



Pharmaceutical Interventions in Metabolic and Nutritional Follow-up of Surgical Patients Receiving Parenteral Nutrition

J. Llop-Talaverón, B. Gracia-García, J.J. Machí-Ribes, M. Perayre-Badia, M.B. Badia-Tahull y R. Jódar-Masanes

Servicio de Farmacia, Hospital Universitari de Bellvitge-IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain

Abstract

Purpose: To assess a control protocol concerning alterations in metabolic follow-up parameters in the context of a pharmaceutical care program designed for surgical patients receiving parenteral nutrition, through determination of the impact of pharmaceutical interventions on associated metabolic complications.

Methods: Prospective interventional study of two-months' duration performed in surgical patients receiving parenteral nutrition. The study variables included predefined biochemical parameters within the metabolic-nutritional profile. Four categories were established to classify the degree to which each parameter was altered: *a*) no alteration (within normal range); *b*) alteration with no associated complication; *c*) moderate complication, and *d*) severe complication. The type of pharmaceutical intervention carried out included a direct intervention on their part or a recommendation. Statistical differences between the mean analytical values before and after the intervention were assessed by parametric and non-parametric tests ($P < 0.05$).

Results: A total of 1055 analytical determinations corresponding to 44 patients were evaluated. Among them, 239 determinations (22.6%) presented some degree of alteration which corresponded to 162 complications. Complication is often defined with more than one parameter. Ninety-three (57.4%) corrective interventions were carried out by direct intervention and 16 (9.9%) by recommendation.

The results showed statistically significant differences or significant trend when the purpose of the pharmaceutical direct intervention was to increase albumin, prealbumin, potassium or phosphate levels or to decrease C-reactive protein, glucose or triglycerides. Significant

differences or significant trend were not seen when no intervention was performed.

Conclusion: Despite the fact that the parameters assessed may have been influenced by factors other than the parenteral nutrition treatment received, our findings show that systematic monitoring of specific analytic parameters can be effective for attaining success in nutritional therapy, in terms of improvement in nutritional status and prevention and control of associated complications.

Key words: Parenteral nutrition. Follow-up study. Pharmaceutical care.

Resumen

Objetivo: Evaluar un protocolo de control de las alteraciones de los parámetros metabólicos en el contexto de un programa de atención farmacéutica dirigido a pacientes quirúrgicos con nutrición parenteral, a través del impacto de las intervenciones farmacéuticas en las complicaciones metabólicas asociadas.

Metodo: Estudio prospectivo de intervención de 2 meses de duración. Se estudia a pacientes quirúrgicos con nutrición parenteral. Como variables de estudio se incluyen los parámetros bioquímicos predefinidos en el perfil metabólico-nutricional. Se establecen 4 categorías para clasificar el grado de alteración de cada parámetro: *a*) sin complicación; *b*) alteración no asociada con complicación; *c*) complicación moderada, y *d*) complicación grave. El tipo de intervención del fármaco se realiza mediante intervención directa o consejo. Las diferencias estadísticamente significativas entre los valores medios de los valores de los parámetros analíticos previos y posteriores a la intervención farmacéutica se establecen con pruebas paramétricas y no paramétrica ($p < 0,05$).

Resultados: Se evaluaron 1055 parámetros correspondientes a 44 pacientes. En total, 239 (22,6%) presentaron alteración, lo que correspondió a 162 complicaciones (para definir algunas complicaciones se utiliza más de un parámetro), de las cuales 93 (57,4%) se intentaron corregir mediante intervención directa y 16 (9,9%), mediante consejo. Los resultados mostraron diferencias estadísticamente significativas o una tendencia hacia la significación cuando el

This study was previously presented on a research poster in the 35th European Symposium on Clinical Pharmacy (Vienna, October 2006).

Correspondence: Josep Llop Talaverón.
Servicio de Farmacia. Hospital Universitari de Bellvitge.
Feixa Llarga, s/n. 08197 L'Hospitalet de Llobregat. Barcelona. España.
E-mail: josep.llop@csub.scs.es

Received: January 4, 2008

Accepted for publication: April 3, 2008.

objetivo de la intervención directa fue incrementar la albúmina, la prealbúmina, el potasio y el fosfato, y disminuir la PCR, la glucosa y los triglicéridos. Cuando no se realizó ninguna intervención no se encontraron diferencias significativas o con tendencia hacia la significación.

Conclusiones: A pesar de que los parámetros evaluados pueden estar influidos por otros factores ajenos al tratamiento con nutrición parenteral, los resultados de este estudio indican que el seguimiento sistemático de éstos puede ser un método eficaz para conseguir el éxito de la terapia nutricional, tanto en la mejora del estado nutricional como en la prevención y el control de las complicaciones asociadas.

Palabras clave: Nutrición parenteral. Estudio de seguimiento. Atención farmacéutica.

INTRODUCTION

Therapy with parenteral nutrition (PN) can be complex because of the characteristics and amount of nutrients administered, and the type of patients that are candidates for this treatment. With the progressive advances in enteral nutrition, the use of PN has become restricted to severely ill patients, generally with acute processes. These patients can present problems in assimilating nutrients and are often in a hypercatabolic state with intense proteolysis, hydroelectrolytic imbalance and organ dysfunction that compromises normal metabolic function; hence, nutritional management of these patients is difficult¹.

