

Original

## Liver function test alterations associated with parenteral nutrition in hospitalized adult patients; incidence and risk factors

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### Abstract

**Background:** Parenteral nutrition-associated liver dysfunction can be progressive and irreversible, particularly in children and patients with long-term treatment. This study has assessed the incidence of abnormal liver function tests in hospitalized adults during short term parenteral nutrition (PN) and has investigated risk factors for developing alterations of each parameter.

**Methods:** A prospective cohort study of parenteral nutrition treated patients with preserved liver function at baseline. Variables examined included nutritional and clinical data and laboratory parameters. Determinations were performed before starting PN and weekly until liver function test alteration was observed. Risk factors were investigated by four stepwise forward logistical regressions.

**Results:** Eighty patients were included, 57.5% had liver function test alterations. PN mean duration was 15.9 (8-54) days. Mean days with PN and additional enteral/oral nutrition were 1.5 (0-20). The following associations were found: gamma-glutamyl-transferase increased with soybean lipid intake and absolute diet; alkaline phosphatase increased with septic shock; alanine transaminase increased with septic shock, hyperglycemia and elevated creatinine; total bilirubin increased with septic shock, absolute diet, low prealbumin and glucose, and high creatinine.

**Conclusions:** The incidence of altered liver function tests is high in adult hospitalized patients treated with short-term PN. However, the effect of nutritional factors in this alteration is low. Oral/enteral nutrition and reduction of soybean lipid supply can reduce increases in some liver function tests such as gamma-glutamyl-transferase and total bilirubin. The high association between all liver function tests and clinical systemic-hypermetabolic variables suggest the importance of specific nutritional strategies for this condition.

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Key words: *Liver dysfunction. Gamma-glutamyl-transferase. Bilirubin. Alanine transaminase. Alkaline phosphatase. Soybean lipid.*

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### ALTERACIONES DE LOS PARÁMETROS HEPÁTICOS ASOCIADOS CON LA ADMINISTRACIÓN DE NUTRICIÓN PARENTERAL EN PACIENTES ADULTOS HOSPITALIZADOS; INCIDENCIA Y FACTORES DE RIESGO

#### Resumen

**Introducción:** La alteración hepática asociada a la nutrición parenteral (NP) puede ser progresiva e irreversible particularmente en niños y en tratamientos de larga duración. El objetivo de este estudio es establecer la incidencia de las alteraciones de los parámetros hepáticos en pacientes adultos hospitalizados en tratamiento con NP y estudiar los factores de riesgo asociados al desarrollo de las alteraciones de cada uno de los parámetros hepáticos.

**Métodos:** Estudio prospectivo de cohortes de los pacientes tratados con NP con función hepática normal al inicio del tratamiento. Se estudiaron parámetros clínicos, nutricionales y analíticos. Las determinaciones se hicieron antes de iniciar la nutrición y semanalmente hasta que se detectó la alteración de algún parámetro hepático. Los factores de riesgo asociados a la alteración hepática se estudiaron con 4 regresiones logísticas.

**Resultados:** Se incluyeron 80 pacientes y 57,5% mostraron alteraciones hepáticas. La media de duración de la NP fue 15,9 días (8-54) y la media de días con nutrición enteral u oral concomitantes fue de 1,5 (0-20). Se encontraron las siguientes asociaciones: la gamma-glutamyl-transferasa aumentaba con la cantidad de lípidos de soja administrados y los días en dieta absoluta; la fosfatasa alcalina con el shock séptico, la alanina-aminotransferasa con el shock séptico, la hiperglucemia y los valores elevados de creatinina; la bilirrubina total con el shock séptico, la dieta absoluta, valores bajos de prealbúmina y glucosa; y valores altos de creatinina.

**Conclusiones:** La incidencia de alteraciones de los parámetros hepáticos es elevada en pacientes adultos hospitalizados tratados con NP, aunque el efecto de los factores nutricionales en esta alteración es bajo. La nutrición oral/enteral y la reducción de los lípidos en forma de soja pueden reducir el aumento de algunos parámetros hepáticos como la gamma-glutamyltransferasa y la bilirrubina total. La gran asociación entre todos los parámetros hepáticos y las variables sistémicas indicadoras de hipermetabolismo apuntan a la importancia de las estrategias nutricionales específicas en esta situación.

