# CUIDADO É FUNDAMENTAL

Universidade Federal do Estado do Rio de Janeiro · Escola de Enfermagem Alfredo Pinto

INTEGRATIVE REVIEW OF THE LITERATURE

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# HYPOGLYCEMIA MINIMIZING TECHNOLOGIES USED IN ADULT PATIENTS DURING CONTINUOUS INFUSION OF INSULIN

Tecnologias utilizadas na minimização da hipoglicemia em pacientes adultos durante a infusão contínua de insulina

Tecnologías utilizadas en la minimización de la hipoglucemia en pacientes adultos durante la infusión continua de la insulina

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#### ABSTRACT

**Objective:** The study's purpose has been to identify existing technologies for minimizing hypoglycemia in adult patients undergoing continuous intravenous insulin infusion. **Methods:** It is an integrative review of scientific literature available in Portuguese, English and Spanish, indexed in the Virtual Health Library (VHL), over the period from 2005 to 2015. **Results:** After accomplishing the search, selection and analysis of the articles, 06 complete studies were found addressing the technologies to minimize hypoglycemia during continuous intravenous insulin infusion. This sample also featured computer protocols and paper protocols used during treatment. **Conclusion:** This research was able to identify technologies that were created to minimize the occurrence of hypoglycemia during continuous infusion of insulin. The computer protocols were considered to be more effective in minimizing hypoglycemic events.

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**Descriptors:** Health technologies, insulin, hypoglycemia, intensive care.

#### RESUMO

**Objetivo:** Identificar as tecnologias existentes para minimização de hipoglicemia em pacientes adultos durante a infusão contínua de insulina (ICI) venosa. **Método:** Revisão integrativa das produções científicas disponíveis em português, inglês e espanhol, indexadas nas bases de dados da Biblioteca Virtual de Saúde (BVS), tendo como recorte temporal os anos de 2005 a 2015. **Resultados:** Após a busca, seleção e análise dos artigos, foram selecionados 06 estudos para compor a amostra, os quais se encontravam disponíveis na integra, e que evidenciavam tecnologias existentes para a minimização da ocorrência de hipoglicemia durante a ICI venosa. A amostra caracterizou protocolos informatizados e protocolos de papel utilizados durante o tratamento. **Conclusão:** O estudo conseguiu identificar tecnologias que foram criadas para minimização da ocorrência de hipoglicemia durante a infusão contínua de insulina. Os protocolos informatizados foram considerados mais eficazes na minimização de eventos hipoglicêmicos.

Descritores: Tecnologias em saúde; Insulina; Hipoglicemia; Terapia intensiva.

#### RESUMÉN

Objetivo: Identificar las tecnologías ya existentes para la minimización de la hipoglucemia en pacientes adultos durante la infusión continua de la insulina por las venas. Metodología: Revisión integrativa de las producciones científicas disponibles en portugués, inglés y español, indexadas en las bases de los datos de la Biblioteca virtual de salud (BVS) utilizando como marco de tiempo los años de 2005 a 2015. Resultados: Después de la búsqueda, selección y analice de los artículos, 06 fueron seleccionados para componer la amostra de estudio que se encuentra disponible, en su totalidad, donde evidenciaban tecnologías para la minimización de la hipoglucemia durante la ICI en las venas. La amostra caracterizó protocolos informatizados y protocolos de papel utilizados durante el tratamiento. Conclusión: El estudio consiguió identificar tecnologías que fueron creadas para minimizar las ocurrencias de hipoglucemias durante la infusión continua de la insulina. Los protocolos informatizados fueron considerados más eficaces en la minimización de las eventualidades hipoglucémicas.

