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## INTEGRATIVE REVIEW OF THE LITERATURE

### Controle glicêmico em pacientes críticos que recebem insulina: revisão integrativa

Glycemic control in patients receiving insulin critics: integrative review

Control de la glucemia en los pacientes que recibieron insulina críticos: revisión integrada

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### ABSTRACT

**Objective:** To discuss the knowledge produced on glycemic control for critically ill patients receiving continuous insulin infusion. **Method:** Integrative review of publications in the literature bases Ovid, Scopus and Science that dealt with continuous insulin infusion in hospitalized patients from 2003 to 2013 and full text available online. Selected eleven publications. **Results:** Glycemic control with intravenous insulin showed higher rates of hypoglycemia despite allowing achieve faster target goal and computerized protocols are effective resources to prevent hypoglycemic events though expensive and still not available on the Brazilian reality. **Conclusion:** It is important for nurses to provide input on the implications of severe hypoglycemia during continuous infusion of insulin for the control of risks in nursing care processes. **Descriptors:** Insulin, Blood glucose, Hypoglycemia, Nursing.

### RESUMO

**Objetivo:** Discutir o conhecimento produzido sobre o controle glicêmico de pacientes críticos que recebem infusão contínua de insulina. **Método:** Revisão integrativa de literatura de publicações nas bases Ovid, Science e Scopus que abordassem a infusão contínua de insulina em pacientes hospitalizados, entre 2003 a 2013 e texto completo disponível on line. Selecionados onze publicações. **Resultados:** O controle glicêmico com insulina intravenosa apresentou maiores taxas de hipoglicemia apesar de permitir alcançar a meta alvo mais rápido, e verificar que protocolos informatizados são recursos eficazes na prevenção de eventos hipoglicêmicos apesar de caros e ainda pouco disponíveis na realidade brasileira. **Conclusão:** É importante fornecer subsídios para o enfermeiro sobre as implicações da hipoglicemia grave durante a infusão contínua de insulina para o controle dos riscos nos processos assistenciais de enfermagem. **Descritores:** Insulina, Glicemia, Hipoglicemia, Enfermagem.

### RESUMEN

**Objetivo:** Discutir el conocimiento producido acerca del control glucémico en pacientes críticamente enfermos que recibieron infusión continua de insulina. **Método:** Revisión integradora de literatura en bases de datos de Ovid, Science y Scopus que hablasen de infusión continua de insulina en pacientes hospitalizados, entre 2003 a 2013 y texto completo disponible on line. Selecionados onze publicaciones. **Resultados:** El control glicémico con insulina intravenosa indicó tasas más grandes de hipoglicemia apesar de permitir alcançar la meta alvo mas rápido y protocolos informatizados son recursos eficazes en la prevención de eventos hipoglicêmicos apesar de caros y poco disponibles. **Conclusión:** És importante que se informe al enfermero acerca de la hipoglicemia grave que ocurre encunto se administra insulina intravenosa. **Descritores:** Insulina, Glucemia, Hipoglicemia, Enfermería

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## INTRODUCTION

**S**trict glycemic control has been used mainly in intensive care units (ICU), through intravenous insulin employment, by continuous infusion.<sup>1</sup>

Its use frequently occurs as a result of hyperglycemia, which until a few years ago, was considered a beneficial response of stress that affects the critical patient, but currently is considered an increased mortality risk factor.<sup>1</sup>

Hyperglycemia is responsible for increased gluconeogenesis and peripheral resistance to insulin's action as one of the responses to the cytokine secretion and counter-regulatory hormones.<sup>1</sup>

A few years ago, it was demonstrated that strict glycemic control kept it between 80 and 110 mg/dl, using continuous insulin infusion (CII), was associated with reduced mortality and reduction of complications, especially in surgical patients of cranial trauma with stroke and acute myocardial infarction.<sup>1</sup>

Despite the proven benefits with the use of intravenous insulin to achieve glycemic-physiological levels, there is the adoption of this therapy a faint threshold between offering patients a protective care and a potentially harmful approach, significantly increasing the risk of severe hypoglycemia.<sup>2</sup>