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Palabras clave: *Disfunción hepática. Gamma glutamiltransferasa. Bilirrubina. Alanina aminotransferasa. Fosfatasa alcalina. Lípido de soja.*

## Abbreviations

LD: Liver disease.  
LFT: Liver function test.  
PNALD: Parenteral nutrition-associated liver disease.  
PN: Parenteral nutrition.  
GGT: Gamma-glutamyl-transferase.  
AP: Alkaline phosphatase.  
ALT: Alanine aminotransferase.  
TB: Total bilirubin.

## Introduction

Parenteral nutrition-associated liver disease (PNALD) which is usually a mild, transient complication, can become progressive, irreversible and fatal in patients receiving long-term parenteral nutrition (PN), in neonates and children.<sup>1,2,3</sup> During PN the main manifestation of PNALD starts with the alteration of a part or the entire liver function test (LFT) obtained from the blood analysis. The etiopathogenesis of this process is unknown, but several factors have been invoked as possible causes.<sup>4,5</sup> These include nutritional factors, such as an excessive supply of glucose or lipids in the PN formula, lack of balance in the amount of nitrogen and carbohydrates provided, the type of lipids administered,<sup>6</sup> the amount of phytosterols in the PN<sup>7</sup> and the production of amino acid metabolites due to photo-oxidation.<sup>8,9</sup> In addition, sepsis and the lack of enteral intake have also been cited, as well as factors associated with LFT alterations. Both sepsis and the lack of enteral feeding have been associated with an increase in fatty acid release from triglycerides and an increase in triglyceride uptake and synthesis by the liver.<sup>4</sup>

Many reviews have focused on the populations at highest risk of developing PNALD.<sup>10,11,12</sup> In the case of children, and particularly, premature neonates, it is believed that a reduced bile acid pool size and immature enterohepatic circulation, together with other factors, contribute to the high incidence of PNALD in this vulnerable group.<sup>2</sup> In long-term PN-dependent patients, the abnormalities have been described as steatosis and steatohepatitis, fibrosis, cholestasis, and cirrhosis.<sup>5</sup> Some of the additional factors implicated in PNALD in these patients are the length of the remnant bowel, altered bile absorption, altered release of gut hormones, bacterial translocation, tumor necrosis factor associated with sepsis, and bacterial overgrowth.<sup>13,14,15</sup>

Nevertheless, in adults under short-term PN treatment, PNALD has received little attention, being considered a reversible complication that resolves when nutritional therapy is withdrawn. In this study, we have evaluated LFT alterations as the first markers of possible PNALD.

## Objective

The aims of this study were to assess the incidence of abnormal LFT in hospitalized adult patients, including

critically ill patients, during PN treatment and to establish the risk factors for the alteration of each LFT parameter by a multivariate approach.

## Methods

### Design

This is a prospective cohort study of incidence of liver test alterations in patients admitted in a tertiary hospital from October 2006 to June 2007. Patients were included in the study when they were expected to need PN for at least five days. The definition of LFT alterations was established before starting the study.

In the patients' follow up, two points were established for comparison purposes in the analysis: *baseline time point* was the time just before PN was started and *final time point* was defined as the time of maximal LFT alteration or the time of PN withdrawal, in case of no LFT alteration.

### Patients

The inclusion criteria were patients aged 18 years or more, with preserved liver function at baseline and expected to receive PN treatment for at least five days. Patients with prior hepatic disease or hepatic involvement established as altered LFT over the normal range were excluded.

Age, sex, weight, past medical history (diabetes mellitus, hypertension, and dyslipidemia), primary diagnosis, surgery interventions and the indication for PN were recorded at the beginning of the study. Length of hospital stay and mortality were collected during the study.

### Nutrition

Following the hospital protocol, PN was administered through a central venous catheter using "all in one" ternary mixtures and a continuous pump infusion. The PN bag was replaced every 24 hours. The calculated nutritional requirements were 25 kcal/kg/day with an intake of 1 to 1.5 g protein/kg and a ratio of carbohydrates/fat kcal range from 70:30 to 60:40.

In this study, the supply of nitrogen, lipid and glucose were expressed as the accumulative supply. Aminoacids supply was administered as Aminomix® and Vamin®. Lipids were administered as Structolipid® based on purified structured triglyceride as an inter-esterified mixture of equimolar amounts of long chain triglycerides (LCT) (64%) and medium chain triglycerides (MCT) (36%), Clinoleic® based on a mixture of purified olive oil (approximately 80%) and soybean oil (approximately 20%) and SMOF® based on soybean oil (30%), medium chain triglycerides (30%), olive oil (25%) and fish oil (15%), depending on patients

requirements. While Structolipid® and Clinoleic® were administered in stable patients; SMOF® was administered in patients with systemic inflammatory response syndrome (SIRS) or inflammatory processes. Lipid administration was disaggregated as soybean oil, medium-chain triglycerides, olive oil and fish oil.

