



Farmacia Hospitalaria

ISSN: 1130-6343

[farmhosp@grupoaulamedica.com](mailto:farmhosp@grupoaulamedica.com)

Sociedad Española de Farmacia  
Hospitalaria  
España

Sevilla Sánchez, D.; Placeres Alsina, M.M.; Miana Mena, M.T.; López Suñé, E.; Codina  
Jané, C.; Ribas Sala, J.

Pharmaceutical intervention with parenteral nutrition  
Farmacia Hospitalaria, vol. 34, núm. 1, 2010, pp. 9-15  
Sociedad Española de Farmacia Hospitalaria  
Madrid, España

Available in: <http://www.redalyc.org/articulo.oa?id=365961363002>

- How to cite
- Complete issue
- More information about this article
- Journal's homepage in [redalyc.org](http://redalyc.org)

[redalyc.org](http://redalyc.org)

Scientific Information System

Network of Scientific Journals from Latin America, the Caribbean, Spain and Portugal

Non-profit academic project, developed under the open access initiative

# Pharmaceutical intervention with parenteral nutrition<sup>☆</sup>

D. Sevilla Sánchez,\* M.M. Placeres Alsina, M.T. Miana Mena, E. López Suñé,  
C. Codina Jané, and J. Ribas Sala

Pharmacy Division, Hospital Clínic de Barcelona, Barcelona, Spain

Received April 27, 2009; accepted September 15, 2009

Available online January 22, 2010

## KEYWORDS

Pharmacist  
intervention;  
Parenteral nutrition;  
Acceptance

## Abstract

**Objective:** Description and analysis of pharmaceutical interventions for patients with parenteral nutrition and an assessment of the degree of acceptance.

**Method:** Prospective six-month study. Design of a data collection sheet (with personal data, the indication for parenteral nutrition, hospital area, nutrition type, time and type of intervention, type of notification, acceptance) for recording interventions carried out based on normal activities: complete review of pharmacotherapy and clinical history.

**Results:** A total of 265 interventions were carried out during the study period (1.5 interventions/day) with a mean of 2.1 interventions/patient. The overall degree of acceptance was 83.77%; significant differences were found between type of communication for the intervention (oral and/or written) and the degree of acceptance.

**Conclusions:** Adding a pharmacist to the care team permits direct intervention in partnership with the doctor, and it is an effective method for preventing and resolving the complications, generally metabolic, that are associated with parenteral nutrition. Using this process for resolving medication-related problems in hospitalised patients, principally in surgical areas, is an addition to the pharmacist's activities in the area of nutritional support.

© 2009 SEFH. Published by Elsevier España, S.L. All rights reserved.

## PALABRAS CLAVE

Intervención  
farmacéutica;  
Nutrición parenteral;  
Aceptación

## Intervención farmacéutica en el ámbito de la nutrición parenteral

## Resumen

**Objetivo:** Descripción y análisis de las intervenciones farmacéuticas realizadas en el ámbito de la nutrición parenteral (NP) y valoración del grado de aceptación.

<sup>☆</sup>This study has been presented in part at the LIII Congreso Nacional de la Sociedad Española de Farmacia Hospitalaria held in Valencia from 21 to 24 October 2008.

\*Corresponding author.

E-mail address: danielsevillasanchez@gmail.com (D. Sevilla Sánchez).

**Método:** Estudio prospectivo de 6 meses. Se diseñó una hoja de recogida de datos (datos personales, indicación de NP, sala de hospitalización, tipo de nutrición, momento y tipo de intervención, modo de notificación y aceptación) en la que se registraron las intervenciones realizadas a partir de la actividad diaria: revisión completa de la farmacoterapia y de la historia clínica.

**Resultados:** Se realizaron un total de 265 intervenciones en el período de estudio (1,5 intervenciones/día) con una media de 2,1 intervenciones/paciente. El grado global de aceptación fue del 83,77%, fueron significativas las diferencias encontradas entre el tipo de comunicación de la intervención (oral y/o escrita) y el grado de aceptación.

**Conclusiones:** La integración del farmacéutico en el equipo asistencial permite una intervención directa con el médico, y es un método eficaz para la prevención y resolución de complicaciones asociadas a la NP, principalmente de tipo metabólico. Utilizar este proceso para resolver problemas relacionados con la medicación en los pacientes ingresados, principalmente en salas quirúrgicas, proporciona una calidad añadida a la actividad del farmacéutico en el área del soporte nutricional.

