methods, whose need requires a high level of professional qualification and structural resources that are appropriated to provide a careful attendance to the patient, where the recognition of adverse events and factors attached to them enables the identification of the weak points of this varied care process, as well as to implement interventions aimed at improving the care quality.

In view of this, we conclude that, for achieving the reduction of avoidable adverse events in the potentially dangerous medications administration in intensive care units, it is necessary to simplify the care processes and standardize the administration system of each class of these medicinal drugs. Furthermore, the nurses should also propose prevention strategies for applying in these units, given their potential risk and wide-ranging use thereof, with sight to contribute to the care improvement and safety promotion for the patient who needs it.

It should be noted the importance of conducting and publishing further surveys involving such an issue, since there were few Brazilian data obtained in this study on the occurrence of avoidable adverse events, which hampered the situational diagnosis of the reality experienced by Brazil, as well as the adopted measures to prevent avoidable adverse events related to the potentially dangerous medications administration in the intensive care unit scope.

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