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Predictive factors of hyperglycemia in hospitalized adults receiving total parenteral nutrition

Factores predictivos de hiperglucemia en adultos hospitalizados con nutrición parenteral total

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Abstract

Objective: To know those predictive factors of hyperglycemia that could guide us the design of a parenteral nutrition and it could avoid later complications associated with it.

Methods: A prospective observational study was designed; adult hospitalized patients who received total parenteral nutrition at least 48 hours were included. Nutritional and pharmacotherapeutic follow-up were performed according to usual practice. Variables collected included demographic, clinical, analytical and nutrition and pharmacotherapy.

Results: Fifty-eight patients were included, with 28 patients (48.3%) with glucose restriction. This intervention was statistically associated with elevated glycemia prior to parenteral nutrition (OR: 1.38, 95% CI 1.11-1.73, p=0.004) and BMI (OR: 1.29, 95% CI 1.05-1.58, p=0.014), with more frequent intervention was in patients with BMI>25 (overweight and obese) (OR: 10.00; 95% CI 1.15-86.95, p=0.037).

Conclusions: Pre-parenteral glycemic values, diabetes and BMI values>25 are predictors of hyperglycemia, so a early intervention to prevent and correct hyperglycemia may improve clinical outcomes in patients with parenteral nutrition.

Resumen

Objetivo: Conocer aquellos factores predictivos de hiperglucemia que orienten al diseño de una nutrición parenteral de inicio que nos permita evitar posteriores complicaciones asociadas a la misma.

Métodos: Se diseñó un estudio prospectivo observacional en el que se incluyeron los pacientes adultos hospitalizados con nutrición parenteral total por vía central con al menos 48 horas de duración; se realizó un seguimiento nutricional y farmacoterapéutico según la práctica habitual; se recogieron variables demográficas, clínicas, analíticas y relacionadas con la nutrición y la farmacoterapia.

Resultados: Se incluyeron 58 pacientes, se intervino con restricción de glucosa en 28 pacientes (48,3%). Esta intervención se asoció de manera estadísticamente significativa a glucemia elevada previa a la nutrición parenteral (OR: 1,38; IC 95% 1,11-1,73, p=0,004) e IMC (OR: 1,29; IC 95% 1,05-1,58, p=0,014), siendo más frecuente la intervención en los pacientes con IMC>25 (sobrepeso y obesidad) (OR: 10,00; IC 95% 1,15-86,95, p=0,037).

Conclusiones: Los valores de glucemia previos a la nutrición parenteral, la diabetes y los valores de IMC>25 son predictores de hiperglucemia; por tanto, una temprana intervención para prevenir y corregir la hiperglucemia podría mejorar los resultados clínicos en pacientes con nutrición parenteral.

KEYWORDS
Parenteral nutrition; Hyperglycemia; Risk factors; Body mass index; Diabetes; Glucose.

PALABRAS CLAVES
Nutrición parenteral; Hiperglucemia; Factores de riesgo; Índice de masa corporal; Diabetes; Glucosa.

Introduction

Parenteral nutrition (PN) maintains an adequate nutritional status, which is important in order to improve disease prognosis and sustain an appropriate immune system[1,2]. The beneficial effects of PN have been well established, but some studies have questioned its safety due to the risk of derived complications, such as hyperglycemia, with an incidence ranging from 10 to 88% according to literature[1,3-6].

PN is associated with a higher frequency of hyperglycemia and insulin requirements[7] because glucose in NP will go straight into peripheral circulation, reaching high systemic levels, but remaining low in portal circulation[3]. On the other hand, there is an increase in metabolic pathways (gluconeogenesis and glycogenolysis) mediated by hormonal regulation and proinflammatory cytokines[2,8]. As a consequence, there is sustained hyperglycemia together with hyperinsulinemia and various side effects such as hyperosmolarity, glycosuria, excess of CO_2, liver impairment, etc.[3].

Critical patients will frequently develop hyperglycemia secondary to stress and their hypermetabolic condition due to acute lesion[3]. Some non-critical patients, even without any previous history of diabetes mellitus (DM) or glucose intolerance, will respond to PN with very severe hyperglycemia; this will subsequently entail correction through fast-acting insulin and the modification of the PN formulation as soon as possible[9].

