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Effectiveness of insulin solution: a comparison between different times for maintaining the solution

Eficiência da solução de insulina: comparação entre diferentes tempos de manutenção da solução

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ABSTRACT

Background: Hyperglycemia is frequent in the critically ill patient, and is a risk factor for unfavorable clinical outcomes, including mortality. During the recent years, intensive blood glucose control using intravenous insulin infusion has gained a prominent role in the critically ill patient management. There is important concern on insulin solution continued efficacy over the time, as little the literature available on this subject is poor. Lack of evidence is known to lead to inappropriate practices. This study aimed to compare the blood glucose levels between two different protocols in an intensive care unit in Porto Alegre, using the same solution concentration and two different replacement times during the first 24 hours, and additionally to assess the protocol-related hypoglycemia rate.

Methods: The medical charts of 80 patients under insulin therapy for over 24 hours during 2008 were revised; 40 patients had their insulin solution replaced every 6 hours and for 40 patients the insulin solution was replaced after 24 hours.

Results: The causes for admission to the intensive care unit included more frequently hypertensive (68.8%) and diabetic (45%) patients. No significant capillary blood glucose differences were seen for the every 6 or 24 hours solution replacement groups. Only 3 mild hypoglycemia cases were observed in the every 6 hours replacement group, and no hypoglycemia was seen in the 24 hours replacement group.

Conclusion: We concluded that keeping insulin infusion, replacing the solution every 24 hours is feasible. However, longer infusion time studies are required to check for possible hypoglycemic events as insulin therapy advances.

Keywords: Hyperglycemia; Insulin therapy; Critical patient

INTRODUCTION

The critically ill patient, either previously diabetic or not, trends to show increased blood glucose levels. This hyperglycemia, called "stress hyperglycemia" is characterized by insulin resistance, catecholaminergic reduced pancreas insulin secretion, increased angiotensin II levels, and proinflammatory cytokines release changing the insulin receptors.[1]

Hyperglycemia is a natural body response to metabolic stress caused by hormone changes. Additionally, the critically ill patient care increases hyperglycemic response due to corticosteroids, adrenergic agents and glucose rich nutrition support use. Although being a physiologic body response, blood glucose levels reduction improves the outcome and reduces complications risk, particularly infective.[2]

Increased blood glucose levels change the immune function and ap-

propriate glucose control improves the macrophage/neutrophil function. Insulin has anti-inflammatory effects, as demonstrated by reduced C-reactive protein production. Has anabolic effects, and favorable effects on coagulation and fibrinolysis.[3]

In the last years, intensive blood glucose control, using continued intravenous infusion, took over a relevant role on the critically ill patient management. The premise is that maintaining normal blood glucose levels is associated with lower infection and organ failure rates, and therefore, lower mortality rates.[4]

Hypoglycemia is considered the main complication associated with continued venous insulin therapy, and severe hypoglycemia is seen in 4% to 7% of these patients. Severe hypoglycemia is considered when the blood glucose level is below 40 mg/dL; moderate from 41 to 60 mg/dL; and mild from 61 to 70 mg/dL.[4]

Some explanations are suggested as likely causes of increased hypoglycemia rates during intensive blood glucose control: excess insulin administration, failure of glucagon response to epinephrine, previously reduced consciousness level (sedation and other clinical causes), other hormone deficiencies, other associated drugs, discontinuity of the nutrition support, or organ dysfunction.[5]

Insulin adsorption is an unspecific surface phenomenon, poorly understood, which starts suddenly and disturbs trustful insulin offer to the patient. Due to this phenomenon, in most of the institutions the solution is replaced every 6 hours. It is discussed if glycemic changes would occur in longer time infusion solution replacements.[6] This study aimed to compare the glycemic levels between two different protocols involving different solution replacement times, and to identify protocol-associated hypoglycemic rates.

METHODS

A retrospective, descriptive with quantitative analysis study was conducted, using the medical charts from 80 patients who stayed in the intensive care unit of the Hospital Geral de Porto Alegre and underwent insulin therapy for more than 24 hours; 40 patients were in the protocol with insulin solutions replaced every 6 hours, and 40 patients were in the 24 hours insulin solution replacement protocol. The study was approved by the Hospital Geral de Porto Alegre's Ethics Committee, after signature of a commitment with data use document.

In September 2008 the insulin therapy protocol was changed, keeping the same solution concentration but changing the solution replacement time to every 24 hours. The medical charts were randomly selected both pre- and post- protocol change, and evaluated for the study purposes.

For both protocols (replacement either every 6 or 24 hours), the insulin solutions were similarly prepared, with 50 IU regular insulin in 100 mL 0.9% normal saline, obligatorily infused with an infusion pump at the institution's protocol-defined infusion rate. Capillary blood glucose assessments were made hourly.

The mean blood glucose levels were compared between the protocols on the 7th, 13th, 19th and 25th hours, and hypoglycemic events were checked by the solution replacement times.