The preparation of PN is handled by the hospital Pharmacy Department because of the requirements of sterility and the complexity of the formulations. Over the years and coinciding with advances in Clinical Pharmacy, the hospital pharmacist has become increasingly more implicated in the development of guidelines and protocols, as well as other health care activities in the field of nutrition^{2,3}.

Automation of the formulation processes and systems for dispensing treatment, as well as data integration into computer networks (e.g., clinical and analytical reports, pharmacological treatment administered) facilitate continuous information exchange and enhance the development of evidence- and efficiency-based clinical interventions in this area: that is, pharmaceutical care^{4,5}.

In practice, pharmaceutical care implies the establishment of protocols, work flow-charts, and methods for recording the interventions applied, in order to assess the activity in terms of health benefits, reduce variation in the patients' clinical response, and generate information that will promote continuing improvement in the care provided.

The Parenteral Nutrition Unit of our Pharmacy Department (PNU) have a set of action procedures and protocols, such as nutritional assessment of PN candidates, caloric requirement analyses, the registry, follow-up and prevention of catheter-related complications, the surveillance of the nutritional treatment adherence and the registry of events derived from PN administration.

In total PN nutritional support multidisciplinary teams must provide a high quality nutritional assistance based on evidence and daily follow-up of patients with total PN⁶. In a general context, the PNU is part of a multidisciplinary team which includes endocrines, nutritionists, ICU attendings and surgeons. The PNU actively participates in nutritional design (protocols and guides), nutritional assessment (with its own programme), formulae selection, monitoring and follow-up. In surgical services, the surgeon prescribes the initial PN. From the PNU, the indication of the parenteral support is evaluated and according to nutritional assessment the initially composition is discussed and adjusted during therapy according to clinical and metabolic data. The Endocrinology and Dietetic Services, in charge of the Nutritional Unit, are responsible for the transition to oral or enteral diet and the nutritional follow-up of patients with long evolution artificial nutrition.

In this study we present a control protocol concerning alterations in metabolic follow-up parameters in the context of a pharmaceutical care program for surgical patients receiving PN, developed in the Parenteral Nutrition Unit of the Pharmacy Department with the aim of standardizing, systematizing, and documenting interventional pharmaceutical activity in the hospital setting for patients at a certain level of complexity. The pharmaceutical care program is assessed by determining the impact pharmaceutical interventions have on the patients' metabolic complications.

METHOD

This is a prospective, interventional study of two months' duration. Hospitalized patients receiving PN in the General Surgery and Gastrointestinal Surgery Units during the months of October and November 2005 were included. Patients referred from intensive care units and patients with incomplete records were excluded.

The PN protocol of our unit standardizes the nutritional formulas prescribed depending on the patient's anthropometric characteristics, degree of hypercatabolism and clinical status. Based on the underlying diagnosis, indication, and the patient's clinical condition, the physician prescribes the most appropriate

Table 1. Analytic Parameters Evaluated

Function Measured	Parameter Assessed
Kidney function	Plasma creatinine and urea
Liver function	gamma-glutamyltransferase (GGT), alkaline phosphatase (AP), alanine-aminotransferase (ALT), total bilirubin (Bb)
Synthesis-inflammation	Albumin, prealbumin and C-reactive protein (CRP)
Substrate metabolism	Glucose and triglycerides
Electrolytes	Sodium, potassium, magnesium, phosphates, calcium, chloride