It is worth remembering that insulin is a potentially dangerous medication (PDM), which means that presents a great potential in causing serious injury to patients when a failure occurs in its usage. As potentially dangerous medication, intravenous insulin requires care to maintain the efficiency and safety of its management, because it has side effects, among which hypoglycemia is emphasized as the most important, that if it goes untreated, can cause irreversible brain damage.<sup>2</sup>

It is considered severe hypoglycemia when the level is equal to or less than 40mg/dl; moderate when measures of 41 to 60mg/dl, and light when lies between 61 to 70mg/dl. Hypoglycemia is the primary adverse event associated with continuous intravenous insulin therapy<sup>2</sup>. The literature says that the severe hypoglycemia occurs around 4% to 7% of patients receiving continuous intravenous insulin infusion.<sup>2</sup>

In Brazil, it is nursing who prepares and administers insulin solution in most hospitals, she should therefore be aware of issues that involve not only the management of insulin, but also monitoring it to prevent the occurrence of severe hypoglycemia.<sup>2</sup>

It nursing preparation and monitoring of the validity of the solution, the installation of the infusion, the monitoring of blood glucose and titration of infused doses in order to achieve and maintain the blood glucose, target range to avoid hypoglycemia.<sup>2</sup>

Despite efforts to consolidate protocols that guide how to achieve the goal of the target range in patients, where severe hypoglycaemic episodes still persist in critically ill patients, which may contribute to increased morbidity in these patients.

The concern for hypoglycemia motivated the development of a study that aimed to synthesize and discuss the knowledge produced in the literature on glycemic control in critically ill patients receiving continuous insulin infusion. The contribution of this study is based on the possibility of alerting on nurses aspects of intravenous insulin usage to contribute to the reduction of the frequency of severe hypoglycemia, benefiting patients and hospitals in patient safety issues, which involves intravenous insulin and nursing.

## METHOD

We conducted an integrative review, fulfilling the six steps provided as follows: defining the research question; definition of Articles selection criteria; selection of publications in the sample review; reported data on selected articles, interpretation of results and final report of the review.<sup>3</sup>

The study was guided by the following questions: a) which results in blood sugar control when using insulin subcutaneous or intravenous?; b) what resources exist to decrease the occurrence of hypoglycemia?. We performed a search through the Capes Portal in Ovid databases, Science and Scopus using the keywords: *insulin*, *blood glucose*, *hypoglycemia* and the connector *and* among these descriptors.

Selected articles published in Portuguese, English and Spanish, which addressed continuous insulin infusion in hospitalized patients, between the years of 2003 to 2013 and with full text available *online*. The strategies for the removal of the articles were adapted to each database, according to their specific characteristics. The results have been grouped into categories, which have guided the discussion.

## RESULTS AND DISCUSSION

In the databases surveyed, no nursing publications were found.

We identified 26 articles submitted to the selection criteria resulted in a sample of 11 publications that are shown in Figure 1.

Fifteen articles were excluded because they deal with pediatric patients and not with hospitalized patients.

**Figure 1-**Scientific production on the strict control of glycemia.RJ, 2003-2013.

Base	Year	Authors	Periodical	Method
Scopus	2012	Dumont C, Bourguignon C <sup>4</sup>	<i>American Journal of Critical Care.</i>	Prospective study, case-control, randomized with 141 clinical and surgical patients monitored by electronic protocol and 159 in the control group by conventional protocol.
Scopus	2012	Bouw JW, Campbell N, Hull MA, Juneja R, Guzman O, Overholser BR <sup>5</sup>	<i>Diabetes Technology and Therapeutics</i>	A retrospective cohort study with clinical and surgical patients. N = 61
Scopus	2011	Meyfroidt G, Wouters P, De Becker W, Cotten D, Van Den Berghe G <sup>6</sup>	<i>Intensive Care Medicine</i>	Cohort study of medical and surgical patients. N=729.
Science Direct	2011	Torredà MR, Pérez EC, Aragón MD, Ribe RM, Juvanteny EP, Boreu QF <sup>7</sup>	<i>American Journal of Critical Care</i>	A retrospective study of medical patients. N=144
Scopus	2010	Via MA, Scurlock C, Adams DH, Weiss AJ, Mechanick JI <sup>8</sup>	<i>Endocrine Practice</i>	A prospective study of all patients post-cardiothoracic surgery patients. N=114
Science Direct	2009	Cavalcanti AB, Silva E, Pereira AJ, Caldeira-Filho M, Almeida FP, Westphal GA, et al <sup>9</sup>	<i>Journal of Critical Care</i>	Controlled randomized, multicentered study with clinical patients. N=167
Ovid	2008	Wiener RS, Wiener DC, Larson RJ <sup>10</sup>	<i>Journal of The American Medical Association</i>	Meta-analysis of clinical and surgical patients. N= 8432
Ovid	2008	Brunkhorst FM, Engel C, Bloos F, Meier-Hellmann A, Ragaller M, Weiler N, et al <sup>11</sup>	<i>New England Journal of Medicine</i>	Multicentered experimental study of critically ill patients. N=448
Ovid	2007	Preiser JC, Devos <sup>12</sup>	<i>Intensive Care Medicine</i>	Multicentered, randomized controlled European trial. N=3500
Ovid	2004	Krinsley 13	Mayo Clinic	Controlled study "before and after" with critically ill patients. N=800

