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ORIGINAL ARTICLE

Composition of personalized and standard nutritional mixtures in patients on home parenteral nutrition

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BACKGROUND/OBJECTIVES: The compounding of personalized parenteral nutrition mixtures (PPNMs) for home parenteral nutrition (HPN) gives the possibility to better satisfy nutritional requirements for patients in selected clinical conditions. The objective of this study was to compare the composition of PPNMs prescribed in selected cases, by a practitioner nutritionist, with that of industrially manufactured standard parenteral nutrition mixtures (SPNMs).

SUBJECTS/METHODS: Two hundred and ninety-eight patients (151 men, 147 women, aged 17–87 years) on HPN, followed up in 2011 at our Center, were retrospectively recruited.

RESULTS: Industrially manufactured SPNMs were prescribed in 230 (77.2%) patients, whereas compounded PPNMs were prescribed in 68 (22.8%). Formulation of PPNMs, adjusted for body weight, did not significantly differ from SPNMs as regards total daily calorie amount, but was significantly different as far as nutrient composition is concerned ($P<0.01$). Analysis on the daily amount of nutrients per kg of body weight and per patient disease showed that 16/34 (47%) benign chronic intestinal failure (CIF) patients, 47/233 (20%) cancer patients and 5/31 (16%) patients grouped as 'having other diseases' needed personalized mixtures (in PPNMs 4–9 nutrients were significantly different from those in SPNMs). Moreover, in CIF patients receiving PPNMs, frequent changes in the formulation (mean 6 times per year, range 1–28) were necessary.

CONCLUSIONS: Our data suggest that, presently, PPNMs cannot be completely replaced by SPNMs owing to special needs in macro and/or micronutrients of some patients and/or the necessity of frequent changes in the nutritional mixture composition, at least until stabilization of clinical and metabolic conditions.

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INTRODUCTION

Parenteral nutrition (PN) is indicated in patients who cannot be fed by enteral route, such as those with intestinal failure or obstruction.[1–3] Patients needing PN must be evaluated by a specialized nutritional team[4–6] to establish their fluid, electrolytes, and macro- and micronutrient requirements.[3,7–9] Nutritional guidelines are a valid reference for a safe PN support formulation;[10] however, nutrient requirements can widely vary from one patient to another and for the same patient in time,[11,12] even according to patient's gender, age, weight, hematobiochemical exams, mostly depending on clinical conditions, evolution and characteristics of primary disease. PN consists in intravenous administration of nutrients as elementary components that can also be performed for long periods at home.[13,14] Nutritional mixtures may be compounded (namely prepared in hospital pharmacies and personalized according to patient requirement) or standard (manufactured by pharmaceutical industries). For patients without relevant comorbidities, standard parenteral nutrition mixtures (SPNMs) are often adequate to correct nutrient deficiencies and their related complications.[15] However, for patients with particular comorbidities (heart failure, chronic renal failure, hepatic failure), as well as for critically ill and/or catabolic patients or for patients with benign chronic intestinal failure (CIF), that is, chronic inflammatory bowel diseases and short bowel syndrome, PPNMs are often required.[14]

Aim of the study

This retrospective study compares the formulation of PPNMs and SPNMs, both prescribed by a physician specialized in clinical nutrition at our nutritional center. The study does not aim to debate the appropriateness of the parenteral nutritional mixtures prescriptions, but only to evaluate the differences in nutrient composition, also according to the different diseases treated.

PATIENTS AND METHODS

Patients and medical intervention

Out of 648 patients (303 men, 345 women, aged 16–97 years) followed at the Home Artificial Nutrition Unit of Federico II University Hospital in Naples from January to December 2011,[16] 298 were on home parenteral nutrition (HPN). Patients were grouped into three groups: (1) oncologic; (2) patients with CIF; (3) patients affected by 'other diseases', such as neurologic disease, malabsorption after bariatric surgery, gastrectomy, cystic fibrosis, intractable diarrhea for intestinal infections, primary hypo- or a-gammaglobulinemia, necrotizing enterocolitis, high-output

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enterocutaneous fistulas, intestinal motility disorders, pancreatitis, graft-versus-host disease and intractable vomiting in pregnant.