Table 2. Protocol for Interventions in Metabolic Follow-up

Parameter (Normal Range)	Degree of Alteration	Intervention	Assess
Albumin (35-50 g/L)	Moderate complication: 25-35 g/L Severe complication: < 25 g/L	Increase nitrogen supply (N) in PN Add 50 mL glutamine (2 g N) in PN Add 100 mL glutamine(4 g N) in PN	Degree of stress Estimated start of oral intake Administration intravenous albumin Prealbumin level
Prealbumin (21-41 mg/dL)	Moderate complication: 15-20 mg/dL Severe complication: <15 mg/dL	Increase nitrogen supply (N) Add 50 mL glutamine (2 g N) in PN Add 100 mL glutamine(4 g N) in PN	Degree of stress Estimated start of oral intake Patient has sepsis or polytrauma RF
Glucose (4.1-6.9 mmol/L)	Alteration: 6.9-7.8 mmol/L Moderate complication: 7.8-10, or 3-4 mmol/L Severe complication: >10 or <3 mmol/L	Hyperglycemia >10 Reduce glucose supply PN Hyperglycemia >7.8 and <10 Reduce glucose supply PN if caloric requirements covered Severe hypoglycemia Administer dextrose 10% solution + potassium	Monitor plasma glucose Hypercatabolism Correct insulin dosage Fluid therapy (extra supply)
Triglycerides (≤ 2.3 mmol/L)	Alteration: 2.3-3 mmol/L Moderate complication: 3-5 mmol/L Severe complication:> 5 mmol/L	Hypertriglyceridemia >5 Eliminate PN lipids and increase glucose Hypertriglyceridemia >3 and <5: Reduce PN lipid supply Assess switch from LCT to MCT/LCT Reduce PN lipid supply on alternate days	Liver function Pancreatitis RF, sepsis or elevated plasma glucose levels Treatment with corticoids, cyclosporine, heparin or propofol.
CRP (≤ 5 mg/L)	Alteration: 5-100 mg/L Moderate complication: 100-200 mg/L Severe complication: > 200 mg/L	Use immunomodulators <i>Glutamine (100 mL)</i> in PN: patient has hypercatabolism and/or inflammation (CRP>200) and/or intestinal failure <i>ω-3 FA (100 mL)</i> in PN: patient critical and inflammatory states (CRP>50) CRP 50-200: Add 50 mL ω-3 FA CRP>200: Add 100 mL ω-3 FA	Prealbumin and nitrogen balance RF or liver disease
Urea (3.6-8.6 mmol/L)	Moderate complication: 8.6-15 mmol/L Severe complication: > 15 mmol/L	Acute RF, not under dialysis: Reduce PN supply of nitrogen, lipids and ions. Use histidine-rich essential amino acids Acute RF, under dialysis: Adjust nitrogen supply with pattern of high biological value Decrease lipid supply Extrarenal uremia, due to excess supply. Reduce nitrogen	Cause is renal, extrarenal or iatrogenic If creatinine values are normal: liver function, bleeding, diet protein intake
Creatinine (≤ 111 μmmol/l)	Alteration: 111-200 mmol/L Moderate complication: 200- 500mmol/L Severe complication: > 500 mmol/L	Acute RF, not under dialysis: Same criteria as urea Acute RF, under dialysis: Same criteria as urea	Patient under dialysis or not? If yes, intermittent or continuous?
Hepatic dysfunction	Alteration: Mild hepatic dysfunction (GGT ≥ 3.5 or FA ≥ 4.5) +(BIL ≤ 25 + ALT ≤ 0.83) Moderate complication: Moderate hepatic dysfunction (GGT ≥ 3.5 or FA ≥ 4.5) + (BIL ≤ 25 + ALT ≥ 0.83) Severe complication: Severe cholestatic jaundice (GGT ≥ 3.5 or FA ≥ 4.5)+ BIL ≥ 25	Severe cholestatic jaundice: Lipids with low phytosterol content. Reduce PN lipid supply. Assess switch LCT to MCT/LCT. Reduce PN lipid supply to alternate days. Eliminate PN lipids and increase glucose. Hepatic encephalopathy: Aromatic amino acids reduction and adjust nitrogen	GGT, AP, ALT and bilirubin to calculate degree of hepatic dysfunction

(Continued)

Table 2. Protocol for Interventions in Metabolic Follow-up (*Continuation*)

Parameter (Normal Range)	Degree of alteration	Intervention	Assess
Sodium (135-147 mEq/L)	Alteration: 130-134 mEq/L Moderate complication: 120-130 or 147-150 mEq/L Severe complication: <120 or ≥ 150 mEq/L	Dilutional hyponatremia: Restrict fluids Hyponatremia due to loss: Replace sodium Hyponatremia: control supply	Calculate plasma osmolarity Assess renal function Hydric balance
Potassium (3.5-4.7 mmol/l)	Alteration: 4.7-5.2 mmol/L Moderate complication: 2.5-3.5 mmol/L Severe complication: > 5.2 or < 2.5 mmol/L Hyperpotassemia ≥ 5.2 Hypopotassemia ≤ 3.6	Modify dose according to criteria: K ⁺ Supply(mEq/L) < 2.9 80 3-3.4 60 3.5-4.7 40 4.8-5.2 20 > 5.2 0	Hyperpotassemia: Rule out RF, hyperglycemia, hypoadosteronism Control potassium supply by alternative options other than PN Control diuretic use
Magnesium (0.625-1 mmol/L)	Alteration: 1-1.66 mmol/L Moderate complication: 0.42-0.625 or 1.66-5.2 mmol/L Severe complication: < 0.42 or > 5.2 mmol/L	Hypermagnesemia ≥1: Decrease magnesium supply Hypomagnesemia ≤ 0.625. Increase magnesium supply	
True calcium (2.2-2.54 mmol/L)	Alteration: 2.15-2.2 or 2.54-2.6 mmol/L Moderate complication: 1.88-2.15 or 2.6-3.25 mmol/L Severe complication: < 1.88 or > 3.25 mmol/L	Hypercalcemia ≥ 2.6: Decrease calcium supply Hypocalcemia ≤ 2.15. Increase calcium supply	<i>True total calcium</i> True total = (43 -albumin (g/L))* 0.0204 + calcium (mmol/L)
Phosphate (0.85-1.5 mmol/L)	Alteration: 0.7-0.85 mmol/L Moderate complication: 0.3-0.7 or >1.5 mmol/L Severe complication: ≤ 0.3 or > 2 mmol/L	Hyperphosphatemia > 1.55. Decrease phosphate supply Hypophosphatemia: Increase phosphate supply	Hyperphosphatemia: RF Hypophosphatemia: refeeding syndrome, glucose supply
Chloride (98-116 mmol/L)	Hyperchloremia ≥ 116 Hypochloremia ≤ 98	Hyperchloremia ≥ 116: Decrease chloride supply Hypochloremia ≤ 98: Increase chloride supply	Hyperchloremia: Metabolic acidosis

ALT: Alanine aminotransferase, AP: Alkaline phosphatase, CRP: C-reactive protein, GGT: Gamma glutamyltransferase, LCT: Long-chain triglycerides, MCT: Medium-chain triglycerides, PN: Parenteral nutrition, RF: Renal failure, ω-3 FA: omega-3 fatty acids.

formula to start nutritional support, according to the hospital protocol. This protocol does not establish the amino acid and lipid patterns or set exact amounts of nutrients; instead, it establishes ranges. Once nutritional therapy is started, clinical and metabolic follow-up of the patient is performed up to completion of treatment. For this purpose, the Parenteral Nutrition Unit requests weekly determination of the patient's analytical and nutritional profile, and, if is deemed necessary, the pharmacist assesses, adjusts and modifies the composition of the PN formula according to the patient's metabolic status.