© 2009 SEFH. Publicado por Elsevier España, S.L. Todos los derechos reservados.

## Introduction

Pharmaceutical care, understood to mean the responsible provision of pharmacotherapy for the purpose of obtaining specific results that improve patients' quality of life,<sup>1</sup> is particularly relevant when it comes to parenteral nutrition (PN), considering the clinical nature of this task among the pharmacist's activities. Therefore, the field of artificial nutrition presents one of the best possibilities for a pharmacist to participate as part of a multidisciplinary team and contribute to more effective, safer pharmacotherapy by detecting and resolving medication errors and errors related to nutrition itself.<sup>2</sup>

A pharmacist intervention (PI) is understood to mean any action undertaken by the pharmacist in order to solve a potential or current medication and nutrition-related problem arising from a patient's care needs.<sup>3</sup> The purpose of this study is to complete a description and analysis of the PIs performed in the area of PN, and to evaluate their degree of acceptance and the factors that may affect them.

## Method

For the purpose of recording PIs in the area of PN, we designed a six-month prospective study in a tertiary hospital with 850 beds. We included all patients on PN treatment who were monitored by the PN team in the pharmacy department. These patients were in surgical units (general and digestive tract surgery, thoracic and urological surgery); medical units (gastroenterology, hepatology, internal medicine, nephrology, dermatology and neurology) and intensive care (ICU) and sub-intensive care digestive, respiratory and nephrology units.

As a daily activity, we revised pharmacotherapy and fluid therapy, clinical history and laboratory analyses, and evaluated the indication of PN and the nutritional state of patients observed in the study. A data collection form was designed (Figure 1). The following was recorded for each intervention:

1. Demographic data and date of intervention.
2. Unit type: medical, surgical or ICU.
3. Principal diagnosis and indication for PN.
4. Time at which the PI is undertaken with respect to when PN was prescribed: beginning, follow-up or end.
5. PN Type: Total PN (TPN) or peripheral PN (PPN).
6. Type of PI undertaken:
  - I. Indication of nutrition: modification to PN type, change to enteral nutrition or oral diet, delay start of nutrition, continue PN or end PN.
  - II. Venous accesses and catheters: changing the central or peripheral lines, and selecting the type of route.
  - III. Modifying fluid therapy: type of FT prior to the intervention, motive of the intervention and proposed change of FT.
  - IV. Modification to electrolyte input: type of electrolyte involved, laboratory test result justifying the intervention and prior level received.
  - V. Laboratory test monitoring: request for laboratory testing prior to starting PN, follow-up analysis, capillary glycaemia test and/or diuresis test.
  - VI. Medication-related problems (MRPs) according to the adjustment of the MRP classification system based on Jarabo's criteria<sup>4</sup>:
    - i. Insulin: add to treatment, adjust sliding-scale or set dose according to capillary glycaemia.
    - ii. Propofol: change concentration from 1% to 2% (to reduce the amount of lipids received) depending on the serum triglyceride level.
    - iii. Other pharmacotherapy actions.
7. Type of notification given: oral (doctor and/or nursing staff) and/or written (clinical history and/or treatment chart and/or hospital computer programme).
8. Acceptance: yes, no or not applicable.
9. Remarks: other data of interest.

The PIs were recommendations made to doctors or to nursing staff. Under no circumstances did the pharmacist directly manipulate the pharmacotherapeutic devices. These PIs were evaluated the day after they were performed and entered in a database (Microsoft Access®) created for