Hyperglycemia is a common and undesirable complication of PN, and it represents a good marker for results, morbidity and mortality[1,4,6,10-13]. High glucose levels in blood can lead to severe complications such as infections, sepsis, renal failure or respiratory failure[4].

PN formulation provides glucose continuously, and therefore higher glucose levels in PN are associated with higher hyperglycemia[14]. For this reason, it must be ensured that each patient will receive the adequate intake of carbohydrates and insulin[7], taking into account that nutritional requirements are higher in hypercatabolic states[8].

Glucose restriction in PN is one of the potential strategies for glycemic control in patients on PN, and the one conducted in our setting; but other strategies have also been studied, even though without any conclusive outcomes, such as the combination of PN and enteral nutrition, the delay in PN initiation, the addition of glutamine or chromium, or the use of certain lipid emulsions in PN formulation, etc[15].

Following recommendations by scientific societies, the content of glucose as an energy substrate will be adjusted in order to maintain glycemic values below 150 mg/dl, with the required content of exogenous insulin[16,17]. Values above 180 mg/dl might be associated with worse clinical results[8,11,12]. All this reinforces the need to achieve strict glucose control, because it is associated with a lower risk of complications in hospitalized patients[9].

Previous glucose levels can orientate towards initiating a therapy with glucose restriction in patients with DM; however, in other non-diabetic patients who develop hyperglycemia, no initial restrictions will be usually made. Knowing the predisposing factors before PN initiation would allow to adapt the initial PN formulation for each individual patient, thus reducing the risk of hyperglycemia and its subsequent complications[9].

The primary objective of this study is to understand the predictive factors of hyperglycemia. The secondary objectives are to compare those patients with intervention (glucose reduction in PN) vs. those without intervention, and to determine which factors are associated with a higher efficacy in said intervention.

Methods

A prospective observational study was designed and conducted during six months (November, 2015 to April, 2016), including consecutively all adult patients hospitalized (critical and non-critical) receiving total PN through a central line for at least 48 hours. Those patients included were followed up from PN initiation to its discontinuation, EN initiation, or oral tolerance.

Data collection

The following data were collected during the study:

Demographical variables: gender, age, weight, body mass index (BMI) calculated through weight (kg)/ (height (m))^2.

Clinical variables:

- Clinical Record: insulin-dependent diabetic or not, previous creatinine, basal comorbidities (hypertension, dyslipidemia, heart conditions, COPD).
- Reason for PN (complication of a GI tract neoplasia, abdominal surgery post-operative period, GI hemorrhage, clinical deterioration due to sepsis, oral intolerance due to liver disease, or oral intolerance for other reasons).
- Clinical or surgical condition.
- Stay at the ICU (Intensive Care Unit) or not.

Nutrition and Drug Therapy:

- Type of PN administered (mean volume of glucose, proteins and lipids administered (g/kg/24h)).
- Basal energy expenditure (BEE) (Kcal/24h), Kcal in the PN administered (Kcal/24h) and association between both (proportion).
- Need for insulin during PN: yes (subcutaneous or intravenous) or not.
- Days until development of hyperglycemia.
- Duration of PN (in days).

Lab Test Variables:

- Glucose levels previous to PN (mg/dl)*.
- Mean daily glucose levels during PN*: the daily mean value is estimated from the glucose concentrations measured every 8 hours.
- Days until glycemic normalization after glucose restriction.

*Hyperglycemia was defined as > 150mg/dl glucose levels in plasma.

Protocol for nutritional intervention

The follow-up for patients on PN was conducted according to the usual protocol described below.

After PN prescription, the total PN formulation was calculated based on the caloric and clinical needs of each patient, through the estimation of basal energy expenditure by Harris-Benedict (HB). Formulations with glucose restriction were initiated from the start in patients with DM:

- *D1 Formulations* (50 g glucose restriction from their nutritional needs).
- *D2 Formulations* (100 g glucose restriction from their nutritional needs).

The Pharmacy Unit conducted daily follow-up for patients on PN, taking into account the following premises:

- In any case, the minimum values of glucose in the formulations were 100 g per day.
- In diabetic patients, PN was initiated with a restricted formulation of 100 g glucose *(D2 Formulation*).
- Blood glucose tests (with capillary glucometer) were conducted every 8 hours since PN initiation.
- If glucose restriction was sustained over time, daily Kcal were compensated with lipids.