Several parameters that are predefined in the general protocol are recorded in the weekly monitoring of metabolic profile (Table 1). Four categories were defined to classify the degree of alteration of each parameter: *a*) no alteration: The value falls within the normal analytical range; *b*) alteration: the value is outside the normal range, but is considered to have no clinical relevance within the context of the patient's condition; *c*) moderate

complication: the value lies outside the normal range with potential clinical consequences, considered to be moderate in nature, and *d*) severe complication: the value for the parameter is outside the normal range, with potential clinical consequences considered to be severe in nature.

The type of intervention pharmacists initiated was a direct intervention on their part, or a recommendation. In cases in which the pharmacist acted directly, formula is modified according to the decision algorithm and analytic values. Recommendations to prescribing physicians were carried out in a therapeutic monitoring context already implemented in our service, which includes electronic recordings (unitary doses programme) of the recommendations, its acceptance and impact.

For the analysis of the results, the analytical parameters have been grouped into 5 categories: electrolytes, liver function markers, kidney function markers, substrate metabolism, and synthesis-inflammation (Table 1).

To standardize the pharmaceutical care provided for a metabolic alteration, a protocol or decision algorithm was designed based on clinical evidence and clinical practice guidelines (Table 2). This protocol is an essential tool to assure that the activity is reproducible and to optimize the efficiency of the process.

To assess the impact of pharmaceutical interventions on metabolic complications, differences in the mean analytical values before and after the intervention were analyzed using a parametric test (*t*-test) and a non-parametric test (Wilcoxon *t*-test). The statistical analysis was done with SPSS, version 13.0, and significance was set at a *P*-value of <0.05.

RESULTS

The study included 44 patients. Demographic characteristics are described in Table 3. A total of 2011 analytical values were recorded for the parameters studied. Among them, 1055 were matched results from before and after the pharmaceutical intervention and these were selected for evaluation.

The determinations considered for the analysis were classified according to the complication and the type of corrective pharmaceutical intervention carried out (Table 4). Among the parameters studied, 239 (22.6%) presented some degree of alteration, which represented 162 complications in 40 patients, some complications are defined with more than one altered parameter. Following evaluation of the analytical results, estimation

of when oral intake would start and assessment of the patient's clinical status, the pharmacist carried out 93 direct interventions (57.4% of complications) involving 30 patients and 16 (9.9% of complications) interventions by recommendation involving 14 patients. Interventions consisting of recommendations to the prescribing physician are described in Table 5. In contrast to what would be expected in light of the patients' analytic results and energetic, caloric and protein needs, it was decided not to conduct intervention in 53 cases defined as complications. The pharmacist based this decision on short- or long-term estimation of when oral or enteral ingestion would start and to reduce risk in patients with hyperglycemia, hypertriglyceridemia, considerable hepatic alterations or renal dysfunction (Table 6).

Among the various parameters studied, those encompassed in the group of synthesis-inflammation (albumin, prealbumin, and C-reactive protein [CRP]) presented the largest number of alterations and were more often associated with complications (*n*= 83, 51.2%). The renal function parameters showed relatively few complications (*n*= 9, 5.5%) (Table 4).

Following the pharmaceutical interventions, the mean difference was calculated between the pre- and post-intervention mean values (table 7). Statistically significant differences or trend to signification were found for interventions aimed toward increasing albumin, prealbumin, potassium and phosphate levels, and for decreasing CRP, glucose and triglycerides. For some of the objectives contemplated, such as decreasing creatinine, potassium and phosphate, or increasing sodium and magnesium, the alterations in these parameters were small and the sample studied was insufficient to reflect statistical differences. The objective of decreasing liver function parameters (GGT, AP, ALT and bilirubin) was achieved, but did not show statistically significant differences.

DISCUSSION

In a general context, the PNU activities take part in a model of Pharmaceutical Care from our Pharmacy Service, this implies to assume responsibilities in the assistance team and in pharmacotherapy design, including monitoring and evaluation.

The protocol presented here allows for a series of interventions that, among others (clinical, high quality...) can be included in the patient's final results assessment.

Numerous studies have assessed the importance of protocolled nutrition for the prevention and treatment of various diseases^{1,3,7-16}. Although some of these publications defend the idea that the pharmacist's contribution in the prescription process achieves more successful PN therapy^{4,5}, there are few descriptions of pharmaceutical care in parenteral nutrition based on adjusting the composition of PN formulas according to the clinical status of individual patients at each point of their clinical process. Anoz Jiménez et al¹⁷ identified medication errors and/or drug-related problems associated with both total parenteral nutrition and other pharmacological treatments.

