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Insulinization protocol for burns: glycemic control and outcomes

Protocolo de insulinização para queimados: controle glicêmico e desfechos

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ABSTRACT

Introduction: The stress mechanisms and peripheral insulin resistance of severe burns determine protein glycosylation with increased morbidity and mortality. Thus, glycemic control becomes a priority, as well as an effective and safe insulinization protocol.

Objective: To analyze the insulinization protocol for burn patients and compare it to the general insulinization protocol regarding glycemic results and outcomes of burn patients.

Method: Retrospective cross-sectional analytical observational study that analyzed the medical records of major burn patients. A sample was carried out with 88 patients, divided into 2 groups, one with 41 users of the general protocol and the other with 47 users of the burn protocol.

Result: The glycemic percentage outside the target, with the general protocol, was 23% while with the burn protocol it was 17% (p = 0.0001). The mean daily glycemic variation (p = 0.027) and the mean maximum daily glycemia (p = 0.022) were significantly higher in the general protocol group when compared to the burn protocol group, while the mean minimum daily glycemia (p = 0.71) was similar between both. Mortality predicted by the Abbreviated Burn Severity Index was significantly higher in the group that used the burn protocol when compared to the general protocol (p = 0.004); however, there was no statistical difference between the groups in terms of mortality (p = 0.61).

Conclusion: There was a reduction in the percentage of measurements outside the glycemic target, in the average maximum glycemia and in glycemic variability in the burn protocol, when compared to the general protocol. However, the average minimum daily blood glucose levels were similar between the protocols. Mortality predicted by the Abbreviated Burn Severity Index was higher in the burn protocol when compared to the general protocol; however, mortality was similar between both.

KEYWORDS: Burns. Glycemic control. Clinical protocol. Insulin. Hyperglycemia.

RESUMO

Introdução: Os mecanismos de estresse e resistência periférica à insulina em queimaduras graves determinam a glicosilação proteica com aumento da morbimortalidade. Assim, o controle glicêmico torna-se prioridade, bem como a confecção de um protocolo de insulinização eficaz e seguro.

Objetivo: Analisar o protocolo de insulinização para queimados e compará-lo ao protocolo de insulinização geral quanto a resultados glicêmicos e desfechos de pacientes queimados.

Método: Estudo observacional analítico transversal retrospectivo que analisou o prontuário de grandes queimados em 88 pacientes, divididos em 2 grupos: 41 usuários do protocolo geral, e outro com 47 usuários do protocolo para queimados.

Resultado: A porcentagem glicêmica fora do alvo, com o protocolo geral, foi de 23% enquanto com o para queimados foi de 17% (p = 0,0001). A variação glicêmica média diária (p = 0,027) e a média das glicemias máximas diárias (p = 0,022) foram significativamente maiores no grupo do protocolo geral quando comparado com o do protocolo para queimados, enquanto a média das glicemias mínimas diárias (p = 0,71) foi semelhante entre ambos. A mortalidade predita pelo índice Abbreviated Burn Severity Index encontrada foi significativamente maior no grupo que utilizou o protocolo para queimados quando comparado ao geral (p = 0,004), entretanto não se evidenciou diferença estatística entre os grupos quanto à mortalidade (p = 0,61).

Conclusão: Constatou-se redução da porcentagem de mensurações fora do alvo glicêmico, na média das glicemias máximas e na variabilidade glicêmica no protocolo para queimados, quando comparado com o protocolo geral. Todavia, a média das glicemias mínimas diárias foi semelhante entre os protocolos. A mortalidade predita pelo Abbreviated Burn Severity Index foi maior no protocolo para queimados quando comparado com o geral; contudo, a mortalidade foi semelhante entre ambos.

PALAVRAS-CHAVE: Queimaduras. Controle glicêmico. Protocolo clínico. Insulina. Hiperglicemia.