Case history, physical examination, anthropometric measurements and biochemical exams were mostly performed on a Day Hospital basis, and in a minority of patients during hospitalization.

Data collection

Demographic, clinical and anthropometric data of HPN patients, days of therapy and formulation of nutritional mixtures were routinely recorded by the practitioner nutritionist in a dedicated electronic database, at the first visit of each patient and updated at each clinical control visit. Data for the study were obtained from this dedicated database; no data concerning the appropriateness of care were examined.

Nutritional assessment and indications for PN

Nutritional assessment and indication for PN were applied according to the European Society for Clinical Nutrition and Metabolism (ESPEN) and the Italian Society of Artificial Nutrition and Metabolism (SINPE) guidelines.[3,8] PN was indicated in case of the impossibility to maintain an adequate nutritional status by enteral route only, reduced bowel absorbent function, impaired intestinal transit or mechanical bowel obstruction, severe bowel ischemia, short bowel syndrome, high-output jejunal or ileal fistulas.

Anthropometric measurements

Body weight and height were measured on a standard balance with an attached ruler. Body weight was measured at the nearest 0.1 kg and height at the nearest 1 cm. Body mass index was calculated as weight in kilograms divided by the square of height in meters.

Compounding of PN mixtures

The compounding of PPNMs was in agreement with the 'Good Manufacturing Practices' of Italian Pharmacopoeias[17] and guidelines of the 'Società Italiana di Farmacia Ospedaliera e dei Servizi Farmaceutici delle Aziende Sanitarie' (SIFO) for PN,[18] and was performed using an automatic filling system (CARETRONIC, B Braun Italia SpA, Mirandola, Italy) in a class A contamination area, achieved through the use of a horizontal laminar flow hood equipped with high-efficiency particulate air filters, in a controlled environment with filtrated air. Concentrate of trace elements was regularly added as a supplement in PPNMs. Multivitamin formula for infusion as lyophilized sterile powder was also added to the parenteral mixture immediately before the infusion or was administered separately by dissolving in physiological solution.

Industrial standard nutritional mixtures

Ready-to-use SPNMs were multichamber bags with three prefilled compartments to mix at the time of infusion. These were used off the shelf or as base for further aseptic additions, for example, vitamins, trace elements, glutamine, etc. The formulation of four industrial parenteral mixtures available at the Home Artificial Nutrition Unit of Federico II University Hospital, used for 230 HPN patients, ranged as follows: energy 1000–1900 kcal; fluid 1250–1920 ml; nitrogen 5.4–10.2 g; amino acid 34–72 g; glucose 97–225 g; lipids 50–75 g; sodium 32–75 mmol; potassium 24–52.5 mmol; magnesium 4–6 mmol; calcium 2–6 mmol; phosphorus 11–22.5 mmol. SPNMs of 750 mOsm/l were used either for peripheral or central venous access, whereas those with 1250 mOsm/l osmolarity were used only for central vein.

Statistical analysis

A *post hoc* statistical analysis of patient's data receiving HPN from January to December 2011 was performed using the Statistical Package for Social Sciences version 13 (SPSS Inc., Chicago, IL, USA). Results are expressed as mean ± s.d., median and range (minimum–maximum) or 95% confidence interval (CI). Non-parametric tests were used because variables were not normally distributed. Two-sided *P*-values <0.05 were always considered statistically significant.