<b>PACIENTE:</b> <b>SERVICIO/SALA:</b> <b>TIPO NUTR:</b> <input type="checkbox"/> NPT <input type="checkbox"/> NPP		<b>NHC:</b> <b>FECHA:</b> <b>MOMENTO INTERVENCIÓN:</b>		<b>INDICACIÓN:</b> <input type="checkbox"/> INICIO <input type="checkbox"/> SEGUIMIENTO <input type="checkbox"/> FINALIZACIÓN	
<b>INDICACIÓN:</b> <input type="checkbox"/> NPT <input type="checkbox"/> NPP <input type="checkbox"/> NE <input type="checkbox"/> ORAL <input type="checkbox"/> STOP <input type="checkbox"/> POSPOSICIÓN INICIO <input type="checkbox"/> CONTINUAR <b>VÍAS:</b> <input type="checkbox"/> RECAMBIO <input type="checkbox"/> VIA CENTRAL <input type="checkbox"/> VIA PERIFÉRICA, TIPO:				<b>OBSERVACIONES:</b>	
<b>SUEROTERAPIA:</b> ACTUAL: <input type="checkbox"/> SF <input type="checkbox"/> SG <input type="checkbox"/> SGS <input type="checkbox"/> SR <input type="checkbox"/> Ninguno AJUSTE: <input type="checkbox"/> Por inicio <input type="checkbox"/> Por Stop <input type="checkbox"/> Por glucemias <input type="checkbox"/> Bal. Vol. <input type="checkbox"/> Por electrolitos CAMBIO: <input type="checkbox"/> STOP <input type="checkbox"/> SF <input type="checkbox"/> SG <input type="checkbox"/> OTROS:				<b>NOTIFICACIÓN:</b> <input type="checkbox"/> ORAL: <input type="checkbox"/> médico <input type="checkbox"/> enfermera <input type="checkbox"/> ESCRITO: <input type="checkbox"/> HC <input type="checkbox"/> SAP <input type="checkbox"/> OM	
<b>ELECTROLITOS:</b> <input type="checkbox"/> K <sup>+</sup> <input type="checkbox"/> Na <sup>+</sup> <input type="checkbox"/> Mg <sup>2+</sup> <input type="checkbox"/> Ca <sup>2+</sup> <input type="checkbox"/> P <input type="checkbox"/> OTROS: <input type="checkbox"/> APORTE INICIAL DIA (NP // EXT); <input type="checkbox"/> Analítica Nutricional inicial <b>MONITORIZACIÓN:</b> <input type="checkbox"/> Solicitud Glucemia capilar				<input type="checkbox"/> ANALÍTICA: <input type="checkbox"/> AJUSTE: <input type="checkbox"/> Control-ajuste-seguimiento por electrolitos <input type="checkbox"/> Solicitud control diuresis <input type="checkbox"/> Otros:	
<b>MEDICACIÓN:</b> <input type="checkbox"/> INSULINA (Ajuste pauta a Glucemia capilar): <input type="checkbox"/> PROPOFOL (Ajuste pauta a TAG): <input type="checkbox"/> PRM: <input type="checkbox"/> 1. Med. no indicado <input type="checkbox"/> 2. Omisión tratamiento <input type="checkbox"/> 3. Dosis inapropiada <input type="checkbox"/> 4. Duración inapropiada <input type="checkbox"/> 5. Vía inapropiada <input type="checkbox"/> 6. Interacción <input type="checkbox"/> 7. RAM <input type="checkbox"/> 8. Otros:				<b>ACEPTACIÓN:</b> <input type="checkbox"/> SI <input type="checkbox"/> NO <input type="checkbox"/> NO PROCEDE <b>MOTIVO:</b>	

**Figure 1** Data collection sheet.

CH indicates clinical history; CHN, clinical history number; DS, dextrose solution; EN, enteral nutrition; EXT, external; GSS, glucosaline solution; MO, medical order; MRP, medication-related problem; PN, parenteral nutrition; PPN, peripheral parenteral nutrition; RS, Ringer's solution; SAP, hospital's computer programme; SS, saline solution; TAG, triacylglycerides; TPN, total parenteral nutrition; vol. bal., volume balance.

that purpose. Statistical analysis was performed using the chi-square test for categorical data.  $P$ -values  $< .05$  were considered significant. In the statistical analysis, total acceptance data were grouped as either accepted (yes) or not accepted (no or not applicable). In the latter case, the reason for lack of acceptance was also recorded. Numbers for PN consumption were obtained using the software application for the PN area (Nutridata Braun®).

## Results

During the six-month study period, a total of 265 interventions were carried out (152 in men and 113 in women; mean age, 64.8 years, SD 16.7), which came to 1.45 interventions per day (SD 1.03) in 127 different patients (2.09 interventions/patient, SD 1.40). The mean duration of PN treatment was 15.38 days (ED 11.91). This came to an average of 0.22 interventions per patient per day on nutritional support (SD 0.19). During this period, the total number of PN in the hospital was 5.091, of which 61.28% (3,120) were the responsibility of the pharmacy department's PN team (a mean of 17.05 nutritions per day).