### Analytical data

Blood serum laboratory analyses were carried out just before starting PN and weekly once the PN was started. We recorded gamma-glutamyl-transferase (GGT), alkaline phosphatase (AP) alanine aminotransferase (ALT), and total bilirubin (TB) as LFT. In addition glucose, creatinine, triglycerides, urea, albumin, prealbumin, C-reactive protein, leukocytes, platelets and hematocrit were also recorded.

### Risk factors

Four multivariate models were developed with the following LFT as dependent variables: GGT, AP, ALT and TB. To identify risk factors related with the PN treatment, we included as independent variables in each model: days of PN, lipid supply, type of lipids, protein supply assessed as nitrogen, glucose supply, number of days with PN as the only nutritional support, and number of days with concomitant enteral/oral nutrition.

In addition, in order to adjust their effect, some confounding clinical variables that are known to be associated with liver parameter pattern modifications were also included in each model as independent co-variables. These variables were: sepsis and septic shock; creatinine and urea (renal impairment); albumin, prealbumin and C-reactive protein (inflammation); blood glucose level and blood triglycerides level.

Based on the ACCP/SCCM consensus conference,<sup>16</sup> sepsis was established when the patient presented SIRS due to infection. SIRS was confirmed by at least two of the following criteria: (a) fever  $\geq 38^\circ\text{C}$  or fever  $\leq 36^\circ\text{C}$ , (b) tachycardia with heart rate  $\geq 90$  beats/min, (c) tachypnea with  $\text{paCO}_2 \leq 32$  mmHg or mechanical ventilation; (d) leukocytes  $> 12 \times 10^9$ . If the patient additionally met the criteria for associated persistent hypotension despite adequate fluid resuscitation or the necessity of vasopressor administration to maintain a mean arterial blood pressure of 70 mmHg, this was classified as septic shock.

### Liver function test's definitions

The criteria used in this study to define the patterns of LFT alteration were established as GGT  $> 1 \mu\text{kat/L}$  (60 UI/L), AP  $> 1.5 \mu\text{kat/L}$  (269 UI/L), ALT  $> 0.83 \mu\text{kat/L}$  (49 UI/L), and TB  $> 25 \text{ mol/L}$  (1.4 mg/dL).<sup>17</sup>

Cholestasis pattern was associated with elevated TB coexisting with AP or GGT elevations; cytolysis was

defined as elevated ALT coexisting with AP or GGT elevations; and elevations of GGT and PA were considered as a mixed pattern.

Liver biopsies or image diagnosis were not carried out in this study.

### Statistical analysis

Statistical analyses were performed with SPSS, v.13 (SPSS Inc, Chicago, Illinois, USA). Statistical significance was set at the confidence interval. A student's *t* test was used to compare the mean LFT at baseline time point and at final time point. The multivariate model was a "stepwise forward" logistical regression. Each independent variable was included in the model for  $p < 0.1$ .

## Results

### Patients' description

Eighty patients were included in the study. Twenty-two were women and fifty-eight were men. The mean age of the sample was 60.1 years (range 17-91) and the mean weight 66.8 kg (range 40-99.5). The past medical history included 19 diabetes mellitus type 1 or 2, 14 dyslipidemia, and 31 hypertension. The most common primary diagnosis in the series was gastrointestinal neoplasm (50%) and the most frequent indication for PN was postoperative ileus (35%) (table I).

Mean duration of hospital stay was 38.9 days (range, 8-154). Among the total, 91.3% of patients underwent surgery during hospitalization, and almost one quarter of them (23.3%) required a second operation. Five patients had septic shock and nine died.

### Liver function tests parameters

Among the total, 46 patients (57.5%) developed abnormal LFT: 15% presented jaundice associated

**Table I**  
Primary diagnosis and indications for PN

Primary diagnosis	n (%)
Gastrointestinal neoplasms	40 (50%)
Gastrointestinal disease other than neoplasm	29 (36.25%)
Neoplasms other than gastrointestinal	5 (6.25%)
Others	6 (7.5%)
Indications for PN	n (%)
Postoperative ileus	28 (35.0%)
Gastrointestinal occlusion	17 (21.3%)
Intestinal fistula	9 (11.3%)
Others	26 (32.5%)

PN: Parenteral nutrition.

