Condiciones clínicas y complicaciones asociadas al uso de nutrición parenteral en pacientes con enfermedades críticas ingresados en una unidad de cuidados intensivos de un hospital general

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Condiciones clínicas y complicaciones asociadas al uso de nutrición parenteral en pacientes con enfermedades críticas ingresados en una unidad de cuidados intensivos de un hospital general

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The study project was approved by the Research Ethics Committee of the State Health Department of Brasília, Brazil. Patient information collected during the study will remain confidential.

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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Conflict of interests: The authors declare no conflict of interests.

ABSTRACT

Objective: the aim of this study was to evaluate the clinical conditions, the existing complications, and the drug prescription profile of patients who received parenteral nutrition in the intensive care unit.

Material and methods: this retrospective, analytical cohort study was carried out among individuals admitted to a public general hospital ICU. For data collection, the electronic medical records for the entire period of inpatient treatment were analyzed.

Results: in total, 213 individuals who had received parenteral nutrition for a period greater than 48 hours were included in the study. Most participants were male and mean age was < 60 years; death occurred in 75 % of patients, and abdominal surgery was the main indication for parenteral nutrition. Hyperglycemia was the most common complication. The Mann-Whitney test showed that the individuals who died were using a higher number of medications. The increased use of medications correlated with use of PN and led to an increase in hospital length of stay and death rate (p-value < 0.001). There was a higher proportion of deaths among patients using

standard parenteral nutrition solutions (76.9 %) as compared to the period when patients started receiving custom-made parenteral nutrition solutions (71.7 %). However, there was no statistical evidence of the association between type of nutrition and the outcome of death (p-value = 0.395).

Conclusions: custom-made parenteral nutrition may result in benefits for the patients, such as a decrease in the number of medications used. The relationship between type of nutrition and the outcome of death did not prove to be statistically significant.

Keywords: Intensive care unit. Critical care. Complications. Parenteral nutrition. Hospital mortality.

RESUMEN

Objetivo: el objetivo de este estudio fue evaluar las condiciones clínicas, las complicaciones existentes y el perfil de prescripción de medicamentos de los pacientes que recibieron nutrición parenteral en la unidad de cuidados intensivos.

Material y métodos: este estudio de cohortes analítico y retrospectivo se llevó a cabo entre individuos ingresados en una UCI de un hospital público general. Para la recopilación de datos se analizaron los registros médicos electrónicos de todo el período de tratamiento hospitalario.

Resultados: en total se incluyeron en el estudio 213 individuos que habían recibido nutrición parenteral durante un período superior a 48 horas. La mayoría de los participantes eran hombres y la edad media era < 60 años; se produjo la muerte en el 75 % de los pacientes y la cirugía abdominal fue la principal indicación de la nutrición parenteral. La hiperglucemia fue la complicación más común. La prueba de Mann-Whitney mostró que las personas que murieron estaban usando una mayor cantidad de medicamentos. El aumento en el uso de medicamentos se correlacionó con el uso de la PN y condujo a un aumento de la duración de la estancia hospitalaria y de

la mortalidad (valor p < 0,001). Hubo una mayor proporción de muertes entre los pacientes que usaron soluciones de nutrición parenteral estándar (76,9 %) en comparación con el período en que los pacientes comenzaron a recibir soluciones de nutrición parenteral hechas a medida (71,7 %). Sin embargo, no hubo evidencia estadística de la asociación entre el tipo de nutrición y el resultado de la muerte (valor p = 0,395).

Conclusiones: la nutrición parenteral hecha a medida puede generar beneficios para los pacientes, como una disminución de la cantidad de medicamentos utilizados. La relación entre el tipo de nutrición y el resultado de la muerte no resultó ser estadísticamente significativa.

Palabras clave: Unidad de cuidados intensivos. Cuidados críticos. Complicaciones. Nutrición parenteral. Mortalidad Hospitalaria.

INTRODUCTION

The intensive care unit (ICU) is intended for critically ill individuals and those who require specialized, complex care and continuous monitoring. The technology, devices and equipment involved help health care professionals make quick decisions to benefit severely ill patients (1).

Despite all the technology available in ICUs, patients in specific health situations—such as trauma patients, patients with severe infections, or those in the postoperative period after major surgery—are more susceptible to failing to respond to treatment due to a high risk of malnutrition during inpatient management (2). This malnutrition may contribute to immunosuppression and increase the risk of reduction in nutrient absorption by the intestine, thus leading to several complications that range from susceptibility to pressure injury development to decreased muscle mobility (3).