Most of the PN were hospitalised in the ICUs and surgical units, but the number of PIs was greater in surgical units (60.75%) than in the ICUs (18.11%). Most of the interventions

having to do with the indication of PN affected patients on PN due to prolonged post-operative recovery and its complications (Table 1).

With respect to the time of intervention, more than half of the PIs took place during daily clinical monitoring, while 36.98% took place when PN was initiated and 7.17% when it was ended. Of the total nutritional supports prescribed during this study, 90.90% (2,836) were TPN and 9.10% (284) were PPN. Most of the PIs were performed with TPN (77.74%) (Table 2). The overall acceptance rate for the PIs was 83.77%. Of the PIs that were refused, 11.32 were not accepted and 4.91% were not applicable (Table 3). We found no statistical significance in the correlation between the degree of acceptance and any of the variables described above (unit in question, indication, moment of the PI and type of PN).

The result from the different interventions allows us to see that most of them were performed in two areas: FT adjustment and adjustment of the electrolyte input (Figure 2). Upon beginning PN, 29 patients required an adjustment to the FT, mainly to suspend the input of dextrose solution once PN had been started. Of the 21 interventions carried out to suspend PN, most took place in order to add FT to the treatment. Twelve PIs were carried out to correct glycaemia alterations and 18 to adjust fluid balance.

Interventions caused by changes in electrolyte input were mostly carried out to control potassaemias (12 cases

**Table 1** Pharmacist interventions classified by hospital unit, indication of parenteral nutrition and acceptance

Type of PN indication	ICU/semi-intensive	Medical units	Surgical units	Total	Acceptance
1. Mechanical obstruction	0	3	15	18	14
2. Dynamic obstruction (ileum)	1	5	8	14	13
3. Prolonged post-op period and complications	13	3	86	102	87
4. Severe malabsorption and diarrhoea	0	0	0	0	0
5. Incoercible vomiting	0	1	0	1	0
6. Digestive haemorrhage	1	3	2	6	6
7. Severe acute pancreatitis	0	14	5	19	16
8. Digestive fistulas and suture dehiscence	2	2	24	28	21
9. IID + perforation, megacolon and stenosis	0	9	0	9	7
10. Aesophagitis	0	8	0	8	7
11. Polytrauma and/or SCT	0	0	0	0	0
12. Abdominal sepsis and peritonitis	2	0	0	2	2
13. Contraindications of EN, shock, instability	10	0	2	12	10
14. High risk of bronchoaspiration + NIMV	7	1	0	8	7
15. Anorexia nervosa or 2 <sup>nd</sup>	0	0	0	0	0
16. Coadjuvant CT/RT	3	0	0	3	2
17. Pre-op for major surgery in patient with severe malnutrition	0	0	3	3	3
18. EN intolerance and/or insufficient ingestion. Other	9	7	16	32	27
Total	48	56	161	265	222

CT/RT indicates chemotherapy/radiotherapy; EN, enteral nutrition; ICU, intensive care unit; IID, inflammatory intestinal disease; NIMV, non-invasive mechanical ventilation; PN, parenteral nutrition; SCT, spinal or cranial trauma.

**Table 2** Correlation between the time of intervention and the nutrition type, listing units and acceptance

	ICU	Medical units	Surgical units	Total	Acceptance
<b>Moment of intervention</b>					
Start	13	21	64	98	84
Follow-up	34	32	82	148	120
End	1	3	15	19	18
Total	48	56	161	265	222
<b>Type of PN for the intervention</b>					
PPN	0	9	50	59	49
TPN	48	47	111	206	173
Total	48	56	161	265	222

ICU indicates intensive care unit; PN, parenteral nutrition; PPN, peripheral parenteral nutrition; TPN, total parenteral nutrition.