Central Message

The mechanisms of stress and peripheral insulin resistance in severe burns determine protein glycosylation with increased morbidity and mortality. Thus, glycemic control becomes a priority, as well as the preparation of an effective and safe insulinization protocol. Thus, analyzing the insulinization protocol for burn patients and comparing it to the general insulinization protocol in terms of glycemic results and outcomes of burn patients is interesting and timely in the treatment of major burn patients.

Perspective

Among the differences between the protocols, it can be mentioned that the ICP protocol predefines the intervals for measuring glycemic values and the initial dose of intravenous insulinization, as well as indicating its increase, reduction, interruption and migration from intermittent to continuous and vice versa. Although it has shown that it can be effective in restricting blood glucose at its glycemic target, this complexity of directions requires specific training of the team for its safe use.

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INTRODUCTION

Burns represent the fourth most frequent cause of trauma and with a relevant incidence in regions where poverty and misinformation predominate.[1,2] Severe burns have high morbidity and mortality, and hypermetabolism is one of the culprits,3,4 which can persist for up to 2 years with multiple organ dysfunction.[5]

Catecholamines and corticosteroids are the primary mediators of this response6 with peripheral insulin resistance and increased catabolism of glycogen, proteins, and lipids.[7] Stress-induced hyperglycemia determines protein glycosylation, with increased catabolism and risk of infections and increased mortality.[8,9] However, insulinization increases the risk of hypoglycemia, which is associated with a worse prognosis,10,11 findings that make glycemic control essential for a better outcome, but controversy persists regarding the limits of the glycemic target.[9]

Adequate glycemic control with insulin and blood glucose monitoring improve clinical outcomes and survival of major burn patients, because it can reduce infectious complications and organ dysfunctions, with attenuation of hypermetabolism, healing improvement, and preservation of muscle mass.[12] The implementation of a protocol can improve glycemic control and reduce glucose variability,13 as the concern is not restricted to hyperglycemia, but also includes the variation of blood glucose values.[12]

The Abbreviated Burn Severity Index (ABSI) is widely used, as it is a simple method for estimating the mortality of burn patients.[14] The ABSI derives from a multivariate logistic regression and its values are simple deaths without the need for laboratory tests.[15] Mortality prediction helps in clinical decisions, alleviating individual suffering, and improving the allocation of health resources.[16]

This study aimed to compare the glycemic results and outcomes of the insulinization protocol for burns (PIQ)17 compared to a general insulinization protocol (PIG); to verify the percentage of measurements outside the glycemic target in the 2 protocols; to compare the mean daily glycemic variation to the mean of the maximum and minimum daily blood glucose; and to verify the mortality predicted by the ABSI and that in the 2 groups.

METHOD

This is a retrospective analytical observational study of the medical records of major burn patients admitted from June 2022 to April 2023 in the burn ICU of a burns reference hospital and was approved by the Research Ethics Committee under opinion 6.262.039.

The research was carried out by comparing the SGA, which was used in the ICU, with the PIQ (Figure), from the moment of its implementation. Data from the medical records of burn patients admitted to the ICU over 18 years of age were included, and those whose medical records did not contain the necessary information, diabetics, and those under 18 years of age were excluded.

Age, gender, weight, comorbidities, burned body surface, depth, and inhalation injury were verified. A glycemic target was established between 80-160 mg/dl. The ABSI index was calculated to obtain the predicted mortality between the groups, as well as to compare it with the mortality observed in the 2 groups. To obtain the mean maximum and minimum blood glucose, their values were collected throughout each day, and from these values the daily glycemic variation was obtained. Blood glucose values lower than 80 mg/dl were considered hypoglycemia and hyperglycemia higher than 160 mg/dl.

Statistical analysis

Statistical analysis was performed by observing the lack of normality in the study data, based on the Shapiro Wilk test. To compare the groups in relation to categorical variables, the chi-square test was applied, and in relation to quantitative variables, the non-parametric Mann-Whitney test was applied. To verify the relationship between 2 quantitative variables, Spearman's correlation coefficient was calculated. Statistical significance was set at $p < 0.05$.