Nutritional therapy is part of the treatment provided to hospitalized patients, and is essential for their recovery. When nutrient supply is lower than required by patients, their nutritional status may worsen,

which may lead to malnutrition. Studies have shown that malnutrition in critically ill individuals is a risk factor for increased mortality, longer hospital length of stay, and even the occurrence of complications such as organ dysfunction (3-5).

Most patients admitted to an ICU are unable to receive oral nutrition. This may be due to their underlying pathology or orotracheal intubation, among other factors. When oral nutrition is impossible, patients must receive enteral or parenteral nutrition. Enteral nutrition (EN) is regulated by Resolution n. 63/2000 of the Brazilian Health Regulatory Agency (ANVISA, from the Portuguese *Agência Nacional de Vigilância Sanitária*) and is the most appropriate nutritional therapy for individuals whose ability to eat is severely compromised, as it maintains gastrointestinal tract function as the diet is administered through a nasoenteral or percutaneous endoscopic gastrostomy (PEG) tube or similar (3,5).

Parenteral nutrition (PN) is indicated when the patient is unable to receive food through the digestive system due to inaccessibility or low functionality. PN may be administered as partial (PPN) or total (TPN) parenteral nutrition. Partial parenteral nutrition consists of amino acids, carbohydrates, minerals and vitamins. It is administered through a peripheral venous access due to its low osmolarity and shorter infusion period, when compared to TPN. TPN may have higher osmolarity and is more complete in caloric and nutritional terms for critically ill patients when compared to PPN, as it also includes lipids (3,6).

The disadvantage of using PN is a higher risk of bacterial translocation, mainly due to bowel disuse, and a higher risk of infectious complications, including central venous catheter-related bloodstream infections, as well as venous access-related mechanical problems and metabolic or electrolyte changes, dehydration and hyperglycemia (3,5-10). Parenteral nutrition is regulated by Administrative Rule n. 272/1998 of the Brazilian Health Regulatory Agency (ANVISA) (3).

PN may either consist of premixed/standard solutions or custom-made products made in the hospital or a specialized pharmacy, ready for immediate use. The standard PN obtained from different laboratories consists of amino acid solutions with or without electrolytes, and lipid solutions at 10 % or 20 %, always at fixed concentrations, with macro and micronutrients supplied in multi-chamber bags by the manufacturer (7,11).

The choice of a PN origin is associated with the assessment of benefits, associated safety-related risks (contamination and the possibility of infection), and costs to the patient and institution (7,12). Critically ill individuals admitted to intensive care units undergo invasive procedures, are exposed to polypharmacy, and have complex clinical pictures requiring the use of medications and parenteral nutrition, often jointly through a venous access with continuous infusion. The study of these conditions may increase the safety of hospital procedures that critically ill patients undergo (13).

The aim of this study was to perform a survey of the epidemiological aspects, and to evaluate the clinical conditions, existing complications and drug prescription profile of patients receiving parenteral nutrition in the intensive care unit of a general hospital in Brasília, Brazil.

METHODS

This was a retrospective, analytical cohort study, also considering epidemiological aspects, carried out among individuals admitted to a public general hospital ICU in Brasília, Brazil, from March 2010 to December 2016. All individuals who were hospitalized for more than 48 hours in the intensive care unit were included in the study. Electronic medical records were investigated to provide additional information and to check out existing data. Individuals whose electronic medical records could not be found, or were incomplete, due to errors in the recording of data at admission to hospital were excluded, causing a loss of 18 % of the potential participants.

To achieve the study objectives a data collection form was created, which contained the information related to the overall evaluation of the participants. During data collection, the information obtained consisted of medical and nursing progress notes and prescriptions. As PN use varied among the patients included in the study, the median prescription was established during the period of parenteral nutrition use. For the other variables, all information was considered regarding the hospitalization period during which the patient received PN.

The data collection tool was created using the following variables: a) sociodemographic characteristics: registration number, age, origin, outcome (discharge/transfer or death), associated syndromal and nosological diagnoses, and hospital length of stay; b) evaluation of the parenteral nutrition therapy prescription: indication, access route used for administration and type of parenteral nutrition (standard or custom-made PN); c) clinical situations at the time of nutritional therapy prescription: unstable hemodynamics, acute pulmonary edema, patients with anuria but who were not receiving dialysis, presence of severe electrolyte and metabolic disorders; d) complications due to nutritional therapy use: local or systemic secondary infection due to central venous access use, glycemic disorders, significant electrolyte losses, hypertriglyceridemia, hepatic steatosis or cholestasis; e) drug interaction assessment of the PN-drug association: name of the prescribed drug, dosage, administration route, ATC (Anatomical Therapeutic Chemical) classification of prescribed drugs, and prescription of drugs from clinical trials which were not registered in Brazil at that time.