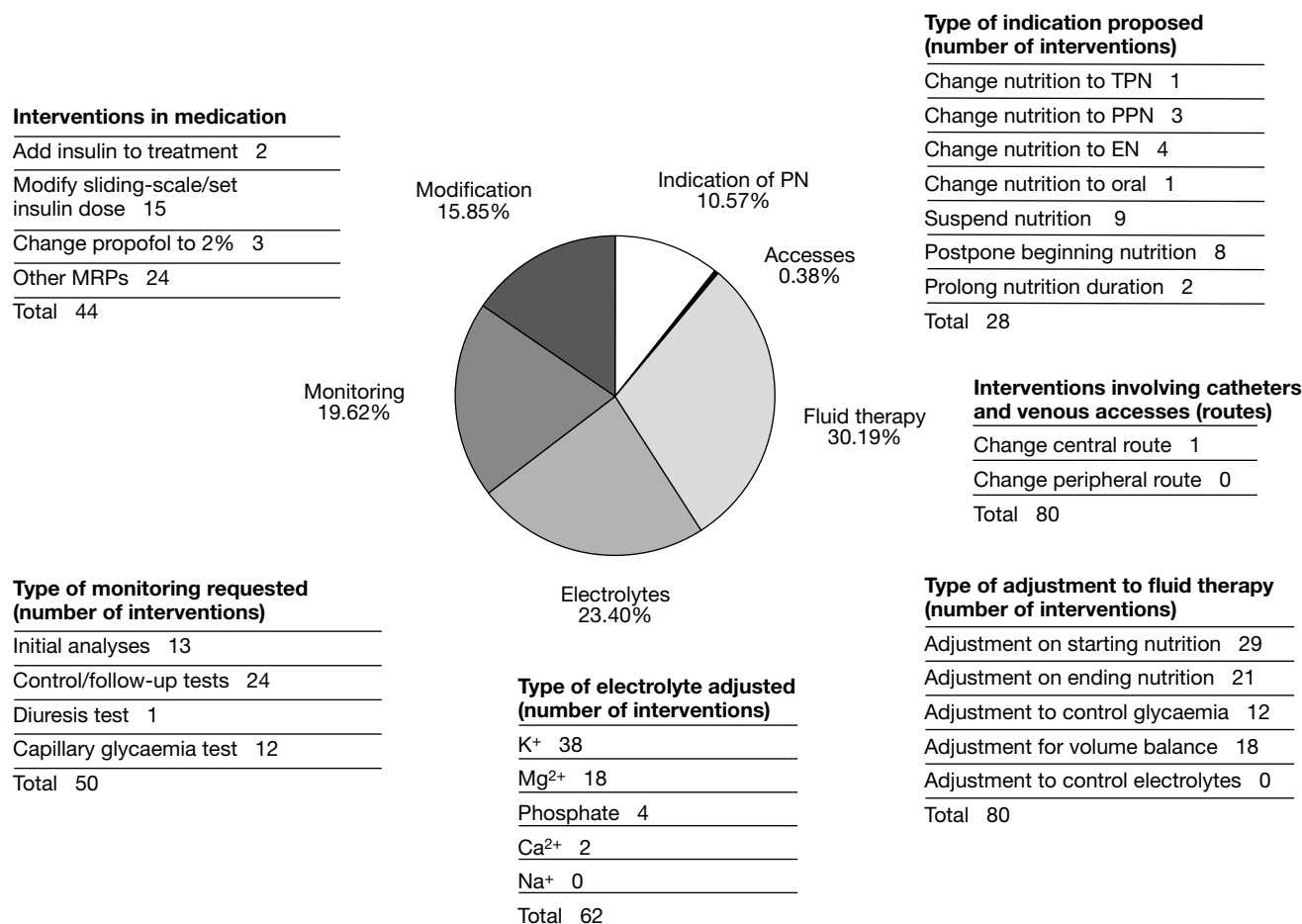
**Table 3** Correlation between units, number of interventions and acceptance rates

Unit type	No. PIs	No. PN treatments	No. PN/day	Acceptance
ICU	48	1,177	6.44	37 (77.08%)
Medical units	56	731	3.99	51 (91.07%)
Surgical units	161	1,212	6.62	134 (83.23%)
Total	265	3,120	17.05	222 (83.77%)

ICU indicates intensive care unit; PI, pharmaceutical intervention; PN, parenteral nutrition.

required adding an external source, 5 required increasing the existing dose, 17 required suspending treatment and 4 required reducing it) and magnaesaemias (it was necessary

to add an external source in 15 cases, increase the dose in two cases and decrease it in one). More rarely, interventions were carried out for phosphataemias (four cases),



**Figure 2** Distribution and breakdown of different types of pharmacist intervention. EN indicates enteral nutrition; MRP, medication-related problem; PN, parenteral nutrition; PPN, peripheral parenteral nutrition; TPN, total parenteral nutrition.