**Descriptores:** Tecnologías en la salud; Insulina; Hipoglucemia; Terapia intensiva.

# INTRODUCTION

In recent years, Continuous Infusion of Insulin (CII) has been used for glycemic control, gaining prominence in the treatment of critically ill patients.<sup>1</sup>

In the past ten years, many prospective, randomized studies have shown that intensive glycemic control reduced, in the short and long term, mortality, multiple organ failure, systemic infections, hospital, and Intensive Care Unit (ICU) stays, and as a consequence, total hospital costs.<sup>2,3</sup>

Hypoglycemia is considered an important complication associated with the use of CII and severe hypoglycemia occurs in about 4% to 7% of patients. Severe hypoglycemia is considered when the blood glucose level is below 40 mg/dL; moderate hypoglycemia, 41 to 60 mg/dL; and mild hypoglycemia, 61 to 70 mg/dL.<sup>4</sup>

Some hypotheses have been suggested as probable risk factors that increase the incidence of hypoglycemia in

intensive glycemic control: excess insulin administered, impaired response to glucagon and epinephrine, decreased level of consciousness (sedation or other clinical causes), other deficiencies hormones, other associated drugs, suspension of nutritional support or organ dysfunction.<sup>2</sup>

When performing the CII, it is essential to implement strict glycemic control to adopt a protocol that allows keeping blood glucose within the selected range and that either prevents or reduces the occurrence of hypoglycemia.<sup>5</sup>

There are several advantages to the use of assistance protocols, such as: greater safety for users and professionals, reduction of the variability of care actions, improvement in the qualification of professionals for decision-making in assistance, ease in the incorporation of new technologies, innovation care, more rational use of available resources and greater transparency and cost control. It can also be highlighted that the use of protocols facilitates the development of process and results indicators, the dissemination of knowledge, professional communication and the coordination of care.<sup>6</sup>

Protocols are considered a type of light-hard technology focused on care. Therefore, they must be created in a systematic way to assist professionals and clients in deciding on the appropriate care to meet specific health conditions.<sup>7</sup>

Technology must be understood as a comprehensive concept, where it will make it possible to understand the work process of nurses and, consequently, the systematization of care. Hence, it is possible to innovate in the search for an instrument that has a scientific approach to the work performed by nurses, being able to promote their professional autonomy.<sup>8</sup>

This research will enable the dissemination of existing technologies that can provide confidence to nurses who provide assistance to patients who are undergoing CII. Therefore, this study meant to identify existing technologies for minimizing hypoglycemia in adult patients undergoing continuous intravenous insulin infusion.

### **METHODS**

It is an integrative review of the scientific literature. The six stages of this method being respected: definition of the guiding question; definition of article selection criteria; selection of publications that participated in the review sample; description of the findings in the articles that were selected; interpretation of results and final report of the review.<sup>9</sup>

The question that guided the research was the following: What are the existing technologies to minimize the occurrence of hypoglycemia in adult patients undergoing continuous infusion of insulin?

Data collection took place electronically, at the Virtual Health Library (VHL), over the period from 2005 to 2015. During this research, the following descriptors were crossed using the Boolean operator "and": "protocols", "hypoglycemia" and "insulin".

The following inclusion criteria were used: national and international articles published in Portuguese, English, and Spanish; that contemplated the objective of the study; published between 2005 and 2015. Exclusion criteria: publications that were not available in full; pediatric and neonatal studies, studies that had the same type of technology as studies already nominated. Doing a careful reading of the titles and abstracts, articles containing technologies were selected to minimize the occurrence of hypoglycemia in adult patients undergoing continuous infusion of insulin.

The articles were selected and organized using the instrument developed by the authors, according to Table 1.

## RESULTS

Based on the controlled descriptors "protocol", "hypoglycemia", "insulin", 45 articles were found in the Virtual Health Library (VHL), through the inclusion and exclusion criteria six articles were then selected. It was observed that in the *Literatura Latino-americana e do Caribe em Ciências da Saúde (LILACS)* [Latin-American and Caribbean Literature in Health Sciences] database, two articles were found addressing the study and in the Medical Literature Analysis and Retrieval System Online (MEDLINE) database, there were found four articles.