Glucose adjustments in PN were made according to the current protocol prepared by the Pharmacy Unit and the Endocrinology Unit (Figure 1). The mode of action consisted in the daily adjustment of glucose volume in the PN formulation, based on the glycemic values recorded in the 24 previous hours (blood glucose tests):

- If three consecutive glucose levels > 150 mg/l or two > 180 mg/l were observed, there was a glucose reduction of 50 g per day, up to a minimum 100 g glucose in PN.
- If high glycemic values continued subsequently, insulin was added to PN (the volume was two thirds of the fast-acting insulin administered the day before, according to the outcomes of the sliding scale).

The PN formulations prepared were standardized according to protein and glucose grams; and initially contained the same volume of lipids, micronutrients and electrolytes. These were the basis for PN prescription and preparation, and were used as a model to modify the adjustment to the individual requirements of each patient according to their daily clinical and lab test evolution.

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Statistical Analysis

A descriptive analysis of the individual characteristics of patients was conducted, both in the total sample and by groups with intervention (patients who had undergone glucose reduction or insulin addition in their PN according to the protocol in figure 1) and without intervention. There was an estimation of the mean value, standard deviation, maximum and minimum values of quantitative variables; while qualitative or discrete variables were described through absolute (N) and relative (%) frequency throughout the sample. A univariate logistical regression analysis was conducted in order to identify which individual characteristics were associated with the intervention. The odds ratio of the intervention was estimated in each case, as well as their 95% Confidence Interval, and the relevant p-value (Square Chi Test). It was decided to exclude diabetic patients for this analysis, because they would require intervention by protocol. A second stage intended to determine which individual factors would be associated with higher efficacy in the intervention; to this end, a Cox Regression Analysis was conducted, considering the time from intervention to stabilization as time scale, and stabilization as final outcome. There was an estimation of hazard ratio, its 95% Confidence Interval, and the relevant p-value (Square Chi Test). There was an adjustment by the diabetes variable in the model. The STATA (version 11) statistical program was used.

Results

Fifty-eight (58) patients on PN were included; there was nutritional and pharmacotherapeutical follow-up according to usual practice. PN was administered through central line to all 58 patients, with a continuous perfusion during 24 hours (not cyclic). The mean contents (± standard deviation) of carbohydrates were 2.2 (± 0.8) g/kg/day, the protein contents were 0.9 (± 0.3) g/kg/day, and 0.8 (± 0.3) g/kg/day of lipids. The mean BEE was 1402.27 (± 273.24) kcal/day, with a mean daily intake of 20kcal (± 7) /kg/day, which represented 99.7% of the BEE for each patient estimated through HB. All formulations were supplemented with vitamins and trace elements. There was a mean follow-up of 12 days (from 2 to 51 days). Hyperglycemia developed in diabetic patients on the first day of PN administration, while for non-diabetic patients, this occurred after a mean 2.3 days (from 1 to 10 days).

Forty-five (45) patients (77.5% of the sample) had not been diagnosed with diabetes; however, 40% of them (18 patients) presented hyperglycemia during follow-up. There was an intervention in all diabetic patients, except for three patients who presented 120mg/dl glycaemia before PN, and it was decided not to restrict glucose to 100g. Table 1 shows all variables collected from the 58 patients included in the study.