INTERMITTENT INSULINIZATION

For awake, compensated and non-diabetic patients, measure blood glucose in the morning. For unconscious, decompensated or diabetic patients, measure blood glucose every 6 hours. Target blood glucose between 80 and 160.

BLOOD GLUCOSE (mg/dl)	BOLUS EV – REGULAR INSULINE	MEASUREMENT
160 -180	1U	4/4h
181 -250	2U	414h
251 -310	4U	2/2h
311-360	6U	2/2h
361 -430	8U	2/2h

PUMP INSULINIZATION

Start regular insulin in an infusion pump if blood glucose levels remain higher than 160 mg/dl after 12 hours of intermittent dosing according to the table above. Start the regular insulin infusion pump at 2 ml/hour and administer a bolus dose corresponding to the range of values in the table below:

BLOOD GLUCOSE (mg/dl)	BOLUS EV - REGULAR INSULINE
161 -180	---
181 - 250	2U
251 - 310	4U
311 - 360	6U
361 - 430	8U

Repeat blood glucose levels in 1 hour and readjust the infusion rate according to the table below:

BLOOD GLUCOSE (mg/dl)	CONDUCT	MEASUREMENT
121 - 150	Keep the infusion going.	2/2h (3x) and after 4/4h
151 - 180	1U/h	2/2h
181 - 250	2U bolus EV e ↑ 1 U/h	2/2h
251 - 310	4U bolus EV e ↑ 2U/h	2/2h
311 - 360	6U bolus EV e ↑ 2U/h	2/2h
361 - 430	8U bolus EV e ↑ 2U/h	1/1h
If the current blood glucose level is lower than the value range it was in previously, with blood glucose levels lower than 181 mg/dl, readjust according to the table below:		
<80	Stop the infusion and apply 50ml of 50% glucose. After 30 minutes, if blood glucose levels are between 120 and 160mg/dl, restart with half the previous dose.	30/30min
81 - 120	Stop the infusion. After 45 minutes, if blood glucose levels are between 120 and 160mg/dl, restart with half the previous dose.	45/45min
121 -180	Reduce the infusion by half.	2/2h

Blood glucose levels greater than 160mgldl after turning off the insulin pump: Detection of hyperglycemia in less than 12h, restart the insulin pump protocol. Detection of hyperglycemia after 12h, restart the intermittent insulin protocol

FIGURE 1 – Insulinization protocol for burns (PIQ)

RESULT

The medical records of 88 patients were analyzed, among whom 41 used the SGA and 47 the PIQ. A total of 848 blood glucose measurements were obtained from patients who used SGA, of which 183 measurements were detected with values higher than 160 mg/dL and 18 lower than 80 mg/dl, which in percentage represent 22% and 2%. It is noteworthy that no severe hypoglycemia was detected with values lower than 40 mg/dL. The mean values of maximum daily blood glucose levels were 154.91 mg/dL and the mean minimum values were 106.22 mg/dL. The mean daily blood glucose values in this group was 130.57 mg/dL and the mean daily variations were 48.69 mg/dL.

A total of 1577 blood glucose measurements were obtained from the patients who used PIQ; of these, 252 were detected with values greater than 160 mg/dL and 16 lower than 80 mg/dL, which in percentage represent 16% and 1%, respectively and which totaled 16% measurements outside the glycemic target. An episode of severe hypoglycemia was detected with values lower than 40 mg/dL. The mean daily maximum blood glucose values were 149.24 mg/dL and the mean minimum values were 105.49 mg/dL. The mean daily blood glucose values in this group was 125.25 mg/dL and the mean daily variations were 43.75 mg/dL.

Table 1 shows the difference in the percentage of blood glucose levels measured outside and inside the glycemic target between the protocols, which totaled 24% in the SGA and 17% in the PIG (p = 0.0001).