A description of the variables and their distribution over time was undertaken for the statistical analysis. For that purpose, qualitative variables were expressed as frequency distribution and percentage (relative frequency). Quantitative variables were expressed as mean and standard error of the mean. The Shapiro-Wilk test was applied to quantitative variables to verify whether the data had a normal distribution. The associations between qualitative variables were

verified by the chi-squared test, and for the quantitative variables their correlation was analyzed. As the normality of the data was not assumed, Spearman's correlation was used, while the non-parametric Mann-Whitney test was used for comparisons between groups.

Finally, the graphical representation was carried out using boxplots as a complement for the comparative analyses between groups. The Statistical Package for the Social Sciences® (SPSS) software, version 23.0, and Microsoft Excel® 2013 were used to analyze the data. Analyses with a p-value < 0.05 were considered significant. The study project was approved by the Research Ethics Committee of the Department of Health of Brasília, Brazil, ensuring the confidentiality of the information collected.

RESULTS

Sociodemographic characteristics

The study included 213 subjects who received parenteral nutrition for a period > 48 hours. The sample consisted of 121 (57 %) individuals under 60 years of age and 92 (43 %) over 60 years of age, of whom 118 were males (55.4 %) and 95 (44.6 %) females (Table I).

Of all the years analyzed, 2011 had the highest number of patients included in the study, when almost one-third of the subjects were assessed. A total of 17 (8 %) individuals were assessed in 2010, 64 (30 %) in 2011, 10 (4.7 %) in 2012, 30 (14.1 %) in 2013, 38 (17.8 %) in 2014, 36 (16.9 %) in 2015, and finally 18 (8.5 %) in 2016.

Regarding the diagnoses, 1,229 medical diagnoses were found, of which each patient had at least two. Diagnoses found in the ICD-10 (International Classification of Diseases, 10th edition), Chapter XI, representing digestive tract diseases, were identified 363 times, followed by diagnoses from Chapter X, diseases of the respiratory system, which were identified 268 times.

Hospitalization time was divided into 5-day intervals, and the interval with the highest prevalence was that from 11 to 15 days in 37 individuals (17.4 %), followed by 6 to 10 days in 36 (16.9 %). There

were 16 cases (7.5 %) with a hospital length of stay > 60 days (Table I).

Inpatient hospitalizations are controlled by the Department of Health of the Federal District (SES/DF) Intensive Care Unit (ICU) bed regulation center. Patients may be from the hospital itself, the hospitals of the public health network of the Federal District, or from the private network contracted by the SES/DF. The hospital emergency unit was responsible for 52 (24.4 %) of the referred patients, followed by the surgical center in 48 cases (22.5 %), and the in-patient wards, with a total of 33 (15.4 %) from the hospital itself. There were 71 (33.4 %) individuals from public hospitals located in Brasília and the Federal District, and 9 (4.2 %) individuals from private hospitals.

For the purposes of analysis, outcome was differentiated as discharged (discharge to the ward or transfer to another ICU) or death. On average, approximately three-quarters of the individuals died, but this proportion varied from year to year, as shown in table II: all individuals analyzed in 2012 died, whereas there was a mortality rate of 50 % in 2015. In 2010, there were 2 (11.8 %) discharges and 15 (88.2 %) deaths; in 2011, 17 (26.6 %) discharges and 47 (73.4 %) deaths; in 2012 all individuals (n = 10) died; in 2013, there were 9 (30 %) discharges and 21 (70 %) deaths; in 2014 there were 4 (10.5 %) discharges and 34 (89.5 %) deaths; in 2015, there were 18 discharges (50 %) and 18 (50 %) deaths, and finally in 2016 there were 4 (22.2 %) discharges and 14 (77.8 %) deaths.

Evaluation of the parenteral nutrition therapy prescription

Regarding the indication of nutritional therapy prescription, the main indication was abdominal surgery with 94 indications, intolerance to enteral nutrition in 48 cases, and peritonitis in 47 cases. The other indications were related to pancreatitis, abdominal distension, surgery in the cervical region, upper digestive bleeding, high gastric residual volumes through the nasogastric tube, persistent diarrhea, increase in

calorie intake, intestinal obstruction, vomiting, reduced intestinal transit to promote wound healing, enteric fistula, abdominal trauma, tracheal fistula, and megaesophagus. Of all individuals assessed, 27 (13 %) had PN indicated for more than one reason.