The results are presented with descriptive statistics, using arithmetic means and respective standard deviations (SD). The inter-group "before-after" comparisons were analyzed using the Wilcoxon test and the inter-groups comparisons ("6 hours" versus "24 hours") analyzed with the Mann-Whitney test. All statistical procedures were performed using the SPSS software (version 16), with a $p \leq 0.05$ significance level.

RESULTS

The study population was characterized according to age, gender, admission cause and comorbidities (Table 1). The most frequent admission causes were related to cardiovascular diseases, showing high incidence of hypertensive and diabetic patients, and increased use of corticosteroids and norepinephrine for both groups. The studied patients had ages ranging between 27 and 90 years (mean 72.2 ± 12.2 years for the group with every 6 hours solution replacement, and 64.0 ± 16.4 for the group with replacement after 24 hours).

Considering H0 as the time of infusion start, and comparing the mean blood glucose levels between the protocols by the insulin solution replacement times, we identified no change on the 25th hour insulin solution effectiveness. The groups comparison failed to show any significant difference for the mean 7th, 13th, 19th and 25th hours blood glucose levels (Table 2, Figure 1).

Only 3 mild hypoglycemia (61 to 71 mg/dL) cases were observed for the every 6 hours solution replacement group, and no hypoglycemia was identified for the 24 hours replacement group. However, this difference was not statistically significant. Hypoglycemia cases were seen on 24th and 25th hours.

Table 1 – Sample characterization by groups

Variable	6 hours re-placement (N=40)	24 hours replacement (N=40)	p value
Male gender	17 (42.5)	24 (60.0)	0.12
Age (years)	72.2 ± 12.2	64.0 ± 16.4	
Cause of admission			
Stroke/cerebral aneurism	6 (15.0)	11 (27.5)	
Sepsis	4 (10.0)	7 (17.5)	
Acute myocardial infarction	5 (12.5)	7 (17.5)	
Respiratory failure	7 (17.5)	4 (10.0)	0.10
BCP/COPD/ pulmonary emphysema	7 (17.5)	3 (7.5)	
Congestive heart failure	4 (10.0)	1 (2.5)	
Others	7 (17.5)	7 (17.5)	
Comorbidities			
Systemic arterial hypertension	26 (65.0)	29 (72.5)	
Diabete mellitus	21 (52.5)	13 (32.5)	
Cancer	6 (15.0)	5 (12.5)	
COPD	7 (17.5)	4 (10.0)	0.42
Urinary tract infection	4 (10.0)	5 (12.5)	
Renal failure	4 (10.0)	2 (5.0)	
Stroke	4 (10.0)	1 (2.5)	
Others	11 (27.5)	8 (20.0)	
Diet			
Enteral	23 (57.5)	13 (32.5)	
No oral ingestion	14 (35.0)	20 (50.0)	0.07
Oral	3 (7.5)	7 (17.5)	
Dialysis			
No	38 (95.0)	36 (90.0)	0.40
Continued hemodialysis	2 (5.0)	4 (10.0)	
Corticoid			
No	14 (60.0)	16 (40.0)	
Hydrocortisone	22 (55.0)	24 (60.0)	0.12
Methylprednisolone	4 (10.0)	0	
Vasoactive drugs			
No	11 (27.5)	13 (32.5)	
Noradrenaline	24 (60.0)	24 (60.0)	0.08
Others	5 (12.5)	3 (7.5)	

BCP – bronchopneumonia; COPD – chronic obstructive pulmonary disease. Results expressed as number (%) or mean ± standard deviation.

Table 2 – Inter-groups blood glucose levels comparison

Collection	6 hours replacement (N=40) Mean ± SD	24 hours replacement (N=40) Mean ± SD	p value
CBG 0 hours	331.2 ± 71.8	355.3 ± 70.3	0.10
CBG 6 hours	247.0 ± 80.5	257.0 ± 62.4	0.53
CBG 7 hours	233.7 ± 78.2	238.2 ± 60.0	0.98
CBG 12 hours	200.2 ± 69.3	184.4 ± 52.1	0.34
CBG 13 hours	194.9 ± 66.2	177.1 ± 48.4	0.24
CBG 18 hours	164.8 ± 54.3	156.6 ± 37.9	0.84
CBG 19 hours	164.1 ± 51.6	154.3 ± 35.0	0.59
CBG 24 hours	139.8 ± 52.5	134.1 ± 22.5	0.46
CBG 25 hours	136.2 ± 51.5	133.5 ± 24.8	0.33

CPG – capillary blood glucose; SD – standard deviation. Results expressed as mean ± standard deviation.
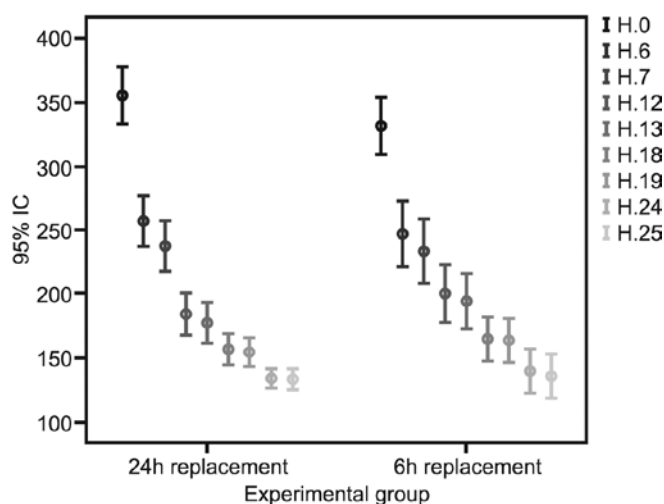
CI – confidence interval.