Table 3. Demographic Characteristics

Sex	Men	28 (65.3%)
	Women	16 (33.7%)
Mean age	61.5 years	
Surgery	Hemicolectomy	8 (19.5%)
	Exploratory laparotomy	6 (14.6%)
	Gastroenterostomy	3 (7.3%)
	Esophagectomy	3 (7.3%)
	Duodenopancreatectomy	3 (7.3%)
	Hepatectomy	3 (7.3%)
	Catheter colocation	2 (4.8%)
	Total gastrectomy	2 (4.8%)
	Colecistectomy	1 (2.4%)
	Other	10 (24.4%)
Non surgical	Pancreatitis 3	
Main reasons NP	Paralitic ileum	16 (36.4%)
	Esophag disease	6 (13.6%)
	Intraabdominal process- perforation	6 (13.6%)
	Bowel stenosis	5 (11.4%)
	Acute pancreatitis	4 (9.1%)
	Piloric stenosis	3 (6.8%)
	Malabsorption	2 (4.5%)
	Other	2 (4.5%)

Table 4. Complications in Analytic Parameters and Type of Interventions (PI)

Group	Complication	n	Parameters	n	Direct Intervention	Advice	Key Criteria
Synthesis and inflammation	Protein synthesis markers reduction	64	Albumin < 35 mmol/L	22	9	–	Prealbumin > albumin
			Prealbumin < 20.01 mmol/L	3	2	–	
			Prealbumin + albumin	39 (78)	22	–	
	Inflammatory response increase	19	C reactive protein > 9,99 mg/L	19	17	–	
Nutritional metabolism	Hyperglycemia	25	Glucose > 7.8 mmol/L	25	8	13	
	Hypoglycemia	0	Glucose < 4.01 mmol/L	–	–	–	
	Hypertriglyceridemia	6	Triglycerides > 2.31 mmol/L	6	5	–	
Renal function	Renal failure	9	Urea > 8.6 mmol/L	7	1	1	
			Creatinine > 199.99	2	2	–	
Liver function	Hepatic dysfunction	13	Moderate hepatic dysfunction (GGT ≥ 3.5 or AP ≥ 4.5) + (BIL ≤ 25 + ALT ≥ 0.83)	5 (20)	2	–	
			Severe cholestatic jaundice (GGT ≥ 3.5 or AP ≥ 4.5)+ BIL ≥ 25	8 (31)	6	–	
Electrolytes	Hyponatremia	2	Sodium < 130.01 mmol/L	2	1	1	
	Hypopotasemia	10	Potassium < 3.50 mmol/L	10	9	1	
	Hyperpotasemia	1	Potassium > 5.19 mmol/L	1	1	–	
	Hypomagnesemia	2	Magnesium < 0.62 mmol/L	2	1	–	
	Hypophosphatemia	5	Phosphate < 0.71 mmol/L	5	4	–	
	Hyperphosphatemia	2	Phosphate > 1.5 mmol/L	2	2	–	
	Hypocloremia	4	Chloride < 98 mmol/L	4	1	–	
TOTAL		162		162 (239)	93	16	

It is clear that the response obtained in the present study has a multifactorial aspect; nevertheless the results show that protocolled pharmaceutical interventions have an impact on the clinical and metabolic outcome of patients receiving PN. These interventions

mainly consisted of changes in the PN formula and additional support measures.

Increases in plasma albumin and prealbumin concentrations are related to improvements in nutritional status, by indicating

Table 5. Therapeutic Recommendations Given to Prescribing Physicians

Group	Complication	Advice
Nutritional metabolism	Hyperglycemia	Modify insuline regimen Review complementary fluid therapy Substitute dextrose 5%
Renal function	Renal failure	Review electrolytic balance and consult nephrology service
Electrolytes	Hypopotasemia	Review electrolytic balance and complementary fluid therapy
	Hyponatremia	Review electrolytic balance and complementary fluid therapy

Table 6. Criteria and Reasons for Non-Intervention in Patients With Metabolic Complications

Group	No intervention criteria	No intervention reason
Synthesis and inflammation	Nitrogen supply maintenance and/or no glutamine addition	Oral/enteral tolerance Oral intake in short-time period Post-surgery moderate hypoalbuminemia with acceptable prealbumin levels Nitrogen supply in the upper limit Encephalopathy risk Not worsening renal function
	No omega 3 fatty acids	Hipertriglyceridemia
Substrate metabolism	Maintenance glucose supply	Moderate hyperglycemia and need to keep caloric supply
	Maintenance lipid supply	Hipertriglyceridemia with minimum lipid supply
Renal function	Maintenance nitrogen supply	High urea levels not related with renal failure or excessive nitrogen supply (normal plasmatic creatinine levels)
Liver function	Maintenance lipid supply	Oral/enteral tolerance
		Oral intake in short-time period
Electrolytes	Maintenance initial supply	Moderate hypophosphatemia
		Moderate and transitory hypocloremia

an increase in protein synthesis or a decrease in proteolysis. In the present study the results for albumin did not show significant changes following the pharmaceutical intervention, a fact possibly attributable to problems of postoperative hemodilution or the elevated half-life of this protein. In contrast, the results for prealbumin indicate that it is more suitable than albumin as an early indicator of improved protein synthesis, both for assessing the clinical evolution of the patient and for evaluating the impact of the nutrients provided.