The access route used for TPN administration in 171 (80.3 %) individuals was the subclavian vein, followed by the internal jugular vein in 27 (12.7 %), and the femoral vein in 15 (7 %) individuals. The catheter used in 100 % of the cases was a double-lumen catheter, which is the standard type used by the public health network of the Federal District. The type of parenteral nutrition provided to patients was selected according to the current supply contract: the standard parenteral nutrition was supplied from 2010 to 2013 and the custom-made parenteral nutrition, supplied by an outsourced company, was provided from 2014 on, and was still being supplied when the study ended in 2016. Thus, a total of 121 (56.8 %) individuals received standard parenteral nutrition and 92 (43.2 %) received custom-made parenteral nutrition.

Clinical situations at the time of nutritional therapy prescription

Regarding the clinical situations at the time of parenteral nutrition use, there were 73 (34 %) individuals with severe electrolyte and metabolic disorders; 56 individuals (27 %) with hemodynamic instability; 17 (8 %) were anuric; and a mere 4 individuals (2 %) were receiving hemodialysis. There were no cases of acute pulmonary edema.

Complications due to nutritional therapy use

Regarding the possible complications due to nutritional therapy use, there were no cases of significant electrolyte loss, hypertriglyceridemia, hepatic steatosis or cholestasis among the individuals who received parenteral nutrition. Secondary infections related to central venous access use were mentioned in the medical

records in only 14 cases (7 %), although the authors suspect under-reporting. Glycemic disorders were the complications found most frequently, with 148 (69 %) cases, and consisted of hyperglycemia, hypoglycemia, or both.

Patient's prescription assessment

The drugs prescribed to the individuals were classified according to the ATC (Anatomical Therapeutic Chemical) classification. No drugs from clinical trials not listed by the Department of Health of the Federal District were identified. The mean number of prescribed drugs was calculated separately per year, as shown in table I.

A total of 3,156 drugs was prescribed during the study period. Regarding the type of medication used, the most frequently prescribed classes of medication were for the digestive tract and metabolism, with 31.62 % (ATC classification = A), followed by drugs for the nervous system class with 18.85 % (ATC classification = N), and thirdly the antimicrobial class for systemic use, with 17.68 % (ATC classification = J) of the total drugs prescribed.

There were some associations between variables and an individual's clinical outcome (discharge or death). Despite the higher death rate observed in women (80 % *vs*. 70.3 % in men), there was no correlation between outcome and sex. Since five variables did not show any cases (acute pulmonary edema, drug not listed by SES-DF, significant electrolyte losses, hypertriglyceridemia, hepatic steatosis, and cholestasis), the chi-squared test was not performed.

All individuals who were hemodynamically unstable died; accordingly, this variable is associated with outcome (p-value < 0.000). Individuals with severe metabolic disorders were more likely to die than those without them. This association between severe electrolyte and metabolic disorders and outcome was also significant (p-value = 0.013). Glycemic disorder was also associated with outcome (p-value < 0.000).

In the case of patients who were anuric, were receiving hemodialysis, or had a secondary infection due to the use of a venous access, although the descriptive analysis showed a greater probability of death, there was no significant association with outcome (p-value = 0.054, p-value = 0.105, and p-value = 727, respectively, as shown in table II.

The normality test showed that a normal distribution could not be assumed for the following variables: length of hospital stay, number of diagnoses, and total number of medications. As a Gaussian distribution was assumed only for the variable of age, it was not possible to use parametric tests. Hence, nonparametric tests were applied to the analyses, as well as the nonparametric Spearman's correlation.

Spearman's nonparametric correlation (Spearman's rho) was applied to identify the associations between quantitative variables, as a normal distribution of these variables could not be assumed. When analyzing the correlations between quantitative variables, it was observed that age had an inversely proportional association with the total number of medications used by the patient. The strength of this association, however, although significant, is weak. There is no significant correlation between age and number of diagnoses or hospital length of stay.

In addition to the inversely proportional association with age, the total number of medications is also correlated with hospital length of stay. The variables are directly proportional, as the higher the number of medications, the longer the hospital length of stay tends to be. The intensity of this correlation is weak. Regarding the number of diagnoses, it is associated only with hospital length of stay. The two variables are directly proportional, that is, the higher the number of diagnoses, the longer hospital length of stay tends to be, but the intensity of the correlation is weak, as shown in table III.