**Table II**  
Cumulative supply

Cumulative supply (g/kg)	Mean (range)
Glucose	44.5 (11.3-116.6)
Nitrogen	2.9 (0.49-8.7)
Lipid	11.6 (2.9-32.6)
Soybean oil	5.6 (0.6-20)
Medium-chain triglycerides	3.0 (0-11.3)
Olive oil	2.5 (0-11.3)
Fish oil (Omega-3 fatty acids)	0.5 (0-5)

with a colestatic pattern; 27.5% presented cytolysis and 15% suffered GGT or AP alterations.

A comparison of baseline LFT between the group that later presented LFT alteration and those that did not, showed no significant differences: AP 1.30  $\mu$ kat/L vs 1.16  $\mu$ kat/L; GGT 0.89  $\mu$ kat/L vs 0.64  $\mu$ kat/L; ALT 0.54  $\mu$ kat/L vs 0.31  $\mu$ kat/L and TB 9.95 mmol/L vs 10.34 mmol/L.

A comparison of the mean LFT results using student's *t* test showed that the AP, GGT and TB were significantly higher at the final time point than at baseline time point ( $P < 0.05$ ): AP 3.2  $\mu$ kat/L vs 1.23  $\mu$ kat/L, GGT 4.16  $\mu$ kat/L vs 0.85  $\mu$ kat/L and TB 18.43  $\mu$ mol/L vs 10.21  $\mu$ mol/L. In ALT, the differences were not significant but showed a tendency: 2.26  $\mu$ kat/L vs 0.44  $\mu$ kat/L ( $p = 0.057$ ).

### Characteristics of nutrition support

The mean daily parenteral energy supply per patient presented as a percentage of total calories was 48.2% for glucose, 20% for nitrogen and 31.8% for lipids. The mean daily parenteral energy supply per patient was 23 kcal/kg (range, 15.7-33.7) distributed as 0.74 (range, 0.4-1.1) g/kg of lipids, 2.8 (range, 2.3-3.8) g/kg of glucose and 0.18 (range, 0.1-0.3) g/kg of nitrogen. Mean cumulative nutrient supply per patient at final time point of the study and mean cumulative supply according to the type of lipid are shown in table II.

At the final time point of the study, patients received PN for a mean of 15.9 (range, 8-54) days, PN and enteral nutrition or oral diet coexisted for 1.5 days (range, 0-20). PN as the only nutritional support was maintained for 14.4 (range, 8-34) days.

### Multivariate analysis

The results of the multiple linear regression models developed for each of the LFT are shown in table III. A high determination factor (from 0.399 to 0.785) was obtained in the four models indicating that the alteration of each of the LFT parameters was highly explained by the variables included in each model.

The mentioned co-variables that could be related with LFT alterations (sepsis, renal function, inflammation, glycaemia and triglyceridemia) were included in

**Table III**  
Linear regression models for the dependent variables

Predictive variables showing significance or a trend	Models			
	GGT <sup>1</sup> B (95% CI)	AP <sup>2</sup> B (95% CI)	ALT <sup>3</sup> B (95% CI)	TB <sup>4</sup> B (95% CI)
Days on additional enteral or oral nutrition	-0.251 (-0.478; -0.025)	-	-	-1.302 (-2.569; -0.034)
Cumulative lipid supply with soy (g/kg)	0.401 (0.007-0.868)	-	-	-
Patient has septic shock	-	3.688 (1.266-6.149)	17.279 (9.095-25.462)	34.034 (13.910-54.157)
Plasma glucose (mmol/L)	-	-	0.849 (0.304-1.395)	-1.423 (-2.764; -0.082)
Plasma creatinine (mg/L)	-	-	0.025 (0.001-0.052)	0.269 (0.205-0.333)
Plasma triglycerides (mmol/L)	-	-	-	-
Prealbumin (mg/dL)	-	-	-	-0.093 (-0.186; -0.001)
Constant	0.005	-0.239	-8.927	11.355

GGT: Gamma-glutamyl-transferase; AP: Alkaline phosphatase; ALT: Alanine transaminase; TB: Total bilirubin.