Ovid	2003	Van den Berghe G, Wouters PJ, Bouillon R, Weekers F, Verwaest C, Schetz M <sup>14</sup>	Critical Care Medicine	Prospective randomized study with surgical critical patients. N=1548
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**Figure 1-** Scientific production on the strict control of glycemia. RJ, 2003-2013.

According to the questions, two categories were identified: computerized or conventional protocols in glycemic control<sup>4-6</sup> and the use of subcutaneous insulin (SC) and intravenous (IV) in glycemic control.<sup>7-14</sup>

The results were described by category.

#### **Computerized or conventional protocols in glycemic control (n=3)<sup>4-6</sup>**

Study looked at the effects of a computerized Protocol compared to a conventional Protocol for glycemic control in critical clinical and/or surgical patients. It was concluded that there were fewer hypoglycemic events in the computerized group (28%) compared to the conventional protocol (72%).<sup>4</sup>

The publication evaluated the impact of a computerized Protocol for Glycemic Control compared to conventional intensive therapy protocol. The hypoglycemic events were reduced in the computerized group of 26% to 6%.<sup>5</sup>

Another article aimed to evaluate the impact of a computerized glycemic alert. There was a reduction in the proportion of patients who have hypoglycemia from 6.5% to 4%, with the employment of this alert.<sup>6</sup>

#### **The use of subcutaneous (SC) and intravenous insulin (IV) on glycemic control (n=7)<sup>7-14</sup>**

The study established the number of hypoglycemic events related to critical patients in relation to the administration of IV insulin and SC insulin in the treatment of hyperglycemia. The hypoglycemia rate was greater when insulin was administered intravenously (3.2%), in relation to subcutaneous administration (2.3 percent), considering a target range of 110-140mg/dL.<sup>7</sup>

Research described the conventional glycemic control with insulin SC applied to cardiothoracic surgery patients. Acute postoperative hyperglycemia and its immediate correction with intravenous insulin were associated with good results for critical patients.<sup>8</sup>

A publication checked the safety of two insulin Protocols with intravenous and subcutaneous administration. It was concluded that there were fewer hypoglycemia cases (3.8%) when used for subcutaneous insulin only had greater than 150mg/dL.<sup>9</sup>

A study evaluated a protocol of intravenous infusion of insulin compared to insulin usage by subcutaneous scale. With the use of intravenous insulin, there was a hypoglycemic rate of 13.7% and with subcutaneous insulin, a rate of 2.5%.<sup>10</sup>

Research developed a multicenter study comparing the glycemic control with intravenous insulin with the conventional insulin therapy. Hypoglycemia was reported at 12.1% and 2.1% in the group with intravenous insulin and in conventional therapy, respectively.<sup>11</sup>

A randomized trial compared a standard protocol with two target groups: an 80 to 110mg/dL in the group with venous insulin and another 140-180mg/dL in the control group. The study was stopped because the incidence of hypoglycemia was very high in the group receiving intravenous insulin (8.69%) compared to the conventional protocol (2.4%).<sup>12</sup>

A study evaluated the glycemic control in critical patients who use IV and SC insulin. The protocol involved intensive monitoring in order to maintain blood sugar levels below 140mg/dL. We obtained a 56.3% reduction in the mean blood glucose levels (from 152mg/dL to 130mg/dl) under strict control, but there was no significant change in hypoglycemia with the use of intravenous insulin (1.02%) when compared to SC insulin (0.35%).<sup>13</sup>

Other research has evaluated a protocol for control of blood glucose (80-110mg/dL) through IV insulin or through the conventional subcutaneous approach. Hypoglycemia affected 5.2% of patients on intensive insulin therapy compared with 0.8% of patients treated conventionally.<sup>14</sup>

Figure two, shows the maximum and minimum rates of hypoglycemia found in the publications.