Although the individuals who died had an older mean age than those who were discharged or transferred (56.97 and 52.56, respectively),

this difference was not significant (p-value = 0.118). This comparison was carried out using Student's t-test for the comparison of means, and equal variances were assumed between the groups (Levene's test was not significant, with a p-value = 0.665).

The Mann-Whitney test revealed a significant difference in the total number of medications between the individuals who died and those who were discharged or transferred (p-value = 0.018). Those who died used a higher number of medications. A similar situation occurs when we analyze the number of diagnoses, as those who died had a higher number of diagnosed comorbidities. This difference between groups was also significant (p-value < 0.000),

Figure 1 shows that the individuals who died were mostly among those who received the highest number of medications.

One can observe from the above graph that the highest number of deaths was among the individuals being prescribed the most medications. The Mann-Whitney test showed there was a significant difference between the number of drugs prescribed to the individuals who died and to those who were discharged or transferred (p-value = 0.018). Those who died used a larger number of drugs. A similar situation is found when one analyzes the number of diagnoses; those who died had a larger number of comorbidities diagnosed. This difference between the groups was also significant (p-value < 0.000).

A higher number of deaths was observed in the individuals who received standard parenteral nutrition. In 2014, when the custom-made TPN began to be used, there was a 5 % decrease in mortality. Despite this difference, the chi-squared test did not show any association between type of nutrition and outcome (p-value = 0.395), as may be seen in tables IV and V.

A higher number of deaths was observed in the individuals who received standard parenteral nutrition. In 2014, when the custom-made TPN started being used, there was a 5 % decrease in mortality. Despite this difference, the chi-squared test did not show any association between type of nutrition and outcome (p-value = 0.395).

Figure 2 shows the number of diagnoses and the outcome (discharge/transfer or death) in individuals, and a higher number of deaths was observed in individuals with more diagnoses.

Figure 3 shows that the total number of medications was lower when custom-made parenteral nutrition began to be supplied by an outsourced company.

DISCUSSION

If patients are to avoid complications resulting from the use of parenteral nutrition, its provision has to be a central element of the care provided by the entire multiprofessional team. In order to be able to prevent or mitigate the effects of PN therapy, it is important to know the patient's clinical situation, the risks and benefits posed by PN, and what possible complications may occur.

The present study showed a prevalence of patients under 60 years of age (57 %) with a mean ± standard deviation age ranging from 50 ± 2 years in 2011 up to a maximum mean of 63 ± 2 years in 2014. There is no significant correlation between age and number of diagnoses or hospital length of stay. The older the patient, the greater the number of drugs administered tended to be. Corroborating this study, the literature presents a mean age ranging from 54 to 65 years in the patients who receive TPN (14-18).

It was found that the majority of participants in the present study were male, a profile similar to that of other studies (14,16,17); only in one study were most participants female (52 %) (15).

A higher number of diagnoses was directly associated with longer hospital length of stay; the patients who died had been diagnosed with a higher number of comorbidities.

This difference between groups was also significant (p-value < 0.000). Only one study carried out a survey of the diagnoses of patients receiving TPN, with enterocutaneous fistula being found in 31 %, in addition to short bowel syndrome, pancreatic fistula, and sepsis, among others (15). Thus, it may be observed that gastrointestinal

disorders are the main factor responsible for the use of parenteral nutrition.

The most frequent hospital length of stay found in this study was 11 to 15 days, observed in 17.4 % of the individuals included in the study, with a mean that varied according to the year in which the study was undertaken, with the lowest mean of 12 days in 2016 and the highest mean of 17 days in 2013. The literature shows greater variations regarding hospital length of stay when compared to the present study, ranging from 28 days (16), 29.3 ± 10.6 days of hospitalization (17), to a mean hospital length of stay of 42.2 days (14). The statistical analysis of the present study showed that the higher the number of medications, the longer the hospital length of stay tended to be (p-value < 0.000).

Approximately three quarters of the individuals included in the study died, thus representing 75 % of deaths and 25 % of discharges. Student's t test showed there was no significant difference between age and outcome. The literature assessed shows a much lower death rate than that found in this study, such as 9.6 % of deaths (16), up to a total mortality rate of 16.9 % (17). There have been no studies that analyzed patient outcome (discharge, death or transfer) with TPN use. Several surgical and some clinical pathologies were the reasons for TPN indication and, in this study, the most common indication was abdominal surgery, followed by intolerance to enteral nutrition and peritonitis. Other studies corroborate abdominal surgery as the main indication for parenteral nutrition (14,18), in addition to indications such as gastrointestinal tract alterations or obstruction (16), and short bowel syndrome in 68 % of cases (19).