<sup>1</sup>  $r^2 = 0.399$ ;  $F = 2.780$ ;  $P = 0.007$

<sup>2</sup>  $r^2 = 0.403$ ;  $F = 4.847$ ;  $P = 0.000$

<sup>3</sup>  $r^2 = 0.506$ ;  $F = 4.821$ ;  $P = 0.000$

<sup>4</sup>  $r^2 = 0.785$ ;  $F = 17.124$ ;  $P = 0.000$

No association with mean daily lipid supply, cumulative lipid supply, mean daily nitrogen supply, cumulative nitrogen supply, mean daily glucose supply, cumulative glucose supply, or plasma urea, albumin, CRP, leukocytes, platelets, or hematocrit.

each model in order to obtain more adjusted results of the weight that nutritional parameters could have in the LFT alterations. Regarding this, we found that GGT and TB were influenced by some of the variables related with the PN. GGT values increased with increasing cumulative soy lipid supply and less days of concomitant enteral or oral nutrition. TB increases were associated with less days on concomitant enteral or oral nutrition; low plasma glucose values; high plasma levels of creatinine and septic shock. Each cumulative g/kg of soybean lipid during the treatment increases GGT values in 0.4  $\mu$ kat/L (95% CI: 0.007-0.868) and each day with oral or enteral nutrition concomitant with the PN decreases GGT values in 0.25  $\mu$ kat/L (95% CI: 0.025-0.478) and decreases TB values in 1.3 mmol/L (95% CI: 0.034-2.569).

Finally, AP and ALT values were not influenced by any of the studied factors related to the nutrition but were for some of the co-variables included. AP and ALT were elevated in patients with septic shock and ALT increased with high plasma glucose and creatinine values.

## Discussion

Our study shows that the incidence of LFT alteration related to PN could be situated in the middle range (57%) of published data since results vary considerably between studies. PNALD is a widely described complication with a highly variable reported incidence that goes from 25% to 100%.<sup>18,19</sup> More specifically, in patients receiving home PN, the incidence of steatosis has been estimated at 0% to 40%,<sup>20</sup> while in seriously ill patients receiving PN it has been estimated at 30%.<sup>17</sup> Nevertheless, our incidence of cholestatic jaundice (15%) was higher than the 4% or 10% indicated in prior publications.<sup>17,18</sup> All these differences may be explained by the fact that several hepatic function markers can be used to establish PNALD, and the criteria to set thresholds as well as the decision values used to combine the alterations in these parameters differ among the related studies.

PN-related hepatobiliary complications generally manifest as steatosis, cholestasis or cholelithiasis. In exceptional cases, non-alcoholic steatohepatitis, fibrosis and cirrhosis can occur.<sup>1,4</sup> The most common manifestation of PNALD is transaminase elevation between 1 and 3 weeks after starting PN, whereas significant bilirubina increases in this period are infrequent in adult patients.<sup>21</sup> Focusing in the values of the isolated LFT measures, we found that in our study significant elevations of three of them (GGT, AP and bilirubina) were observed after a mean of 15.9 days. However, the increases observed in AP and TB did not exceed 3-fold normal values, in accordance with reported results.<sup>22,23</sup>

The second aim of the study was to identify risk factors related to the incidence of each LFT alteration and the use of PN, taking into account specific clinical

issues of the patient situation which can act as confusion factors, mainly sepsis and inflammation. It is well established that sepsis and inflammation can increase the production of cytokines, which are potent inhibitors of bile secretion with the consequent development of cholestasis.<sup>24</sup> The four LFT multivariate models obtained are quite strong according to the values of each determination factor (table III). This factor was 0.785 in the case of TB, meaning that the alteration of TB in our study is highly related with clinical and analytical data associated with SIRS and/or catabolic states. When controlling these confusing variables in the four models, mainly two factors related with the nutrition treatment have significant influence in the LFT values: concomitant use of enteral or oral nutrition and soy lipid supply.

Following other studies,<sup>6,8,9</sup> we found that concomitant administration of enteral or oral nutrition had significant importance for preventing PNALD, as evidenced by an association with a decreases in both GGT and bilirubina. Several changes are produced by the lack of biliary stimulation by intraluminal nutrients leading to the development of PNALD due to a reduction in cholecystokinin secretion as well as an intestinal excessive bacterial growth, intestinal atrophy and permeability. In 1979, Fedorowski et al.<sup>25</sup> demonstrated the capacity of bacteria to transform chenodeoxycholic acid into lithocholic acid, a more hydrophobic and hepatotoxic biliary acid. The combination of all these factors predisposes to bacterial translocation<sup>26</sup> and endotoxemia that induces cytokine production.