Authors	Insulin SC (%)	Insulin IV (%)
<i>Torredà MR, Pérez EC, Aragón MD, Ribe RM, Juvanteny EP, Boreu QF<sup>7</sup></i>	2,3	3,2
<i>Via MA, Scurlock C, Adams DH, Weiss AJ, Mechanick JI<sup>8</sup></i>	NI*	0,03
<i>Cavalcanti AB, Silva E, Pereira AJ, Caldeira-Filho M, Almeida FP, Westphal GA, et al<sup>9</sup></i>	3,8	41,4
<i>Wiener RS, Wiener DC, Larson RJ<sup>10</sup></i>	2,5	13,7
<i>Brunkhorst FM, Engel C, Bloos F, Meier-Hellmann A, Ragaller M, Weiler N, et al<sup>11</sup></i>	2,1	12,1
<i>Preiser JC, Devos<sup>12</sup></i>	2,4	8,6
<i>Krinsley<sup>13</sup></i>	0,3	1,0
<i>Van den Berghe G, Wouters PJ, Bouillon R, Weekers F, Verwaest C, Schetz M<sup>14</sup></i>	0,8	5,2

NI\_ not indicated

**Figure 2-** Hypoglycemic events associated with the use of insulin, RJ, 2003-2013.

### Computerized protocols or not in the control of glycaemia

Studies have shown that with computerized protocols of hypoglycemic events there has been a reduction of almost half in relation to the conventional, in most publications with a decrease ranging between 4% to 28%.

The computerized reservation systems proved to be more effective for predicting hypoglycemia once the system is capable of generating visual or audible alerts when the glucose level is less than 60mg/dl, which facilitates the early detection of hypoglycemia by nursing, allowing time to correct the flow rate of insulin..<sup>15</sup>

Computerized systems for glycemic control, to detect blood glucose levels descendants, calculate the probability of hypoglycemia and launch alerts for insulin flow rate

reduction. So that, although they are expensive systems, they are considered effective in preventing hypoglycemia episodes and optimize the nursing work.

The system informs, depending on the patient condition, which is the best blood sample and indicates the immediate reduction of the insulin flow rate. The effect of a computer alert system on the behavior of the team, with multiple cognitive demands, in a tense environment, serves to establish priorities for actions, every time that alert sounds.<sup>16</sup>

With computerized protocols, the nurses save time in assistance, decreasing the number of dose calculation errors, since the system does the calculations and reports show that nurses who work with this tool had greater satisfaction.<sup>17</sup>

It should be remembered that the calculations of wrong doses could lead to inappropriate insulin infusions and, consequently, the adverse events, increasing, in some cases, episodes of hypoglycemia.<sup>17</sup>

Another advantage of the computerized system is that it can be fed with information on patient condition that may favor the occurrence of hypoglycemia, such as nutritional status, the suspension of nutritional therapy, the type of nutrition, development of renal dysfunction, hepatic and use of dialysis or corticosteroid therapy.<sup>18</sup>

On the other hand, it is known that there are imperfections in the conventional glycemic control, particularly associated with the accuracy in measurement of blood glucose by the nursing staff, because it is dependent on a procedure-governed behavior of the team with respect to measuring the glucose hourly.<sup>19</sup>

A study found that critically ill patients benefit from continuous insulin infusion with the use of computerized glucose protocols fully conducted by nurses. This reinforces the practice that, when working with nurses computerized protocols glucose levels are maintained closer to the set target range, decreasing episodes of hypoglycemia.<sup>20</sup>

Computerized protocols are more effective, but they are not yet available in intensive care units for various factors such as the lack of specific training for nurses in the management of these protocols or due to high costs for the implementation of computerized systems.