In 80.3 % of cases, the access route used for TPN infusion was the subclavian vein; the internal jugular vein was used in 27 (12.7 %), and the least commonly used route was the femoral vein, in 15 (7 %) of the study subjects. The literature shows different results, with a predominance of central venous access in the internal jugular vein, with the subclavian vein being used less often (10,14,17-20).

Central venous catheter location is a risk factor for catheter-related bloodstream infections in patients receiving TPN (14,20), and studies have shown that the use of the jugular vein was a risk factor for the development of infections (10,18,19). Catheter use duration also influences the development of central venous catheter-related bloodstream infections in patients receiving TPN (15,18).

The type of catheter used in all patients in this study was the double lumen type. In the study by O'Connor (2013), the triple lumen catheter was the most frequently used type in 69 %, followed by the double lumen type in 20 %. Another study showed that the double lumen catheter was the one used most often, in 42 % of cases (18).

Central venous catheters are crucial in the treatment of critically ill individuals, as they are used in different ICU scenarios with several indications for their use, such as medication administration, procedures such as hemodialysis, and even hemodynamic monitoring (7).

In the case of individuals with electrolyte or metabolic disorders, and of those with glycemic disorders, there was a statistical correlation with the outcome of death. Likewise, all patients who were hemodynamically unstable also died. The fact that a patient was anuric or undergoing hemodialysis or had a central venous access-related secondary infection was associated with a higher probability of death, but the association was not significant. No study was found that assessed patient status at the time of TPN prescription.

The analysis of a patient's clinical situation when parenteral nutrition is prescribed should be undertaken by a multidisciplinary team involving physicians, nurses, nutritionists and pharmacists, so that a broad analysis of the case can be carried out and the prescription can benefit the patient (7).

Complications that may occur due to the use of TPN include electrolyte alterations, changes in hydration, and hyperglycemia, which are classified as metabolic complications. Among the most severe complications are hepatic steatosis, cholestasis, gallstones,

and even changes in bone metabolism (7). The present study found no evidence of metabolic complications caused by TPN use in terms of severe electrolyte or metabolic disorders, hypertriglyceridemia, hepatic steatosis, or cholestasis.

Regarding glycemic disorders (hyperglycemia, hypoglycemia, or both), these were identified in 69 % of the individuals included in the study throughout the period of TPN use. The presence of a glycemic disorder had a statistical correlation with the outcome of death (p-value < 0.000).

When hyperglycemia occurs in critically ill individuals, it can aggravate the clinical picture and lead to severe infections, organ and system dysfunctions, and even death (7,21). Because TPN involves a glucose-rich medium, it can lead to persistent hyperglycemia. As a result, it becomes a favorable medium for microorganism growth and the development of infections in these patients (16).

Central venous access-related secondary infection was found in 7 % of cases, a lower rate than that found in the literature, with positive blood cultures (catheter-related bloodstream infections) showing results ranging from 11.2 % (10) to 12 % (20), 14.2 % (14), 19 % (15), and 21.4 % (7), reaching an incidence of 56 % (19). There is evidence that one in every six patients who received TPN developed a bloodstream infection (16). Infectious complications are responsible for a mortality rate ranging from 20 % to 35 %, a hospital length of stay prolonged by around 7 days, and an increase in costs related to hospitalization (20).

As for the medications prescribed to the patients receiving TPN, 3,156 drugs were prescribed, with those for the digestive tract and metabolism being the most frequent ones with 31.62 % of prescriptions. Individuals who died were prescribed a greater number of medications when compared to those who were discharged. A p-value < 0.000 was found in the correlation between number of diagnoses and death. It was observed that death occurred more frequently in individuals receiving a higher number of medications.

Mortality decreased when custom-made TPN was used, although there was no statistical association between type of nutrition and outcome (p-value = 0.395). The use of custom-made TPN was also associated with a reduction in the total number of medications. When TPN is used with multi-chamber bags, the chances of metabolic complications, infections, and administration errors increase, due to an increase in the manipulation of the intravenous system (21). The literature search showed that no studies assessing the type of parenteral nutrition that would be best for patients (custom-made or standard type) had been carried out without the support of the pharmaceutical industry.

As limitations, this study had a low number of participants despite taking place over a six-year period, as the study ICU mainly treats patients with conditions related to internal medicine, surgical patients being a minority. The low number of studies on the same topic did not allow a broader discussion of the results found.