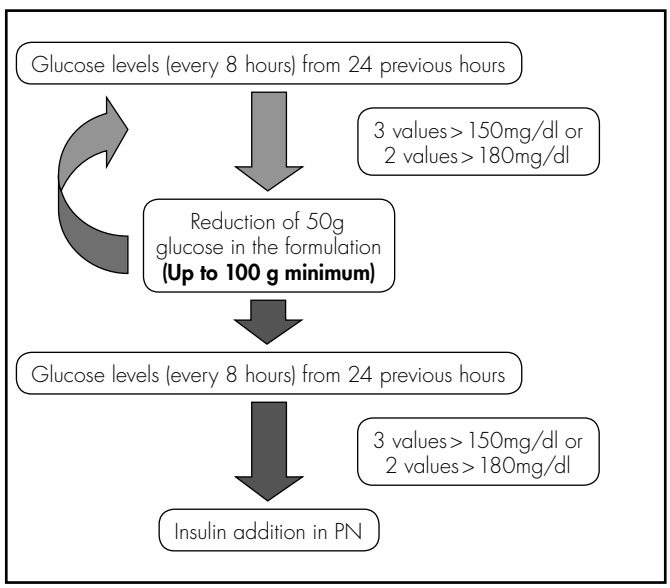

Figure 1. *Protocol for Glucose Reduction in PN.*

There was a glucose restriction intervention in 28 patients (48.3%). Analysis by logistical regression was conducted in two arms: 28 patients with intervention for alteration of glucose levels (with intervention) and 30 patients for whom no glucose modification was conducted in their PN (without intervention). Given that diabetes determines intervention by protocol (OR: 5; CI 95% 1.21-20.77, p = 0.026), statistical analysis was conducted excluding diabetic patients (10 patients in the intervention group arm and 3 patients without intervention). Table 2 shows the outcomes of the logistical regression.

The intervention was associated in a statistically significant way to previous high glucose levels (OR: 1.38; CI 95% 1.11-1.73, p = 0.004) and BMI (OR: 1.29; CI 95% 1.05-1.58, p = 0.014); intervention was more frequent in patients with BMI > 25 (overweight and obese) (OR: 10.00; CI 95% 1.15-86.95, p = 0.037).

Mean glucose levels during PN were higher in the intervention arm (OR: 1.83; CI 95% 1.24-2.72, p = 0.002), as well as insulin administration (OR: 12.25; CI 95% 2.92-51.42, p = 0.001) and the number of insulin units (OR: 2.70; CI 95% 1.05-6.94, p = 0.038). A trend towards significance was observed in the association with intervention in patients with neoplasia and with the higher duration of PN. No statistical significance was achieved for the intervention with gender, age, stay at ICU, reason for admission, and comorbidities.

There was an analysis of the intervention efficacy based on time. The analysis results are shown in table 3. The fast glucose normalization was not associated in a statistically significant way with any of the factors studied. There is a trend for fast glucose normalization after the intervention in women (HRc: 1.73; CI 95% 0.97-1.04, p = 0.180) and with clinical reason (HRc: 0.43; CI 95% 0.14-1.42, p = 0.170).

Discussion

As other authors have already stated[9], understanding the predisposing factors previous to PN initiation will allow us to adapt the initial PN formulation individually for each patient, thus reducing the risk of hyperglycemia and its subsequent complications. For this reason, high glucose levels during PN administration, applying the described protocol, will orientate us towards the modification of glucose volume and/or the addition of insulin to the formulation. On the other hand, the study outcomes show that BMI is a parameter predicting the need for glucose restriction in the PN formulation. Therefore, those patients who present excess weight or obesity (BMI ≥ 25) are associated with hyperglycemia linked to the use of PN. Other studies have determined that previous surgery, renal failure and age are predictors of hyperglycemia, as well as obesity and excess weight[4,6,12,18]. We must point out that DM has been excluded from our analysis, because this is a factor that has determined glucose restriction in the formulation since the start, according to the application of the protocol described.

It is worth highlighting that no statistical association was observed in patients hospitalized in the ICU, against what was expected and described by other authors[4,6]: this result could be explained by the reduced sample size of the study, because it is well known that metabolic alterations of critical patients entail an elevation in glucose levels and insulin resistance due to an increase in glycogenolysis and gluconeogenesis. PN duration showed a trend towards intervention, but was not associated in a statistically significant way with a higher risk of hyperglycemia, unlike other authors who even associated it with longer hospital stays[4]. These factors, as well as the daily concentrations of glucose in blood, are available in clinical records for hospitalized patients, and therefore it would be convenient to take them into account at the time of designing the PN formulation.

Special formulations for renal failure were initiated in seven patients. Due to the characteristics of their composition (reduced protein content), these require a low volume of glucose (100 g) to maintain an adequate ratio of non-protein calories per nitrogen gram. This glucose reduction is conducted when choosing the formulation, and therefore it has not been taken as a glucose restriction intervention, because there are other reasons for the intervention. In order to avoid this bias, these were initially excluded from logistical regression, but outcomes were not modified, so they were finally included in the analysis.