TABLE 1 — Proportion of blood glucose levels outside and inside the glycemic target

	SGA	PIQ
Off target glycemic (%)	647 (76%)	1309 (83%)
Within the glycemic target (%)	201 (24%)	268(17%)
Total	848	1577

To characterize the groups, gender, age, % of burned body surface (SCQ) in relation to extent and depth, inhalation lesions, and mortality predicted by ABSI were compared. The mean age of the patients who used the PIQ, which was 41.34 years, was compared with the mean age of those who used the PIG, which was 37.88 years (p = 0.18), and in relation to the gender that used the PIQ, 22% belonged to the females, while in those who used the PIG 25.5% belonged to the women (p = 0.69).

Regarding the extent of burns, the percentage of burned body surface area (SCQ) was compared in those who used the PIG and observed a mean of 32.6% of SCQ and in those who used the PIG, a mean of 28.59% of SCQ (p = 0.20). Regarding depth, the mean % of SCQ affected by second-degree burns was compared, which was 20.15% in patients who used the PIG and 15.85% in those who used the PIG (p = 0.17), as well as the mean % of SCQ affected by third-degree burns, which was 14.34% in the patients who used the PIQ and 12.73% in the PIG (p = 0.47). In the comparison of the incidence of inhalation lesions, a statistically significant difference was observed, as it was found to be present in 40.43% of the patients who used the PIQ and 17.$^{07\%}$ of those who used it (p = 0.014).

Table 2 shows the results of the ABSI index score of both groups, as well as the respective predicted mortality of each of the groups. Among those who used the PIG, the mean score was 6.76, while among those who used the PIQ it was 7.89 (p = 0.011) with respective predicted mortality of 27.61% and 44.89% (p = 0.004).

TABLE 2 — Mean ABSI score and the percentage of predicted mortality.

	Average	n	DP	Min.	Max.	Average	n	DP	Min.	Max.
SGA	6,8	41	2,28	1	12	27,6 %	41	27,93	2	90
PIQ	7,9	47	1,97	4	11	44,9 %	47	27,78	2	80
Total	7,4	88	2,18	1	12	36,8 %	88	29,02	2	90

However, as shown in Table 3, the mortality found was similar in the comparison between the protocols with death in 24.63% of the patients who used the PIG and 24.89% in those with the PIQ (p = 0.61).

TABLE 3 — Proportion of outcome by protocol

Denouement	PIG	PIQ	Total
Survived (%)	35 (85,37%)	40 (85,11%)	75
Death (%)	6 (24,63%)	7 (24,89%)	13
Total (%)	41 (100%)	47 (100%)	88

Table 4 shows the comparison between the groups of mean daily glycemic variations and mean daily maximum and minimum blood glucose levels of the patients per protocol, as well as the standard deviation (SD) and the maximum and minimum values found for this variable.

TABLE 4 — Mean of maximum and minimum blood glucose levels and daily variation.

		Average	n	DP	Minimum	Maximum	P-value
Variation glycemic	PIG	48,69	41	19,93	20	108	0,027
	PIQ	43,75	47	34,06	7	176	
	Total	46,05	88	28,32	7	176	
Blood glucose Maximum	PIG	154,92	41	22,31	119,00	206,51	0,022
	PIQ	149,24	47	40,19	106,50	296,14	
	Total	151,88	88	33,03	106,50	296,14	
Blood glucose Minimum	PIG	106,23	41	12,39	79,00	136,95	0,71
	PIQ	105,49	47	9,6	89,13	135,67	
	Total	105,83	88	11,00	79,00	136,95	

Regarding the mean daily glycemic variation of the patients who used the PIG, it was 48.69 mg/dL and in those who used the PIQ, 43.75 mg/dL (p = 0.027). The mean maximum daily blood glucose levels in the patients who used the PIG were 154.92 mg/dL and in the PIQ was 149.24 mg/dL (p = 0.022), while the mean minimum daily blood glucose levels in those who used the PIG were 106.23 mg/dL and in those with the PIQ was 105.49 mg/dL (p = 0.71).