**Table 4** Correlation between the type of communication, hospital unit and acceptance rates

Type of communication	ICU	Medical units	Surgical units	Total	Acceptance
Verbal	39	44	68	151 (56.98%)	137 (90.73%)
Written	1	2	30	33 (12.45%)	23 (69.70%)
Verbal+written	8	10	63	81 (30.57%)	62 (76.54%)
<b>Total</b>	<b>48</b>	<b>56</b>	<b>161</b>	<b>265 (100%)</b>	<b>222 (83.77%)</b>

ICU indicates intensive care unit.

calcaemias (two cases) and natraemias, for which no intervention was recorded.

A single PI was undertaken to recommend changing a central venous catheter and it was not accepted. Of the interventions referring to the type of indication, most were carried out to suspend PN (32.14%) or postpone it being started (28.57%). Regarding the type of monitoring requested, a complete round of analytical tests was run in 48% of all cases due to daily follow-up.

With respect to MRPs, pharmacist actions were caused by modifications to insulin treatment in 39% of all cases. The main pharmacological groups involved, apart from insulin

and propofol, were antibiotics with 14 PIs (six due to incorrect treatment duration, three due to treatment omissions, three due to plasma level monitoring results, one due to erroneous administration frequency and one due to a non-indicated drug) and antihypertensive drugs with six interventions (five due to treatment omissions and one due to incorrect dose). There was no statistically significant correlation between PI acceptance and the different intervention types listed above.

The global acceptance rate for PIs was 83.77%. Variation existed between PIs communicated verbally to the staff involved in the case and those issued in written form, with

acceptance rates of 90.73% and 69.70%, respectively. However, acceptance of the PIs communicated by both methods, verbally and in writing, was 76.54%. The differences between degree of acceptance and the type of communication were found to be statistically significant ( $P < .005$ ) (Table 4). Verbal recommendations were made directly to doctors in 49% of the cases (acceptance rate of 89.19%), to nursing staff (acceptance rate of 92%) and 12% to both doctors and nursing staff (94% acceptance rate). Written communications were issued using the hospital's computer system (54.55%), by writing in the patient's medical chart (15.15%), or using both methods (30.30%). Of the recommendations made using verbal and written channels simultaneously, 12.35% were directed to doctors (acceptance rate of 90%), 80.25% to nursing staff (acceptance rate of 73.85%) and 7.41% to both groups (acceptance rate of 83.33%).

## Discussion

Proper nutritional support has been shown to reduce morbidity and mortality in hospitalised patients, and to reduce associated costs.<sup>5</sup> Therefore, increasing the hospitalised patient's nutritional state makes the PIs that a pharmacist may make in this area especially relevant. In our hospital, the responsibility for artificial nutritional support is shared between doctors, who order the nutrition, and the pharmacist (assigned to certain units) who determines the composition of the PN. This shared responsibility grants the pharmacist a privileged position that allows him/her to exert an influence on the rest of the pharmacotherapeutic process.

Therefore, the area of PN allows for important interventions in different hospital units. According to results obtained in our study, the one receiving the most benefit is the surgical patient, which is supported by previously published studies.<sup>2,6,7</sup> Another patient type that could potentially benefit from pharmacist intervention is the critical care patient. Patients in this condition frequently need PN, and furthermore, incorporating a pharmacist in the ICU is a practice that is being adopted in an increasing number of centres.<sup>8,9</sup>

The high acceptance rate of the recommendations shows that the pharmacist is considered a member of the multidisciplinary clinical team. The PIs that were most frequently carried out included adjusting the patient's FT and electrolytes, and this took place mostly during daily monitoring. In our study, 2.1 PIs took place per patient, which is comparable to results listed in the studies by Anoz et al<sup>2</sup> and Cerulli et al.<sup>10</sup>

MRP are complications that cause 6% to 8% of all hospitalisations<sup>11-13</sup> and occur in approximately 2% of all hospitalised patients.<sup>14,15</sup> Preliminary studies show the rate of problems related to clinical nutrition between 30% and 60%.<sup>2,6,10</sup> In the present study, interventions to resolve MRPs represented 16.6% of cases, but reach 70.18% if we consider electrolytes and FT to be part of the medication these patients received. We must stress that antibiotics were the main drug group involved in these MRPs, as was the case in the study by Cerulli et al.<sup>10</sup>

The data obtained strongly show that personal interaction and verbal communication favour PI being accepted.