Table 1. Characteristics of patients (N = 58)

		N/mean	%/ SD	Min	Max
Demographical Variables					
Gender	Male	31	53.5		
	Female	27	46.6		
Age	(number)	66.3	14.0	27	87
	≤ 65-year-old	25	43.1		
	> 65-year-old	33	56.9		
BMI	(number)	26.3	4.1	16.2	35.2
	Normal weight (< 25)	17	29.3		
	Overweight/Obesity (≥ 25)	41	20.7		
Clinical Variables					
Diabetes Mellitus		13	22.4		
Previous Creatinine	(number)	1.2	1.0	0.4	6.3
	< 1.5 mg/dl	48	82.8		
	≥ 1.5 mg/dl	10	17.2		
Comorbidities	Hypertension (YES)	32	55.2		
	Dyslipidemia (YES)	15	25.9		
	Heart conditions (YES)	14	24.1		
	COPD (YES)	5	8.6		
Reason for PN	Complication of GI tract neoplasia	14	24.1		
	Post-operative period after abdominal surgery	25	43.1		
	GI hemorrhage	9	15.5		
	Clinical deterioration due to sepsis	3	5.2		
	Oral intolerance due to liver disease	4	6.9		
	Oral intolerance for other reasons	3	5.2		
ICU (YES)		22	37.9		
Reason for admission	Surgical	45	77.6		
	Clinical	13	22.4		
Nutrition and drugs					
Mean glucose in PN (g)		145.8	41.8	100	250
Glucose (g/kg/day)		2.2	0.8	1.1	4.4
Proteins (g/kg/day)		0.9	0.3	0.3	1.5
Lipids (g/kg/day)		0.8	0.3	0.3	1.7
Energy (Kcal/kg/day)		20	7	8	32.8
Basal Energy Expenditure (kcal/day)		1,402.2	273.2	920	2,252
Insulin	YES	28	48.3		
	Units *	15.1	7.4	5	39.4
PN Duration (days)		12.8	10.9	2	51
Lab Test Variables					
Glucose Pc previous to PN		129.3	42.6	59	260
Mean glucose Pc during PN		144.8	29.7	92.4	234.7

*Only patients receiving insulin are considered for this estimation. PN: parenteral nutrition; Pc: plasma concentration. Values are number (N), frequency (%), SD (standard deviation) and Min (minimum) & Max (maximum) range.

Table 2. Logistical regression (excluding diabetic patients) (N = 45)

		Without intervention (N = 27)		With intervention (N = 18)					
		N	%	N	%	OR	IC95%		p-valor
Gender	Male	16	64	9	36	1 ref			
	Female	11	55	9	45	1.45	0.44	4.83	0.541
Age	(number)	63.9	15.2	67	13.7	1.02	0.97	1.06	0.432
	≤65 year-old	12	60	8	40	1 ref			
	>65 year-old	15	60	10	40	1.00	0.30	3.32	1.00
BMI	(number)	25.3	4.2	28.7	2.9	1.29	1.05	1.58	0.014
	Normal weight (<25)	10	91.9	1	9.1	1 ref			
	Overweight or Obese (≥25)	17	50	17	50	10.00	1.15	86.95	0.037
Previous Creatinine	(number)	1.3	0.9	0.9	0.3	0.39	0.12	1.35	0.140
	<1.5 mg/dl	20	52.6	18	47.4				
	≥1.5 mg/dl	7	100						
Hypertension	No	15	68.2	7	31.8	1 ref			
	Yes	12	52.2	11	47.8	1.96	0.58	6.61	0.276
Dyslipidemia	No	20	60.6	13	39.4	1 ref			
	Yes	7	58.3	5	41.7	1.09	0.28	4.21	0.891
Heart conditions	No	18	58.1	13	41.9	1 ref			
	Yes	9	64.3	5	35.7	0.77	0.20	2.83	0.694
COPD	No	24	57.1	18	41.9				
	Yes	3	100						
Reason for PN	Complication of GI tract neoplasia	5	45.5	6	54.5	2.88	0.59	13.98	0.190
	Post-operative period after abdominal surgery	10	58.8	7	41.2	1.68	0.40	6.96	0.474
	Other*	12	70.6	5	29.4	1 ref			
ICU	No	17	65.4	9	34.6	1 ref			
	Yes	10	52.6	9	47.4	1.7	0.39	5.70	0.860
Reason for admission	Surgical	20	60.6	13	39.4	1 ref			
	Clinical	7	58.3	5	41.7	1.09	0.28	4.21	0.891
PN Duration (days)		10.9	9.8	16.6	13.0	1.04	0.98	1.11	0.114
Glucose previous to PN (OR x10 glucose units)		108.9	28.7	153	49.2	1.38	1.10	1.73	0.004
Mean PN glucose (OR x10 glucose units)		127.9	20.6	154.6	21.8	1.83	1.24	2.71	0.002
Insulin	No	21	84	4	16	1 ref			
	Yes	6	30	14	70	12.25	2.92	51.42	0.001
Insulin Units (only those on insulin)		8.1	1.9	16.3	7.9	2.70	1.05	6.94	0.038