CONCLUSION

This study assessed the conditions and clinical course of patients receiving parenteral nutrition in an intensive care unit. The number of patients who died was high, at three quarters of the individuals studied; the most commonly found site of central venous access was the subclavian vein, which in the literature has been shown to pose fewer infection risks than the jugular vein. Although the literature shows that the most common complication is bloodstream infection related to the use of a central venous access for TPN infusion, this study found that the most common complications related to the use of parenteral nutrition were glycemic disorders, followed by infections related to the central venous catheter. Glycemic control was shown to be important in this profile of patients, as high blood glucose levels increase the likelihood of the development of microorganisms responsible for infections and even organ failure—for which reason this is an important factor in worsening mortality rates.

The most commonly used medications are related to the gastrointestinal tract, as these treat disorders that are common among patients who receive parenteral nutrition. These patients are prescribed, on average, more than ten medications, reflecting the polypharmacy to which these patients are exposed. The number of medications and medical diagnoses associated with the patient influence hospital length of stay. There was also an association between the number of patients who died and the number of medications used. Regarding the type of parenteral nutrition used, a higher proportion of deaths was observed in patients receiving standard parenteral nutrition (76.9 %), and when custom-made parenteral nutrition started being used in 2014 mortality rates decreased (71.7 %). Although a small improvement in mortality was found in this study, there is no definite statistical evidence that it was the result of administering bespoke TPN rather than standard feeding regimens, given that the chi-squared test did not show any association between type of nutrition and outcome (p-value = 0.395). Custom-made parenteral nutrition showed benefits to the patients, as the number of medications used by them was found to have decreased among those receiving custom-made parenteral nutrition.

A deeper understanding of patient progress and of the risks faced by patients receiving parenteral nutrition may allow the development of evidence-based clinical protocols for the entire multidisciplinary team, so that necessary measures may be implemented for the benefit of patients.

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Table I. Critically ill patients' age, length of in-hospital stay, number of diagnoses, and total medications/year, represented by mean ± standard error of the mean. Brasília, 2010-16

Year	2010	2011	2012	2013	2014	2015	2016
Age	60 ± 5	50 ± 2	58 ± 7	55 ± 3	63 ± 2	55 ± 3	58 ± 4
Length of in-hospital stay	39 ± 10	23 ± 2	28 ± 8	31 ± 7	32 ± 3	25 ± 3	23 ± 3
Number of diagnoses	5 ± 0	6 ± 0	7 ± 0	6 ± 0	6 ± 0	6 ± 0	6 ± 0
Total medications	16 ± 1	15 ± 1	16 ± 1	17 ± 1	14 ± 0	13 ± 0	12 ± 0

Table II. P-value test for some variables, and outcome in critically ill individuals. Brasília, 2010-16

		Outcome				p-value
		Discharge / Transfer (n = 54)		Death (n = 159)		
		Freq.	%	Freq.	%	
Sex	Male	35	29.7 %	83	70.3 %	0.107
	Female	19	20.0 %	76	80.0 %	
Was the patient anuric?	Yes	1	5.9 %	16	94.1 %	0.054
	No	53	27.0 %	146	73.0 %	
Was the patient undergoing hemodialysis?	Yes	1	7.1 %	13	92.9 %	0.105
	No	53	27.0 %	146	73.0 %	
Did the patient have any severe electrolyte and metabolic disorders?	Yes	11	15.1 %	62	84.9 %	0.013
	No	43	30.7 %	97	69.3 %	
Was there local or systemic secondary infection due to venous access use?	Yes	3	21.4 %	11	78.6 %	0.727
	No	51	25.6 %	148	74.4 %	
Were there glycemic disorders?	Yes	25	16.9 %	123	83.1 %	0.000
	No	29	44.6 %	36	55.4 %	

Table III. Correlations according to Spearman's rho for the variables age, total number of medications, number of diagnoses, and hospital length of stay

Correlations		Age	Total number of medications	Number of diagnoses	Hospital length of stay
Age	Spearman's rho	1.000	-0.159	-0.052	0.009
	p-value	.	0.020	0.449	0.901
	N	213	213	213	213
Total number of medications	Spearman's rho	-0.159	1.000	0.059	0.186*
	p-value	0.020	.	0.389	0.006
	N	213	213	213	213
Number of diagnoses	Spearman's rho	-0.052	0.059	1.000	0.195*
	p-value	0.449	0.389	.	0.004
	N	213	213	213	213
Hospital length of stay	Spearman's rho	0.009	.0186*	0.195*	1.000
	p-value	0.901	0.006	0.004	.
	N	213	213	213	213

*Significant correlations at the 0.01 level.