Prealbumin levels are reduced in malnourished patients and are used as markers of acute malnutrition, mainly due to its short half-life¹⁸. For many years prealbumin has been used as an indicator to evaluate the impact of the nutrients administered, as reduced prealbumin levels can be reversed with refeeding¹⁹.

In spite of this, authors like López Hellín et al²⁰ have questioned pre-albumin's role, and they have proposed to substitute it for other indicators with a minor artifactation, such as insulin-like growth factor-1, in order to assess the nutritional supply during the stress phase after surgery.

With the development of the pharmaceutical-nutrient concept, prealbumin has been also considered a response marker in im-

munologic-nutrition treatments (e.g., glutamine, omega 3). Experimental studies have found a direct relationship between the adding of immunologic nutrients and prealbumin levels. This association has also proven to be significant in several studies^{13,20-26}.

To attain an increase in prealbumin values, the nitrogen supply was increased. In the cases associated with post-stress hypercatabolism, this was accomplished with glutamine dipeptides. Glutamine favors faster enterocyte recovery and recuperation of immunocompetence^{7-11,27}.

Decreases in CRP concentration were used as a marker of improvement in the inflammatory state associated with post-stress aggression. When substantially elevated CRP values were noted, the interventional protocol established that omega-3 fatty acids should be added to the PN formula. There is now a sufficiently solid theoretical basis indicating the important immunomodulating and anti-inflammatory activity of omega 3 fatty acids¹²⁻¹⁴.

Omega 3 fatty acids addition was made keeping w3/w6 ratios between 1:2 to 1:3. Lipid emulsions with omega-3 to omega-6 ratio of 1:2 exert the highest LTC5/LTC 4 (leukotriene) ratio and a better immune modulating effect²⁸.

Table 7. Comparison Between Analytic Values Before and After Pharmaceutical Intervention (PI)

Parameter and Objective	Intervention	n	Pre-PI Mean Value	Post-PI Mean Value	Mean Difference	T	W
Increase albumin (g/L)	Direct	31	24.51	25.96	-1.45	0.085	0.057
	No	30	27.30	27.33	-0.03	0.96	0.79
	Advice	—	—	—	—	—	—
Increase prealbumin (mg/dL)	Direct	24	10.08	14.61	-4.61	0.001	0.002
	No	18	14.46	15.53	-1.05	0.52	0.50
	Advice	—	—	—	—	—	—
Decrease C-reactive protein (mg/L)	Direct	17	220.48	133.12	87.35	0.003	0.006
	No	2	207.40	101.70	105.70	0.141	0.180
	Advice	—	—	—	—	—	—
Decrease glucose (mmol/L)	Direct	8	10.88	8.52	2.36	0.107	0.092
	No	4	9.22	9.95	-0.72	0.31	0.27
	Advice	13	10.68	7.63	3.04	0.002	0.001
Decrease triglycerides (mmol/L)	Direct	5	4.40	2.74	1.66	0.053	0.08
	No	1	4.90	5.50	-0.6	—	—
	Advice	—	—	—	—	—	—
Decrease Urea (mmol/L)	Direct	1	34.7	20.5	14.2	—	—
	No	5	14.28	17.30	-3.02	0.67	0.89
	Advice	1	21.4	14.9	6.5	—	—
Decrease creatinine (μmol/L)	Direct	2	217.5	102.00	115.5	0.08	0.18
	No	—	—	—	—	—	—
	Advice	—	—	—	—	—	—
Increase sodium (mEq/L)	Direct	1	130	137	-7	—	—
	No	—	—	—	—	—	—
	Advice	1	129	148	-19	—	—
Decrease potassium (mmol/L)	Direct	1	5.63	4.40	—	—	—
	No	—	—	—	—	—	—
	Advice	—	—	—	—	—	—
Increase potassium (mmol/L)	Direct	9	3.21	4.31	-1.10	0.016	0.066
	No	—	—	—	—	—	—
	Advice	1	2.58	4.45	-1.87	—	—
Increase magnesium (mmol/L)	Direct	1	0.56	0.70	-0.14	—	—
	No	1	0.61	0.6	0.01	—	—
	Advice	—	—	—	—	—	—
Decrease phosphate (mmol/L)	Direct	2	1.61	1.47	0.13	0.54	0.65
	No	—	—	—	—	—	—
	Advice	—	—	—	—	—	—
Increase phosphate (mmol/L)	Direct	4	0.40	1.05	-0.64	0.06	0.068
	No	1	0.66	1.1	-0.44	—	—
	Advice	—	—	—	—	—	—
Increase chloride (mmol/L)	Direct	1	89	91	-2	—	—
	No	3	94	103	-9	—	—
	Advice	—	—	—	—	—	—
Decrease GGT (μkat/L)	Direct	5	6.06	5.12	0.94	0.45	0.34
	No	8	6.22	5.43	0.79	0.38	0.39
	Advice	—	—	—	—	—	—

(Continued)

Table 7. Comparison Between Analytic Values Before and After Pharmaceutical Intervention (PI) (*Continuation*)