A univariate logistical regression analysis was conducted in order to identify which individual characteristics were associated with the intervention. In each case, the raw odds ratio of the intervention was calculated, and its Confidence Interval at 95%, and the relevant p-value (Square Chi Test).

*Other: *GI hemorrhage, clinical deterioration due to sepsis, oral intolerance due to hepatic disease, oral intolerance for other reasons.*

PN: parenteral nutrition; Pc: plasma concentration, The values are number (N), frequency (%), OR (Odds ratio) and CI95% (Confidence Interval of 95%). Significant differences (p<0.05).

In the arm of patients with intervention there are no patients with previous creatinine>1.5 mg/dl, because a formulation with protein and glucose restriction is indicated from the start. For this reasons, no intervention is required in the majority of these patients.

Some authors have observed that the composition of the parenteral formulation can have an impact on glucose levels in plasma (omega 3, glutamine)[9]; these factors have not been taken into account in this study, because lipid sources are the same in all cases, and no glutamine has been used. Moreover, we have no information about all the medication that could affect glucose levels (corticosteroids, vasopressor agents, etc.), given that a great proportion of the patients are in the ICU, and it is difficult for the Pharmacy Unit to obtain a record of the medication administered, as there is no system for medication distribution per units in this hospital unit.

The literature published regarding this shows that glucose levels>180 mg/dl previous to PN will entail an increase in pneumonia, renal failure,

Table 3. Factors associated with the efficacy of intervention

Non-diabetic patients with intervention (n=18)		HRc	CI95%		P value
Gender	Male	1 ref			
	Female	1.73	0.77	3.88	0.180
Age	(number)	1.00	0.97	1.04	0.607
	≤65-year-old	1 ref			
	>65-year-old	0.92	0.42	2.00	0.824
BMI	(number)	1.04	0.92	1.17	0.497
	Normal weight (<25)	1 ref			
	Overweight or Obese≥25)	0.71	0.24	2.06	0.529
Previous Creatinine	(number)	0.78	0.27	2.28	0.661
	<1,5 mg/dl	1 ref			
	≥1,5 mg/dl	0.53	0.11	2.58	0.436
Hypertension	No	1 ref			
	Yes	0.64	0.28	1.47	0.295
Dyslipidemia	No	1 ref			
	Yes	1.52	0.64	3.64	0.343
Heart conditions	No	1 ref			
	Yes	1.05	0.36	2.99	0.932
COPD	No	1 ref			
	Yes	2.02	0.40	10.02	0.389
Reason for PN	Complication of GI tract neoplasia	0.87	0.30	2.48	0.801
	Post-operative period after abdominal surgery	1.35	0.48	3.80	0.566
	Other*	1 ref			
ICU	No	1 ref			
	Yes	1.62	0.65	4.03	0.302
Reason for admission	Surgical	1 ref			
	Clinical	0.43	0.14	1.42	0.170
Glucose previous to PN (OR x10 glucose units)		0.98	0.89	1.06	0.606
Mean PN glucose (OR x10 glucose units)		0.84	0.71	1.01	0.071
Insulin	No	1 ref			
	Yes	0.59	0.23	1.49	0.264
Insulin Units		0.95	0.89	1.01	0.129
Mean glucose (g) in PN (HR x10 Glucose Units)		1.14	0.95	1.38	0.151