**Table 1 -** Distribution of the studies according to their databases, titles, authors/publication year and methods. Rio deJaneiro city, Rio de Janeiro State, Brazil, 2018

N	Database	Title*	Authors/Year	Methods
1	LILACS	Avaliação da percepção de enfermeiros sobre três protocolos para controle glicêmico em pacientes críticos.	Corrêa TD, Almeida FP, Cavalcanti AB, Pereira AJ, Silva E. (2012)	A randomized study comparing three glycemic control protocols in critically ill patients.
2	Medline	Computerized intensive insulin dosing can mitigate hypoglycemia and achieve tight glycemic control when glucose measurement is performed frequently and on time.	Juneja R, Roudebush CP, Nasraway AS, Golas AA, Jacobi J, Carroll J, Nelson D, Abad VJ, Flanders SJ. (2009).	Retrospective analysis of patients who received intravenous insulin from March 2006 to December 2007.
3	LILACS	Avaliação da efetividade e segurança do protocolo de infusão de insulina de Yale para o controle glicêmico intensivo	Diener JRC, Prazeres CEE, Rosa CM, Urubatan C, Ramos CCS. (2006).	Retrospective and comparative study between 2 cohorts of critically ill patients, before and after the implementation of intensive glycemic control.
4	Medline	Computerization of the Yale insulin infusion protocol and potential insights into causes of hypoglycemia with intravenous insulin.	Marvin MR, Inzucchi S, Besterman. (2013)	Retrospective analysis of all patients admitted to the ICU who were treated with insulin infusion directed by an insulin dosage calculator.
5	Medline	Improving IV insulin administration in a community hospital.	Magee MC. (2012)	A randomized study to assess intensive glucose control or conventional glucose control.
6	Medline	Computer-assisted glucose control in critically ill patients	Vogelzang M, Loef BG, Regtien JG, Van der Horst LCC, Van Assen H, Ziilstra F, Nijsten MWN. (2008)	An observational cohort study in three intensive care units at a university hospital.

#### N 1: Assessment of nurses' perception regarding three protocols for glycemic control in critically ill patients

Three technologies were studied: Computer Assisted Insulin Protocol (CAIP), Leuven Protocol (PL) and Conventional Treatment (CT). CAIP is a protocol that targets glycemic levels between 100 and 130 mg/dL, guided by a hand-held device or desktop software, CAIP was considered by the study participants to be easier to manipulate, its adjustments were made quickly with aid of a computer program. Still in the study, it was reported the need for nursing to obtain a broad knowledge about the algorithms to adjust insulin. It is necessary to assess whether the algorithm is effective in maintaining blood glucose, safe and easy to use.<sup>2.3</sup>

CAIP met these criteria. While the PL is a protocol that has a glycemic goal of 80-110 mg/dL, used in continuous infusion of insulin, this is considered a strict glycemic control

protocol and has the characteristic of being long and written.<sup>10</sup> The nurses who participated in the research observed a higher incidence of hypoglycemia with the use of PL. It was concluded in this study that CAIP compared to PL is safer, more effective and easier to use.<sup>11</sup>

#### N 2: Computerized intensive insulin dosing can mitigate hypoglycemia and achieve tight glycemic control when glucose measurement is performed frequently and on time

In a retrospective analysis, a study in adult patients using continuous intravenous insulin infusion underwent a glycemic control protocol using an insulin dosage calculator, where they used the glycemic target of 80 - 110 mg/dL, based on the Leuven protocol. In summary, after measuring the patient's blood glucose, the glycemic value was entered into the system, the program calculates an initial insulin infusion rate. There are reminder alarms that can be pre-programmed. If hypoglycemia occurs, the software returns to a hypoglycemia recovery mode and calculates an appropriate dose to be infused intravenously. An audible alarm alerts the nurse to control capillary blood glucose every 15 minutes until the patient recovers from the hypoglycemic event.<sup>12</sup>

All insulin dosage information is saved in the system database. This computerized protocol was used in several subgroups of diseases (acute myocardial infarction, myocardial revascularization surgery, acute and chronic renal failure, type 1 and 2 Diabetes Mellitus). Delays in blood glucose measurements were considered in this study as an important factor for the occurrence of hypoglycemia, around 67% of the severe hypoglycemia were observed. It is concluded with this study that the use of a computerized protocol decreased the occurrence of hypoglycemia.<sup>12</sup>