RESULTS

In 2011, 298 patients (151 men, 147 women; age 17–87 years; body weight 34.0–105.6 kg; body mass index 12.6–40.6 kg/m^2) received HPN (115 received oral nutritional support in addition),[16] for a total of 14 772 PN mixtures delivered; of these, 10 161 (69%) were SPNMs and delivered to 230 (77.2%) patients, and 4611 (31%) were PPNMs and prescribed to 68 (22.8%) patients. Median HPN days of therapy per patient was 24 (range 8–357), in particular 40 (8–357) for PPNMs and 20 (9–302) for SPNMs. Number of patients, age, men/women ratio and days of parenteral therapy per underlying disease are reported in Table 1. Primary diseases, type of parenteral mixtures (PPNMs or SPNMs) received and days of HPN therapy are summarized in Table 2. Table 3 reports the mean and 95% CI (adjusted for body weight) of parenteral mixture components (compounded and industrial) prescribed to the 298 HPN patients; for patients whose formulation was modified over time, average value was used. When comparing PPNM and SPNM formulations, all constituents resulted statistically different ($P<0.01$, Mann–Whitney test), except for the total calorie amount. In particular, average daily amounts of water, nitrogen, amino acids, glucose, sodium, potassium, magnesium and calcium were significantly greater in the compounded mixtures, whereas lipids and phosphates were significantly lower. Table 4 shows nutrients in parenteral mixtures (compounded and industrial) per kg body weight per day prescribed in all patients, classified according to their primary disease. Except for glucose and potassium, in cancer patients significant differences were found between all other components of PPNMs ($n=47$) when compared with SPNMs ($n=186$). In CIF patients, fluid, nitrogen, amino acids, sodium, potassium, magnesium and calcium were statistically different when comparing PPNMs ($n=16$) with SPNMs ($n=18$) ($P<0.01$, Mann–Whitney test), as well as glucose ($P<0.05$, Mann–Whitney test). In patients grouped as having 'other

Table 1. Number of patients, age, sex and HPN days of treatment of 298 patients (151 men, 147 women) followed in 2011, classified according to their primary disease

Primary disease	*No. of patients (%)*	*Age (years), mean ± s.d.*	*Men/ women*	*Days of therapy median and (range)*
Cancer	233 (78.2)	63 ± 12	122/111	20 (8–303)
CIF	34 (11.4)	55 ± 16	18/16	65 (9–357)
Other diseases	31 (10.4)	59 ± 20	11/20	20 (9–268)

Abbreviations: CIF, chronic intestinal failure; HPN, home parenteral nutrition. Other disease: see Patients and Methods section.

Table 2. Type of parenteral mixture (compounded or industrial), number of patients and HPN days of treatment in 298 patients followed in 2011, classified according to primary disease

Primary disease	*PPNMs No. of patients Days of therapy, median (range)*	*SPNMs No. of patients Days of therapy, median (range)*
Cancer	47 24 (8–303)	186 16 (9–296)
CIF	16 214 (12–357)	18 43 (9–302)
Other Diseases	5 17 (9–169)	26 22 (9–268)

Abbreviations: CIF, chronic intestinal failure; HPN, home parenteral nutrition; PPNMs, personalized parenteral nutrition mixtures; SPNMs, standard parenteral nutrition mixtures. Other disease: see Patients and Methods section.

diseases', fluid, sodium, magnesium and phosphorus in PPNMs ($n = 5$) significantly differed when compared with those in SPNMs ($n = 26$) ($P < 0.01$, Mann–Whitney test). Finally, in the 68 HPN patients receiving compounded mixtures, the formulation changed from 1 to 28 times during the 12-month period of follow-up and, as shown in Table 5, the most frequent variations were for CIF patients. On the other hand, only 5 out of 230 patients receiving SPNMs required formulation modifications and these changes ranged between 1 and 2 in a year.

DISCUSSION

HPN reduces hospitalization rate and significantly decreases the National Health Service expense, as well as allowing patients to live within their family and to return, at least in part, to usual living habits.[16,19,20] In 2011, 298 HPN patients were followed at the Home Artificial Nutrition Unit of Federico II University Hospital in Naples. As expected, most HPN patients suffered from cancer, while CIF patients received HPN for the highest number of days. Generally, for most cancer patients, PN was prescribed intermittently, mainly during cycles of radio- or chemotherapy, while CIF patients needed a continuous lifelong HPN supplementation. Patients grouped as having 'other diseases' were generally treated continuously, until their therapeutic goal was achieved.