A Cox Regression analysis was conducted, considering the time from intervention until stabilization as time scale, and stabilization as final outcome. Hazard ratio was estimated, Confidence Interval at 95%, and the relevant p-value (Chi Square Test). It was adjusted by the diabetes variable in the model.
*Other: *GI hemorrhage, clinical deterioration due to sepsis, oral intolerance due to hepatic disease, oral intolerance for other reasons*. PN: parenteral nutrition, PC: plasma concentration. **Cox Regression analysis, adjusted by diabetes. Values are HR (Hazard ratio) and CI95% (95% Confidence Interval). Significant differences (p<0.05).

and a higher duration of hospital stay[5,9,11]. However, it has been observed that an adequate management of hyperglycemia will reduce complications[13]. There has been no assessment of hyperglycemia complications in our study, but there has been intervention in all patients with glucose levels > 180 mg/dl.

Given that glucose concentrations in plasma are the main lab test value to be considered, it would be adequate to review the values of reference for hyperglycemia. In pre-diabetic or non-diagnosed patients, it could be considered that > 120 mg/dl values of glucose and of glycated haemoglobin (though the latter is not easily available in all non-diabetic patients) are predictors for intervention[6]. High glucose levels should not be taken into account if isolated; it is convenient to have continuous levels of high glucose (as stated in the protocol), because there is risk of hyperglycemia in any high-risk patient who is adequate for PN[4]. For this reason, there is no consensus among clinicians in terms of reducing the glucose volume in the PN for patients who present hyperglycemia[3], and therefore it is important to determine glucose reference levels in order to avoid to a higher extent the development of hypoglycemia associated to a reduction in glucose intake. In this study, repeated values of > 150 mg/dl and/or > 180mg/dl show the safety of the intervention, because no hypoglycemia value has been recorded throughout. In our protocol, unlike other authors[11,19,20] who have included insulin since PN initiation, glucose adjustments are laddered in order to prevent hypoglycemia. Even though it has been observed that there is a low incidence of hypoglycemia in patients on PN, its prevention

is important in patients with risk factors: longer PN nutrition and insulin, diabetic patients, and those in the ICU[21].

The following are considered potential biases in this observational study: data from daily clinical practice have been collected, where the same protocol is used for all patients, there has been a consecutive inclusion of all patients, and no patients have been excluded who could have altered the outcomes. Moreover, low protein contents (0.95 g/kg/day, excluding the seven patients with renal failure), probably due to the widespread practice in our centre of choosing initially (off the morning working hours) marketed three-chamber formulations with low protein contents, could have a negative impact on glucose level control, due to the insulinotropic effect of some amino acids and the insulin resistance induced by this low protein intake[22-25]. The lack of more conclusive results show the convenience of being more conservative in terms of initiation therapy, and not restrictive in terms of glucose contents, in order to prevent the risk of hypoglycemia and meet the needs.

High glucose levels have been associated with a higher risk of complications[4], and therefore it is important to identify those patients with risk of hyperglycemia associated with PN, and to prevent any complications that could appear during the period of administration. The benefit of glucose control is particularly important in patients without diagnosis of diabetes, because it has been observed that mortality associated with hyperglycemia is highly superior in these patients than in already known diabetic patients[26,27]. Future research should include more patients in specific populations, in order to reach conclusive outcomes that will be useful for daily clinical practice.

In conclusion, hyperglycemia is a very frequent alteration in patients receiving PN, and it requires close management. The standardization of formulations and inclusion of interventions in protocols will provide quality and safety to the process. Glucose levels previous to PN, diabetes, and BMI > 25 are predictors of hyperglycemia; therefore, an early intervention to prevent and correct hyperglycemia could improve clinical results in patients receiving PN.

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Conflict of interests

No conflict of interests.

Contribution to scientific literature

The results show the high incidence of hyperglycemia in diabetic patients, with high glycemic values prior to parenteral nutrition and with BMI > 25, and therefore the need for early intervention.

The values of BMI > 25 are added as predictors to the intervention protocol and, together with glycemia before parenteral nutrition and diabetes, guide the design of parenteral nutrition to improve the control of hyperglycemia.

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