#### N 3: Assessment of both effectiveness and safety of the Yale insulin infusion protocol for intensive glycemic control

This study assessed the effectiveness and safety of the Yale protocol when using continuous intravenous insulin infusion. This protocol was developed to be controlled by nursing professionals where the glycemic goal of this protocol is 80 to 140 mg/dL. Blood glucose measurements in this protocol must be performed every hour. The results of this study demonstrated that the Yale protocol is effective and showed significant improvement in glycemic control, the studied population were critical and surgical clinical patients. Hypoglycemic episodes were quickly detected and corrected with the administration of 50% glucose as described in the protocol itself. It is concluded with this study that the Yale protocol is safe and effective for the use of intravenous insulin therapy.<sup>4</sup>

#### N 4: Computerization of the Yale insulin infusion protocol and potential insights into causes of hypoglycemia with intravenous insulin

This work sought to achieve two objectives, as follows: to describe the use of an insulin dosage calculator based on the Yale protocol and to report a critical analysis of all hypoglycemic events that occurred during the use of the protocol, in order to determine its basic efficacy. This calculator is installed in the hospital system after the measurement of capillary blood glucose by the nurse is launched, the system calculates the variation of the insulin infusion rate based on the Yale protocol. An insulin infusion dose adjustment recommendation is sent, and the nurse confirms the change made. An audible alert is triggered indicating the next blood glucose measurement, typically within 1 hour.<sup>13</sup>

The system tracks all blood glucose and previous insulin dosage. Users of the system can decrease or cancel all recommendations, allowing clinical decision to be considered. It is concluded that the use of the insulin dosage calculator showed a low incidence of severe hypoglycemia and an incidence of 1.1% of moderate hypoglycemia.<sup>13</sup>

# N 5: Improving IV insulin administration in a community hospital

In a randomized study, blood glucose was compared when using a paper protocol and another using a computerized protocol. Glycemic targets of 80 - 110 mg/dL were used in a patient in Intensive Care Units (ICUs) and a more flexible target of 95 -120 mg/dL in patients who were not in the ICU, both patients were undergoing continuous intravenous insulin infusion. At this point in the study, blood glucose levels did not reach the planned target for patients, requiring a modification of the paper protocol, increasing the glycemic level to 80-180 mg/dL, there were no significant changes in glycemic targets.<sup>13</sup>

It is worth mentioning that the study reports that 85% of hypoglycemic events were not due to the real protocol, but an error in the use of the paper protocol. After unsatisfactory attempts with the paper protocol, it was decided to implement a computerized glucose system, designed to customize the intravenous administration of insulin according to the needs of each patient. The software can be loaded on a hospital intranet server without the need for additional equipment, uses mathematical modeling to calculate a specific physiological insulin dosage curve for each patient based on each patient's blood glucose measurements.<sup>13</sup>

It has 33 algorithms to analyze and interpret four most recent measurements and thus calculate the appropriate dose at that moment. It is concluded that the computerized system reached target concentrations in more than 75% of the readings, minimizing the risk of hypoglycemia. The prevalence of hypoglycemia with the use of the computerized system was well below 1%.<sup>14</sup>

# N 6: Computer-assisted glucose control in critically ill patients

This study sought to assess the safety and efficacy of a computer-guided glycemic control protocol in a population of critically ill patients. In the research, the glucose regulation computer program for critically ill patients is compared to a "watchdog" who is attentive to blood glucose measurements that occur in delay. This program is installed on a computer that should be next to the blood gas analysis machine, arterial blood was used when the patient had an arterial line and venous blood when there was no arterial line. The program shows an overview of the Intensive Care Unit (ICU) and the colors of the beds signal a specific action that should be performed in a given bed, for example, a new blood glucose measurement or the modification of the insulin infusion dosage.<sup>15</sup>

The algorithm used by the program is based on the blood glucose level and changes in recent blood glucose values. Insulin infusion dosages and blood glucose measurement intervals are calculated at any time. This program was designed to be applied in a practical way and to limit the number of blood glucose measurements, resulting in a reduction in the time spent on glycemic control. The total time analyzed in the study, from measuring blood glucose to changing the dosage in the infusion pump was 4 minutes.<sup>15</sup>

It is concluded with this study that the computer-assisted glycemic control protocol was safe and efficient, low hypoglycemia rates occurred, using a lower number of blood glucose measurements, about 6 measurements per day were required in patients who were submitted to intensive glycemic control through continuous infusion of insulin.<sup>15</sup>

### DISCUSSION

The study discussion was categorized based on its findings.