When compared with PPNMs, ready-to-use SPNMs have a reduced risk of contamination during preparation, lower costs (cost-saving for pharmacy laboratories) and extended shelf life.[21,22] Moreover, a wide range of macronutrient concentrations and volumes are also available, as well as the possibility, depending on the osmolarity, to be infused through central or peripheral venous accesses. Our data support these findings; 77% HPN patients received SPNMs with several benefits on clinical outcomes. However for selected patients (23% of HPN patients), in particular for most CIF patients and for some cancer and 'other diseases' patients, the practitioner nutritionist prescribed PPNMs. The majority of parenteral industrial mixtures allows the addition of electrolytes; alternatively, patient needs could be satisfied by an additional infusion therapy, both of which however are endangered by a high risk of contamination.

Our analysis showed that 47% CIF, 20% cancer patients and 16% patients grouped as having 'other disease' were treated with PPNMs for the necessity of frequent changes in the formulation of the mixtures or to satisfy patients' nutritional needs until clinical and metabolical stabilization were reached. This was true, in particular, in CIF patients.

When possible, an oral nutritional support was added to the PN prescription to encourage 'enterocyte feeding' for a potential weaning off PN. Out of 115 patients on HPN plus oral nutritional support, 16 (14%) received personalized mixtures. Of these, 14 were cancer patients and 2 CIF patients. As regards the formulation changes, patients receiving PPNM plus oral nutritional support were metabolically more stable than the others (16 patients: mean 1.6 (range 1–8) changes vs 52 patients: mean 3 (range 1–28)). Nonetheless, in both groups, the composition of personalized mixtures could not be replaced by the standard ones.

This study does not deal with the possible different outcomes when using compounded or standard mixtures. A stimulating analysis on the costs and on the infection rate resulting from the administration of personalized compounded parenteral nutritional mixtures have already been reported in literature, showing that SPNMs are associated with lower costs than PPNMs with regard to both PN acquisition and potential risks of bloodstream infections.[21,22]

Table 3. Daily nutrients' composition of parenteral (compounded or industrial) mixtures, per kg of body weight, prescribed in 298 HPN patients followed in 2011 at Federico II Home Artificial Nutrition Unit (mean and 95% confidence interval)

Nutrient	*PPNMs* n = *68* *Mean (95% CI)*	*SPNMs* n = *230* *Mean (95% CI)*
Calories (kcal/kg per day)	21 (19–23)	23 (22–24)
Fluid (ml/kg per day)	38 (34–41)[a]	30 (29–31)
Nitrogen (g/kg per day)	0.16 (0.14–0.17)[a]	0.12 (0.11–0.13)
Amino acid (g/kg per day)	1.04 (0.94–1.13)[a]	0.78 (0.74–0.81)
Glucose (g/kg per day)	2.8 (2.5–3.1)[a]	2.3 (2.2–2.4)
Lipids (g/kg per day)	0.7 (0.6–0.8)[a]	1.1 (1.0–1.1)
Sodium (mmol/kg per day)	1.9 (1.6–2.2)[a]	0.8 (0.7–0.8)
Potassium (mmol/kg per day)	0.73 (0.57–0.90)[a]	0.55 (0.53–0.58)
Magnesium (mmol/kg per day)	0.16 (0.13–0.18)[a]	0.08 (0.08–0.09)
Calcium (mmol/kg per day)	0.09 (0.07–0.10)[a]	0.05 (0.04–0.05)
Phosphorus (mmol/kg per day)	0.19 (0.14–0.24)[a]	0.25 (0.24–0.26)

Abbreviations: CI, confidence interval; HPN, home parenteral nutrition; PPNMs, personalized parenteral nutrition mixtures; n, number of patients on HPN treated by compounded or industrial mixtures; SPNMs, standard parenteral nutrition mixtures. [a]Significant difference with industrial mixture ($P < 0.01$, Mann–Whitney test).