Parameter and Objective	Intervention	n	Pre-Pi Mean Value	Post-Pi Mean Value	Mean Difference	T	W
Decrease AP ($\mu\text{kat/L}$)	Direct	6	7.55	9.20	-1.65	0.32	0.46
	No	9	11.71	9.32	2.38	0.52	0.86
	Advice	—	—	—	—	—	—
Decrease ALT ($\mu\text{kat/L}$)	Direct	7	5.21	1.83	3.38	0.33	0.23
	No	8	2.04	2.03	0.01	0.96	0.41
	Advice	—	—	—	—	—	—
Decrease bilirubin total ($\mu\text{mol/L}$)	Direct	4	408	245.3	162.7	0.32	0.28
	No	4	180.5	159.7	20.8	0.20	0.14
	Advice	—	—	—	—	—	—

PI: pharmaceutical intervention; t: t-test, w: Wilcoxon t-test

Adequate control of glucose and triglycerides is essential in nutritional therapy, since elevated levels of these parameters indicate inefficient metabolism and are associated with the development of clinical complications. The interventions to decrease hyperglycemia included reducing glucose content in the PN formula, adjusting fluid therapy, and providing recommendations for modifying insulin dosing. All recommendations were accepted.

To decrease hypertriglyceridemia, lipid content in the PN was decreased and lipid emulsions with faster and more effective plasma clearance were used, such as medium-chain triglyceride emulsions^{29,30}.

One important limitation in PN therapy is the development of hepatic complications associated with the lack of oral intake and factors related to toxicity or deficiencies³¹⁻³⁵. Therefore, the protocol required routine monitoring of various parameters related to liver function and established several interventions to prevent or minimize hepatic alterations. These include limiting potential glucose overload and particularly, decreasing the lipid content, while assuring an adequate caloric supply at all times. The results obtained with protocolled interventions for this purpose in the present study did not show a significant decrease in analytical liver function alterations. Nevertheless, these parameters did not worsen, and given their tendency to increase over the duration of PN, this can be considered a positive achievement for the patient's clinical evolution.

The study did not include patients in intensive care units, since this population presents a high incidence of multiorgan failure. Renal failure is of particular concern because of the problems involved in nutritional management of this condition. Exclusion of these patients explains the relatively low level of alterations in hydroelectrolytes and parameters associated with renal failure. There were, however, statistically significant post-intervention increases in potassium and phosphate values in patients with abnormally low results for these parameters. The PN formulas were adjusted to the patients' hydroelectrolyte status when the analytic and therapeutic situation required an intervention, in keeping with standard practice³⁶. The specific action of the

pharmacist established for these cases consisted of increasing the amount of potassium and phosphate in the PN formula.

In conclusion, with regard to clinical and metabolic status, candidates for PN are complex and difficult to treat with standardize nutritional interventions derived from simple criteria. Nevertheless, the findings of this study indicate that systematic monitoring of specific analytic parameters can be an effective means for attaining success in nutritional therapy, in terms of improvements in nutritional status and prevention and control of associated complications. Therefore, even though the parameters assessed may be influenced by several factors other than the PN treatment received, the results obtained in this study provide further evidence of the importance of protocolled, quantified pharmaceutical interventions in surgery patients.

References

- Huckleberry Y. Nutritional support and the surgical patient. *Am J Health Syst Pharm.* 2004;61:671-82.
- Guidelines for the use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients-ASPEN Board of Directors and the clinical guidelines task force. *JPEN.* 2002; 26 Suppl 1.
- Martínez Romero G, Pérez Ruixo JJ, Jiménez Torres NV. Nutrición parenteral e identificación de subpoblaciones con necesidades nutricionales similares. *Nutr Hosp.* 2002;17:80-92.
- McDermott LA, Albercht JT, Good DH. Nutritional support: pharmacists' influence on the prescribing process. *Top Hosp Pharm Manage.* 1994;14:30-9.
- Mutchie KD, Smith KA, MacKay MW. Pharmacist monitoring of parenteral nutrition: clinical and cost effectiveness. *Am J Hosp Pharm.* 1979;36:385-7.
- Martínez Olmos MA, Martínez Vázquez MJ, Montero Hernández M. Assessment of activity of care of a nutritional support multidisciplinary team in the follow-up of total parenteral nutrition. *Nutr Hosp.* 2006;21:57-63.
- Avenell A. Glutamine in critical care: current evidence from systematic reviews. *Proc Nutr Soc.* 2006;65:236-41.
- Koretz RL. Immunonutrition: fact, fantasy, and future. *Curr Gastroenterol Rep.* 2002;4:332-7.
- Lin MT, Kung SP, Yeh SL, Liaw KY, Wang MY, Kuo ML, et al. The effect of glutamine supplemented total parenteral nutrition on nitrogen economy depends on severity of diseases in surgical patients. *Clin Nutr.* 2002;21:213-8.
- Novak F, Heylan DK, Avenell A, Drover JW, Su X. Glutamine supplementation in serious illness: a systematic review of the evidence. *Crit Care Med.* 2002;30:2022-9.