# Computerized and non-computerized technologies used during continuous infusion of insulin

In a study by Van den Berg and collaborators in 2001, based on a study with surgical patients, it was defined to maintain blood glucose between 80 - 110 mg/dL. From this protocol called Leuven I, studies on the benefits of continuous infusion of insulin in critically ill patients have begun. It was observed that this glycemic range decreased mortality and morbidity. Based on this protocol, the use of continuous intravenous insulin therapy became widespread in intensive care units in all countries. Nonetheless, it was also observed that the chances of hypoglycemia increased with this glycemic range.<sup>2,4</sup>

In the study conducted by Goldberg and collaborators, it was designed to be controlled by the nursing team. This protocol requires that blood glucose measurements be performed every hour at the beginning of the infusion. The purpose of this protocol is to maintain a glycemic range of 80 - 140 mg/dL, it is intended for adult critically ill patients in intensive care, who present with a clinical picture of hyperglycemia, it is not specifically suitable for patients with diabetic emergencies. Through a retrospective study performed in 2006, the Yale protocol was considered effective and safe for handling insulin therapy.<sup>4,5</sup>

Most of the existing protocols, used for glycemic control during continuous infusion of insulin, are based on the Leuven and Yale protocol. Whether they are paper or computerized protocols. The use of computerized protocols has facilitated glycemic control effectively in an intensive care unit. According to the studies carried out, the computerized protocols that are used for intensive glycemic control, are considered expensive, but effective in preventing hypoglycemia, in addition to optimizing the time spent by the nursing professionals.<sup>16,17</sup>

The studies carried out comparing paper protocols and computerized protocols, unanimously highlighted the occurrence of decreased hypoglycemic events in intensive care units and even non-intensive ones that adopted computerized protocols. The computer alert system concerning the behavior of the nursing team, where it has numerous demands and in a tense sector, allows the team to establish priority in care when the alert goes off.<sup>18</sup>

In a study that described the replacement of a paper protocol with a computerized protocol, some characteristics were highlighted in the use of the paper protocol. Among them, the calculations that must be made hourly at the bedside, delays or failure to perform blood glucose measurements and the difficulty in interpreting the protocols, these factors increased the variability of glycemic values and hypoglycemic events occurred more frequently.<sup>16</sup>

In another study that evaluated nursing satisfaction with the use of paper protocols and computerized protocols, obtained a result of nurses' satisfaction using computerized protocols. Still in this study, it was observed that the nursing team deviated from what was required by the protocols, this could be assessed when comparing the insulin infusion doses that were found in the medical records and the doses that should really be included according to what was requested in protocols, so when compared to paper protocols, the computerized protocols suffered less deviation by the nursing team.<sup>19</sup>

It was observed that computerized protocols proved to be more effective, nonetheless, they are not yet available in all units that carry out the treatment with continuous infusion of insulin. The reason for that are the costs that are raised in the implementation of computerized protocols.

# CONCLUSIONS

The study was able to identify technologies that were created to minimize the occurrence of hypoglycemia during continuous infusion of insulin, which are computerized protocols and paper protocols. There is a desire to implement computerized protocols, which leads to the surge of satisfaction in the places where it is used.

It is still a challenge to maintain glycemic levels within a target range, even with the use of existing technologies. Furthermore, the concern and the search for glycemic control continues to take place during the continuous infusion of insulin without the occurrence of hypoglycemic events in the frequency in which they happen.

Bearing in mind the aforementioned findings, it is necessary to develop protocols that enable their implementation at a low cost. The existing computerized systems hold a high cost, therefore, making their implementation difficult in most units that provide assistance to critically ill patients undergoing CII.

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