Table 4. Nutrients (per kg of body weight per day) in parenteral mixtures (compounded or industrial) prescribed for HPN patients, classified according to their primary disease

	Cancer		*CIF*		*Other diseases*	
	PPNMs (n = *47*)	*SPNMs* (n = *186*)	*PPNMs* (n = *16*)	*SPNMs* (n = *18*)	*PPNMs* (n = *5*)	*SPNMs* (n = *26*)
	Mean (95% CI)		*Mean (95% CI)*		*Mean (95% CI)*	
Calories (kcal/kg per day)	19 (16–21)[a]	22 (21–24)	26 (20–31)	24 (21–27)	24 (15–33)	22 (19–26)
Fluid (ml/kg per day)	34 (30–37)[b]	30 (28–31)	47 (39–55)[a]	29 (26–33)	44 (28–60)[a]	30 (25–34)
Nitrogen (g/kg per day)	0.14 (0.13–0.16)[a]	0.12 (0.11–0.12)	0.19 (0.16–0.23)[a]	0.13 (0.11–0.15)	0.16 (0.03–0.30)	0.12 (0.10–0.14)
Amino acid (g/kg per day)	0.94 (0.84–1.04)[a]	0.77 (0.73–0.81)	1.28 (1.04–1.51)[a]	0.85 (0.72–0.98)	1.06 (0.16–1.96)	0.76 (0.64–0.88)
Glucose (g/kg per day)	2.5 (2.2–2.8)	2.3 (2.1–2.4)	3.4 (2.6–4.3)[b]	2.5 (2.1–3.0)	2.9 (1.5–4.2)	2.2 (1.9–2.6)
Lipids (g/kg per day)	0.6 (0.5–0.7)[a]	1.1 (1.0–1.1)	0.8 (0.6–1.1)	1.1 (1.0–1.2)	1.0 (0.6–1.4)	1.1 (0.9–1.2)
Sodium (mmol/kg per day)	1.6 (1.3–1.8)[a]	0.8 (0.7–0.8)	2.8 (2.1–3.5)[a]	0.8 (0.7–1.0)	2.0 (1.2–2.8)[a]	0.7 (0.6–0.9)
Potassium (mmol/kg per day)	0.5 (0.4–0.7)	0.6 (0.5–0.6)	1.4 (1.0–1.8)[a]	0.6 (0.5–0.7)	0.4 (0.0–1.3)	0.5 (0.4–0.6)
Magnesium (mmol/kg per day)	0.11 (0.09–0.13)[b]	0.08 (0.08–0.09)	0.25 (0.17–0.33)[a]	0.09 (0.08–0.10)	0.23 (0.08–0.38)[a]	0.08 (0.07–0.09)
Calcium (mmol/kg per day)	0.07 (0.06–0.08)[a]	0.05 (0.05–0.05)	0.14 (0.11–0.17)[a]	0.06 (0.05–0.07)	0.08 (0.04–0.12)	0.05 (0.04–0.06)
Phosphorus (mmol/kg per day)	0.13 (0.09–0.16)[a]	0.24 (0.23–0.26)	0.38 (0.28–0.49)	0.27 (0.23–0.31)	0.07 (0.00–0.21)[a]	0.24 (0.21–0.28)

Abbreviations: CI, confidence interval; CIF, chronic intestinal failure; HPN, home parenteral nutrition; n, number of patients on HPN treated by compounded or industrial mixture; PPNMs, personalized parenteral nutrition mixtures; SPNMs, standard parenteral nutrition mixtures. Mean and 95% CI. [a]Significant difference with industrial mixtures in the same patients's group ($P < 0.01$, Mann–Whitney test). [b]Significant difference with industrial mixtures in the same patients's group ($P < 0.05$, Mann–Whitney test).

Table 5. Mean and range of the formulation changes and days of treatment (median and range) in the compounded formulation for 68 HPN patients followed in 2011, classified according to primary disease

Primary disease	*Formulation changes Mean (range)*	*Days of treatment Median (range)*
Cancer ($n = 47$)	2 (1–5)	24 (8–303)
CIF ($n = 16$)	6 (1–28)	214 (12–357)
Other diseases ($n = 5$)	3 (1–9)	17 (9–169)

Abbreviations: CIF, chronic intestinal failure; HPN, home parenteral nutrition; n, number of patients on HPN treated by compounded mixtures.

In conclusion, the study does not answer the important question of whether personalized mixtures for PN are more appropriate than standard ones, at least in specific clinical conditions. Although this study is only an illustration of current practice patterns, it demonstrates that in some selective cases PPNM composition is different from the standard ones, in particular when the patient is clinically and metabolically instable.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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