11. Culebras-Fernández JM, De Paz-Arias J, Jorquera-Plaza F, Gracia de Lorenzo A. Nutrición en el paciente quirúrgico: inmunonutrición. *Nutr Hosp*. 2001;16:67-77.
12. Heller AR, Rossler S, Litz RJ, Stehr SN, Heller SC, Koch R, et al. Omega-3 fatty acids improve the diagnosis-related clinical outcome. *Crit Care Med*. 2006;34:972-9.
13. Klek S, Kulig J, Szczepanik AM, Jedrys J, Ko_odziewicz P. The clinical value of parenteral immunonutrition in surgical patients. *Acta Chir Belg*. 2005;105:175-9.
14. Tsekos E, Reuter C, Stehle P, Boeden G. Perioperative administration of parenteral fish oil supplements in a routine clinical setting improves patient outcome after major abdominal surgery. *Clin Nutr* 2004;23:325-30. Fe de erratas en: *Clin Nutr* 2004;23:755-6.
15. Imrie CW, Carter CR, McKay CJ. Enteral and parenteral nutrition in acute pancreatitis [review]. *Best Pract Res Clin Gastroenterol*. 2002;16:391-7.
16. Llop Talaveron JM, Berlana Martin D, Badia Tahul MB. Preparados estándar de nutrición parenteral en situaciones clínicas complejas. *Nutr Hosp*. 2004;19:229-35.
17. Anoz Jiménez L, Borrás Almenar C, Cavero Rodrigo E. Actuaciones farmacéuticas en pacientes en tratamiento con Nutrición Parenteral Total. *Farm Hosp*. 2004;5:349-55.
18. Michael E, Kupferman ME, Rombeau JL. Parenteral nutrition in inflammatory bowel disease. En: Rombeau JL, Rolandelli RH, editors. *Clinical nutrition: parenteral nutrition*. Philadelphia: Saunders; 2001. p. 212.
19. Prealbumin in Nutritional Care Consensus Group: Measurement of visceral protein status in assessing protein and energy malnutrition: Standards of care. *Nutrition*. 1995;11:169-71.
20. López Hellin J, Baena-Fustegueras JA, Schwartz Riera S, Garcia Arumi E. Usefulness of short-lived proteins as nutritional indicators surgical patients. *Clin Nutr*. 2002;21:119-25.
21. Puskás LG, Kitajka K, Nyakas C, Barcelo-Coblijn G, Farkas T. Short-term administration of omega 3 fatty acids from fish oil results in increased transthyretin transcription in old rat hippocampus. *Proc Natl Acad Sci USA*. 2003;100:1580-5.
22. Gianotti L, Braga M, Fortis C, L Sodini, Vignali A, Colombo S, et al. A prospective, randomized clinical trial on perioperative feeding with an arginine-, omega 3 fatty acid-, and RNA-enriched enteral diet: effect on host response and nutritional status. *JPEN*. 1999;23:314-20.
23. Chen DW, Wei Fei Z, Zhang YC, Ou JM, Xu J. Role of enteral immunonutrition in patients with gastric carcinoma undergoing major surgery. *Asian J Surg*. 2005;28:121-4.
24. Braga M, Gianotti L, Vignali A, Di Carlo V. Immunonutrition in gastric cancer surgical patients. *Nutrition*. 1998;14:831-5.
25. Wischmeyer PE, Lynch J, Liedel J, Wolfson R, Riehman J, Gottlieb L, et al. Glutamine administration reduces Gram-negative bacteremia in severely burned patients: a prospective, randomized, double-blind trial versus isonitrogenous control. *Crit Care Med*. 2001;29:2075-80.
26. Mercadal G, Llop J, Gracia B, Martorell C, Badía M, Tubau M, et al. Utilización de glutamina en nutrición parenteral en paciente crítico: efectos sobre la morb-mortalidad. *Nutr Hosp*. 2007;22:61-7.
27. Cardona Pera D. Administration of glutamine and its dipeptides in parenteral nutrition. Which patients are candidates? [review]. *Nutr Hosp*. 1998;13:8-20.
28. Morlion BJ, Torwesten E, Wrenger K, Puchstein C Fürst P. What is the optimum w-3 to w-6 fatty acid (FA) ratio of parenteral lipid emulsions in postoperative trauma? *Clin Nutr*. 1997;16 Supl 2.
29. Driscoll DF. Lipid injectable emulsions: 2006 [review]. *Nutr Clin Pract*. 2006;21:381-6.
30. Shirai K, Kobayashi J, Inadera H, Ohkubo Y, Mori S, Saito Y, et al. Type I hyperlipoproteinemia caused by lipoprotein lipase defect in lipid-interface recognition was relieved by administration of medium-chain triglyceride. *Metabolism*. 1992;41:1161-4.
31. Boncompain MG, Claudel JP, Gaussorgues P, Salord F, Sirodot M, Chevallier M, et al. Hepatic cytolytic and cholestatic changes related to a change of lipid emulsions in four long-term parenteral nutrition with short bowel. *JPEN*. 1992;16:78-83.
32. Morán Penco JM, Salas Martínez J, Maciá Botejara E. ¿Qué sucede en el hígado durante la alimentación artificial? *Nutr Hosp*. 2001;16:145-51.
33. Kumpf VJ. Parenteral nutrition-associated liver disease in adult and pediatric patients. *Nutr Clin Pract*. 2006;21:279-90.
34. Clayton PT, Bowron A, Mills KA, Massoud A, Casteels M, Milla PJ. Phytosterolemia in children with parenteral nutrition-associated cholestatic liver disease. *Gastroenterology*. 1993;105:1806-13.
35. Kelly DA. Intestinal failure-associated liver disease: what do we know today? *Gastroenterology*. 2006;130 Suppl 1:S70-7.
36. Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. *Am J Health Syst Pharm*. 2005;62:1663-82.