Although it may seem paradoxical to have a lower acceptance rate for combined communication, both written and verbal, this can be explained by the fact that most of the oral recommendations were made to doctors, while combined verbal and written recommendations were mainly made to nursing staff. This involves an increase in the number of speakers and dilutes direct communication.

Therefore, the current tendency to include the pharmacist in the hospitalised patient units is justified, since it fosters direct interaction with personnel involved in patient care, increased participation in treatment decisions and better acceptance of the recommendations that are made.

In conclusion, a direct PI with the doctor, and therefore, integration of the pharmacist in the care team, may be the best and most effective means of preventing and resolving complications associated with PN, which are primarily metabolic. Furthermore, using this process to detect, prevent and resolve MRPs in patients hospitalised in different units, particularly surgical units, provides added quality to the pharmacist's activities in the area of nutritional support.

## Conflict of interest

The authors affirm that they have no conflicts of interest.

## References

1. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm.* 1990;47:533-43.
2. Anoz Jiménez L, Borrás Almenar C, Caverro Rodrigo E. Actuaciones farmacéuticas en pacientes en tratamiento con nutrición parenteral total. *Farm Hosp.* 2004;28:349-55.
3. Levy DB. Documentation of clinical and cost-saving pharmacy interventions in the emergency room. *Hosp Pharm.* 1993;28:624-53.
4. Otero López MJ, Codina Jané C, Tamés Alonso MJ, Pérez Encinas M. Errores de medicación: estandarización de la terminología y clasificación. Resultados de la beca Ruiz-Jarabo 2000. *Farm Hosp.* 2003;27:137-49.
5. American Society of Parenteral and Enteral Nutrition. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *JPEN.* 2002;26:9.
6. Heyland DK, Montalvo M, MacDonald S, Keefe L, Su XY, Drover JW. Total parenteral nutrition in the surgical patient: A meta-analysis. *Can J Surg.* 2001;44:102-11.
7. Llop-Talaverón J, Gracia-García B, Machí-Ribes JJ, Perayre-Badia M, Badia-Tahull MB, Jódar-Masanes R. Pharmaceutical interventions in metabolic and nutritional follow-up of surgical patients receiving parenteral nutrition. *Farm Hosp.* 2008;32:216-225.
8. Leblanc JM, Seoane-Vazques E, Arbo TC, Dasta JF. International critical care hospital pharmacist activities. *Intensive Care Med.* 2008;34:538-42.
9. Heyland DK, MacDonald S, Keefe L, Drover JW. Total parenteral nutrition in the critically ill patient: A meta-analysis. *JAMA.* 1998;280:2013-9.
10. Cerulli J, Malone M. Assessment of drug-related problems in clinical nutrition patients. *JPEN J Parenter Enteral Nutr.* 1999;23:218-21.
11. Otero MJ, Alonso P, Maderuelo JA, Ceruelo J, Domínguez-Gil A, Sánchez A. Prevalencia y factores asociados a los

- acontecimientos adversos prevenibles por medicamentos que causan el ingreso hospitalario. *Farm Hosp*. 2006;30:161-70.
12. Howard RL, Avey AJ, Howard PD, Partridge M. Investigation into the reasons for preventable drug related admissions to a medical admission unit: Observational study. *Qual Saf Health Care*. 2003;12:280-5.
13. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, et al. Adverse drug reactions as a cause of admissions to hospital: Prospective analysis of 18820 patients. *BMJ*. 2004;329:15-9.
14. Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. *JAMA*. 1997;277:307-11.
15. Cullen DJ, Bates DW, Leape LL. Prevention of adverse drug events: A decade of progress in patient safety. *J Clin Anesth*. 2000;12:600-14.