Table IV. Frequency of type of nutrition according to outcome in critically ill individuals. Brasília, 2010-16

		Outcome		
		Discharge/Transfer	Death	Total
Type of parenteral nutrition	Standard TPN	28 (23.1 %)	93 (76.9 %)	121
	Custom-made TPN	26 (28.2 %)	66 (71.7 %)	92
Total		54	159	213

Table V. Ranks associating total number of medications and type of parenteral nutrition used by critically ill individuals. Brasília, 2010-16

Ranks				
	Type of parental nutrition	N	Mean Rank	Sum of ranks
Total number of medications	Standard TPN	121	121.57	14,710.50
	Custom-made TPN	92	87.83	8,080.50
	Total	213		
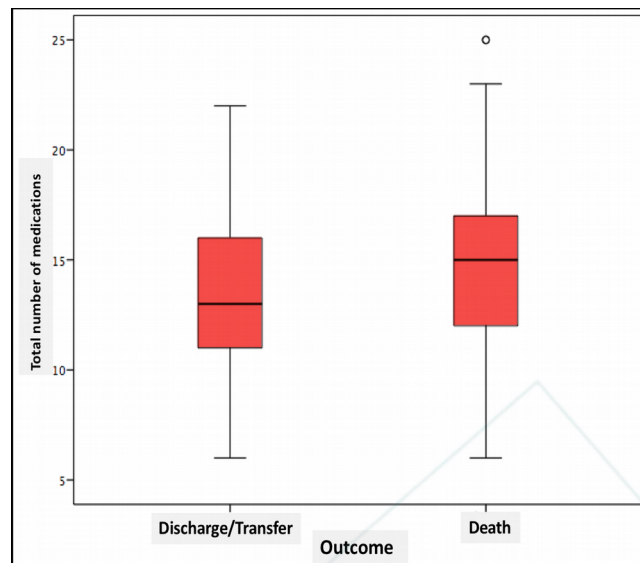
Fig. 1. Boxplot chart displaying total number of medications and outcome in critically ill individuals. Brasília, 2010-16.
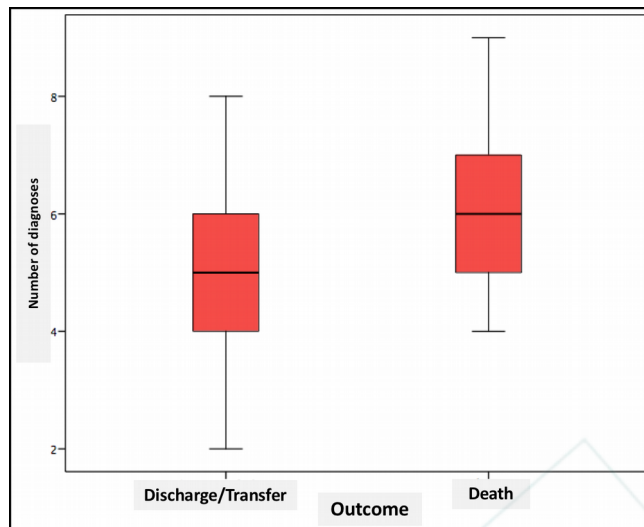
Fig. 2. Boxplot chart showing number of diagnoses and outcome in critically ill individuals. Brasília, 2010-16.
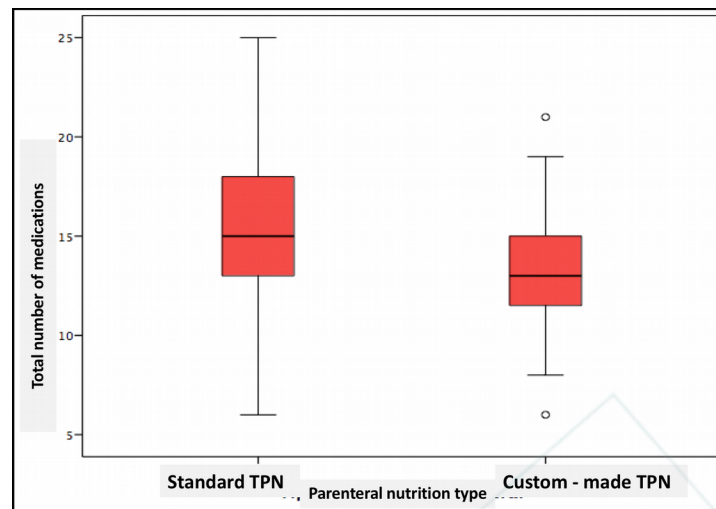
Fig. 3. Boxplot chart displaying total number of medications and parenteral nutrition type in critically ill individuals. Brasília, 2010-16.