DISCUSSION

Maximum values set at 180 mg/dL can reduce mortality. It is pointed out that the range of blood glucose values between 90-140 mg/dL may be ideal, because it avoids hypoglycemia and, at the same time, the glycosylation of hemoglobin that occurs at 150 mg/dL.[7] The concern is not restricted to hyperglycemia, but to the variation in blood glucose values.[12] In the PIQ protocol, the range between 80-160 mg/dL was established as expected, and when comparing it with the PIG protocol, lower values were observed, both in the mean blood glucose variation and in the mean of the maximum blood glucose, indicating a value below that necessary for hemoglobin glycosylation.

Hypoglycemia was found to be associated with increased risk of death and adverse outcomes. Hypoglycemia is considered harmful and dangerous, either moderate when values are less than 60 mg/dL, or severe with values below 40 mg/dL.[7] In this study, 18 (2.12%) patients who used PIG were found to have measurements lower than 80 mg/dl, while 16 (1.01%) had 1 episode of severe hypoglycemia recorded with PIQ. The mean values of the minimum blood glucose levels were similar between the 2 protocols.

It has been observed that a glycemic target with blood glucose below 180 mg/dl can reduce mortality and dwell time.[18] However, there is a hypothesis that the glycemic target should remain at levels close to 130 mg/dl, which is based on the fact that it would avoid episodes of hypoglycemia, as well as hyperglycemia with protein glycosylation.[9] In this study, the mean value of the PIG protocol coincided with that recommended by these authors, while with the use of the PIQ the mean value was 125.25 mg/dL, which corresponds to a lower value. However, the percentage of blood glucose levels below 80 mg/dL was higher in PIG, with 2.2% of measurements versus 1.01% in PIQ. In addition, there was no statistical difference in the mean minimum blood glucose levels, indicating its safety in maintaining the minimum glycemic target.

It was found that staying within the glycemic target of 70-139 mg/dL 80% of the time can reduce mortality in critically ill non-diabetic patients, but not in previously diabetic patients.[19] In this study, the percentage of measurements inside and outside the glycemic target of both protocols was observed, where the results showed significant differences with 76% of the blood glucose levels within the target in the PIG and 83% in the PIQ.

The ABSI is simple and reliable to predict mortality, consisting of 5 variables: gender, age, presence of airway injury, presence of third-degree burns, and percentage of total body surface area burned.[16] The ABSI score found in patients who used the PIQ was higher than in those with the PIC, determined by the presence of a greater number of airway lesions. In this study, the mortality rate of those who used PIG was 27.61%, which was similar to the mortality rate found at 24.63%. However, the predicted mortality rate in patients who used the PIQ was 44.89% and was not similar to that found at 24.89%. Positive results for the PIQ protocol cannot be affirmed that they occurred due to its use, and further studies will be needed to determine the factors that determined these results and interfered with mortality.

Among the differences between the protocols, it can be mentioned that the PIC protocol predefines the intervals for measuring glycemic values and the initial dose of intravenous insulinization, as well as indicating its increase, reduction, interruption and migration from intermittent to continuous and vice-versa. Although it has shown that it can be effective in restricting blood glucose at its glycemic target, this complexity of directions requires specific training of the team for its safe use.

CONCLUSION

The PIQ is promising, because in the comparative analysis with the PIG in burn patients, a reduction in the percentage of measurements outside the glycemic target was found, the mean maximum blood glucose and glycemic variability were lower, and the mean minimum daily blood glucose was similar between the protocols. The mortality predicted by the ABSI was higher in the PIQ when compared to the PIG, however the mortality between the groups was similar.

Authors' contributions
Conceptualization: Claudio Luciano Franck
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