Figure 1 - Evolution of blood glucose between the groups.

DISCUSSION

From the results, both insulin solution and protocol were shown to be effective. We could identify that patients in both protocols are receiving the insulin doses required to lower their blood glucose levels, with no significant influence of the time for the solution replacement, either after 6 or 24 hours.

In hospital practice, the nursing team is responsible for the health care facilities management. Regarding material resources management, the nurse is responsible for forecasting, providing, organizing and controlling these materials. As an example of the purposes and relevance of management of

healthcare resources management, we could mention the costs issue. I.e., every manager should take into consideration the cost-benefit ratio.[7] Institutions that use insulin therapy for blood glucose normalization do so based on their patients characteristics and their technical team. The protocol will guide how the solution must be prepared, its concentration, cautions for infusion and insulin therapy patients' management.

In our literature research, we couldn't find any guidance on the insulin solution time of effectiveness; neither could find any information on relationship of the hypoglycemia rate with the time of the solution replacement.

This study showed that both protocols, either replacing the insulin solution after 6 hours or 24 hours, are safe regarding hypoglycemia, and effective for lowering capillary blood glucose to the target levels. No change was observed on the 25th hour solution effectiveness, thus suggesting that it is not necessary replacing the solution every 6 hours. Hypoglycemia is concerning, as it is the main continued venous insulin therapy complication, however was infrequently seen in this study. Only mild hypoglycemia cases were identified in the most frequent solution replacement (every 6 hours); however, one should bear in mind that, as those were the first 24 hours in the protocol and during this time blood glucose levels are still normalizing, hypoglycemia incidence rates may increase later.

From this study we concluded that institutions replacing the venous insulin therapy solutions every 24 hours are not wrong, as this causes no harm to the patient. Both protocols may be considered safe, however one should have in mind that shorter than every 24 hours replacements lead to increased material and human resources expenditures.

We should highlight that this was a retrospective trial evaluating a very small number of patients per group, and that this evaluation only covered the protocol first 24 hours, while the blood glucose levels are still adjusting. However, comparing the blood glucose levels at 6 hours intervals, the blood glucose levels were found similar.

CONCLUSION

Although this trial evaluated a small number of patients, and the evaluation covered only the first 24 hours of infusion, we conclude that it is possible to keep the insulin solution infusion with every 24 hours replacement. Studies evaluating longer infusion times, looking for eventual hypoglycemic events as insulin therapy advances, are suggested.

RESUMO

Objetivos: A hiperglicemia ocorre com frequência nos doentes críticos, sendo um fator de risco para evolução clínica desfavorável e aumento da mortalidade. Nos últimos anos, o controle glicêmico intensivo, obtido pela infusão venosa contínua de insulina, passou a ocupar lugar de destaque no manejo dos pacientes críticos. Há dúvidas frequentes e importantes sobre o tempo de eficiência da solução de insulina, por não existir referência na literatura. Sabe-se que a falta de evidências frequentemente favorece práticas impróprias. O objetivo deste estudo foi comparar glicemias entre dois protocolos diferentes, utilizados na unidade de terapia intensiva de uma instituição de Porto Alegre, quanto ao tempo de troca da solução, nas primeiras 24 horas de uso, sendo a concentração da solução a mesma; e verificar a taxa de hipoglicemia relacionada aos protocolos.

Métodos: Foram avaliados 80 prontuários de pacientes que utilizaram insulinoterapia por mais de 24 horas no ano de 2008, sendo que 40 deles fizeram uso do protocolo com troca da solução de insulina a cada 6 horas e 40 com troca a cada 24 horas.

Resultados: Observou-se entre os motivos de internação elevada incidência de pacientes hipertensos (68,8%) e diabéticos (45%). Não houve diferenças significativas entre as trocas a cada 6 e 24 horas durante todo o período da coleta com relação a glicemia capilar. Houve apenas 3 casos de hipoglicemia leve, todos no grupo de troca a cada 6 horas.

Conclusão: Com o presente estudo, concluiu-se que é possível manter infusões de insulina promovendo a troca da solução a cada 24 horas. Sugerem-se, porém, estudos avaliando maior tempo de infusão em busca de possíveis eventos hipoglicêmicos com o avanço da insulinoterapia.

Descritores: Hiperglicemia; Insulinoterapia; Paciente crítico

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