Lipid emulsions administered at a dose more than 1 g/kg/day has been associated with the development of PNALD, while dosing lipids at 1 g/kg/day or less has been proposed as a preventing factor of developing PNALD<sup>10,27</sup>. According to these results, possibly because in our sample patients were treated with a mean of 0.74 g/kg/day, we did not find a relation between this parameter and alterations in any LFT. Nevertheless, when we studied the type of lipids used in PN we found that every g/kg of soy lipid provided increased between 0.007 and 0.868 the value of GGT. While the importance of higher PN lipid doses in PNALD has already been emphasized, the quality of the lipid emulsions is also a relevant factor that is increasingly under consideration. Boncompain et al.<sup>28</sup> and Sluijter et al.<sup>29</sup> hypothesized that there is a link between the composition of the emulsions and clinical factors, but no qualitative analyses were performed. Both *in vitro* and animal studies have described the liver toxicity potential of soybean oil-based lipid emulsions.<sup>30,31</sup> Findings suggest that large amounts of omega-6 fatty acids contribute to increased proinflammatory products and the presence of hepatotoxic phytosterols in soybean oil-based emulsions lead to PNALD. In a study in 29 children, Clayton et al.<sup>32</sup> reported a link between the phytosterols in commercial lipid emulsions used in standard PN and PNALD (cholestasis). Further research based on experimental and human models suggests that PN-administered phy-

tosterols may indeed trigger PNALD by affecting bile acid synthesis and flow.<sup>33,34,35,36</sup> However, an accurate model of the actual mechanism is still lacking and the role of phytosterol intake remains to be elucidated. Furthermore, in reference to the type of lipids used, recent studies have indicated that omega-3 fatty acids may be beneficial in cases of hepatic cholestasis in newborns.<sup>37,38</sup> Moreover, alternative lipid emulsions, other than soybean oil-based lipid emulsions, such as fish oil could be used since several studies suggest an improvement in inflammation and clinical response. The immunomodulation effect of fish oil, rich in omega-3 fatty acids, can be explained by three mechanisms: an increased antioxidative protection, a reduction of inflammatory mediators and no phytosterols, since they are in vegetal oil.<sup>39</sup>

Other main cause of PNALD described in the studies is overfeeding. Excess of macronutrients has been classically associated with PNALD.<sup>3,10,15</sup> In our patients none of the parameters related with the total amount of nutrient supply was related with LFT alterations. Comparing with the results reported in other publications we found that our supplies are in the lower range as a mean of 23 kcal/kg per day. Furthermore, analyzing the carbohydrate/fat kcal ratio in our patients, we found a result of 60:40 which is reported as being safe and as preventing abnormalities in liver tests in other studies.<sup>17,40</sup> The fact that in our series the PN supply of nutrients, glucose and lipids was low, in keeping with our hospital protocol, would partially explain the low impact of these factors on LFT alteration.

Therefore, according to our models, in our series of patients, LFT alterations are more influenced by the patient clinical situation than the PN itself, except in the case of GGT. Given that PNALD is a multifactorial process, we investigated several factors that can modulate each of the liver function markers studied. There are several clinical situations in which a hypermetabolic status is associated with the development of liver disease (LD). Among them, sepsis has been widely cited, although the mechanism by which it induces LD is unknown. It has been suggested that hepatic endotoxemia can saturate the ability to detoxify the Kupffer cells, leading to an accumulation of toxins in the liver that cause hepatic injury.<sup>41</sup> In our sample, an association was found between septic shock and elevated plasma levels of AP, ALT and TB. These findings support a relationship between sepsis and LFT alteration, with ALT being an indicator of hepatic injury. In addition to septic shock, other indicators of hypermetabolic status, such as hypoprealbuminemia, hyperglycemia or hypoglycemia and elevated creatinine were also related to high levels of AP, ALT and TB in the present study. Grau et al.<sup>17</sup> analyzed factors associated with LD in a sample of 725 adult intensive care patients treated with PN or enteral nutrition and concluded that patients who developed LD had higher multiple organ dysfunction score, were septic and preferably received PN as nutritional support over enteral nutrition. In our study, septic shock

is the most potent factor associated with increases in AP, ALT and TB; and renal impairment expressed as high levels of creatinin also increases TB levels.

## Conclusion

Our results show a considerable incidence of LFT alterations occurring in our hospitalized adults under PN treatment. These alterations are more related with the patient clinical situation than with the nutrient supply. However, we have to take into account that we use a low amount of nutrients in the PN composition, following our protocol of not overfeeding.

There are two main factors related with nutrition that have a significant influence in the alteration of some LFT: enteral or oral ingestion concomitantly with PN in preventing GGT and TB increases; and the supply of soybean lipid in worsening GGT values.

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