#### **Use of subcutaneous (SC) and intravenous (IV) insulin in the control of blood glucose.**

The findings in this category show that, when the glycemic control happens by intravenous insulin, there is an increase in the rates of severe hypoglycemia when compared to conventional insulin administration. It was found that the hypoglycemia rates among patients were up 3.8% when SC insulin was used and up 41.4% when intravenous insulin was used.

The subcutaneous insulin regimen should mimic the physiologic secretion of insulin. However, when hospitalized, patients undergo a radical change in your routine, by various factors such as the stress of the disease responsible for their hospitalization, changing the nutritional scheme and the use of medications that can affect blood glucose. Namely, in addition to the physiological components, including basal and postprandial glucose insulin, we must conduct with insulin adjustments according to the clinical evolution of the patient. The total insulin dose is the sum of the basal and postprandial requirement and is the amount of insulin required in a day.<sup>21</sup>

The basal insulin (glargine) slow absorption begins 2 hours of action, and has no peak action (so it causes less hypoglycemia) with duration of action 18-24 hours. On the other hand, insulin protein called protamine or NPH, intermediate action, onset of action 2-4 hours duration of action 14-18 hours equally effective; but with a higher incidence of hypoglycemia as a function of peak activity (6 to 10 hours).<sup>21</sup>

The prandial insulin exhibits the onset of action 10 to 15 minutes and peak 30 to 90 minutes lasting 3 to 6 hours, applied immediately before nutrition (meal or enteral nutrition). Since a fast-acting regular insulin with peak activity 2 to 3 hours lasts 6 to 8 hours and presents the disadvantage of early action for 15 to 30 min.<sup>22</sup>

The administration of continuous intravenous insulin in the intensive care environment is an efficient system to control blood glucose. Preferably, regular human insulin is used in a solution of 100 units diluted in 100 ml of 0.9% saline solution (1 U / ml). It is known that insulin IV half-life is 4-5 min, and the short half-life it is an advantage when there is excessive glucose falls, they can be controlled by reducing or interrupting the flow rate of infusion insulin. This short half-life of insulin allows quick control of possible hypoglycemia, as soon the infusion pump is stopped.<sup>23</sup>

In the ICU, the blood glucose measurement for the titration of insulin solution is made in large part, using portable glucose meters; often using capillary blood samples obtained using lancets. However, studies have shown that glycemic digital collection may be inaccurate in critically ill patients due to the injury of peripheral perfusion, caused by the use of vasoactive drugs, the presence of edema and microcirculation disorders, as well as the collection of blood through venous access contaminated by intravenous solutions rich in glucose.<sup>24</sup>

It is recommended that during the IV insulin infusion, the nurse should measure blood glucose every hour; this interval be increased every 2 or 3 hours in individuals with glucose control within the target in the last 6 to 12 hours, respectively.<sup>22</sup>

The glycemic variability, i.e. the amplitude of changes in glucose levels is an important factor for increased mortality, independent of glycemic value, the induction of cellular oxidative stress, i.e. an accumulation of free radicals (superoxide, peroxynitrite, nitrosamine) which trigger the activation pathways of various deleterious to the organism and can potentially contribute to the development of complications. In addition, blood glucose variability has been associated with increased risk of severe hypoglycemia, with endothelial dysfunction and consequently, cardiovascular mortality.<sup>22</sup>

In daily practice, it persists, often with episodes of hypoglycemia during continuous infusion of insulin, despite monitoring by nursing; consisting of measure for digit-puncture the time of glucose in time, monitor the patient's vital signs, in addition to maintaining a continuous supply of glucose, both oral nutrition, enteral and parenteral, guided by protocols of the units.<sup>22</sup>

## CONCLUSION

The monitoring conducted shows that glycemic control with insulin IV had higher rates of hypoglycemia despite allowing to achieve a target goal faster and computerized protocols are effective remedies to prevent hypoglycemic events though expensive and still not available in the Brazilian scenario.

No studies were found comparing the benefit of SC and IV insulin in specific patient groups as in postoperative neurological surgery, cardiac or addressing the nursing workload with both approaches.

The monitoring identified that there is a need for randomized studies justifying the need for scheduled glucose control, as well as studies that address the various factors that can interfere with blood glucose measurement performed by nurses.

Thus indicating the need for studies on the influence of different risk factors for hypoglycemia as prolonged fasting, mismatch between the administration of insulin and carbohydrate intake, inotropic support, kidney failure and sepsis in the glucose levels.

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