ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Standard versus individualized parenteral nutrition

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A R T I C L E I N F O

1. Methods

Literature search
Timeframe: New publications from 2004 until December 2014 were included. Relevant "older" historic references related to these were also considered. A second literature search for RCTs and significant publications was conducted until the end of November 2016.

Type of publications: Randomized trials, observational studies (case-controls, prospective cohort studies, time series, and retrospective data), meta-analyses, and systematic reviews.

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Table: Recommendations for standardized versus individualized parenteral nutrition (PN)

R 13.1	Standard PN solutions should generally be used over individualized PN solutions in the majority of pediatric and newborn patients, including VLBW premature infants (LOE 2 in premature infants and LOE 3 in children, RG 0, Conditional recommendation for)
R 13.2	Individually tailored PN solution should generally be used when the nutritional requirements cannot be met by the available range of standard PN formulations (i.e. in very sick and metabolically unstable patients such as those with abnormal fluid and electrolyte losses; and in infants and children requiring PN for prolonged periods such as those with short bowel syndrome (LoE 2, RG B, Strong recommendation for)
R 13.3	Computerized prescription, whether standardized or individualized, should be used in the ordering process of PN when possible (LoE 2+, RG B, Strong recommendation for)

Key words: Standard parenteral nutrition, individualized parenteral nutrition, individually-tailored or prescribed parenteral nutrition, computerized prescription, premature or preterm infants, very-low-birthweight infants, pediatric patients, infants, children.

Language: English

Search: Searches were performed in three stages. First, all the titles on the relevant key words were retrieved. Members of the Working Group subsequently read all the titles and abstracts, and selected potentially relevant ones. These were retrieved and full articles were assessed.

2. Introduction

PN can be provided as a standard, usually commercial, formulation that is designed to meet the nutritional needs of most patients of the same age group with a similar condition. The aim of standardizing parenteral nutrition (PN) is to improve patient safety (minimize procedural incidents) and optimize resource efficiency at the same time as providing clinically appropriate nutrition (meeting individual patient requirements) [1].

Alternatively, an individually tailored PN formulation, adapted to the individual patient's nutritional needs, can be prescribed. Both types of PN preparations have advantages and disadvantages. Stability of the final product, time pressures on the pharmacy, quality control and cost benefit considerations make the use of standard solutions an attractive option. These standard formulas do not necessarily meet all the requirements of newborns, infants and children [2,3], although even in those units that rely on individualized prescribing, there is some scope for their use in stable patients [4].

The following questions were addressed regarding standardized versus individualized PN:

- Can Standard PN cover the needs of all paediatric patients?
- Is it essential to use computerized prescription?
- Should Standard PN be preferred over individualized PN?
- Can Standard PN be ordered for long periods of time?

Table 1 summarizes studies comparing standardized vs. individualized PN in neonates, infants and children based on their level of evidence. In general, there are very few randomized controlled studies, and unfortunately these are relatively small or methodologically problematic. Overall the level of evidence is low and this is reflected in the strength of our statements and recommendations.

3. Individually prescribed parenteral solutions

The main advantage of individually prescribed PN solutions is that these are tailored to suit a specific patient, and to provide optimal nutrition, assuming that all nutrients are delivered in a safe and bioavailable manner. The prescription can be changed on a daily basis, reflecting the patient's medical condition and most recent laboratory tests [4]. In contrast to individualized prescriptions, standardization carries the risk of turning into "cookbook medicine" that lacks continuous clinical judgment of the patients' changing nutritional requirements. This risk may be increased when the patient is a tiny fragile very-low-birth-weight (VLBW) premature infant with very high nutritional requirements and at risk of developing significant nutrient deficits and sometimes life-threatening, metabolic disturbances (e.g. hypo- or hyperglycemia, hypo- or hypernatremia, hypo- or hyperkalemia). Studies in VLBW infants as well as in pediatric patients suggest that compared to infants on standard PN, infants given individually tailored PN received more optimal nutrition, achieved better growth without clinical or laboratory complications, had a shorter period of exclusive PN and required fewer electrolyte corrections [5—7]. A randomized controlled study comparing individualized versus standard PN formulation in premature infants demonstrated higher intakes of amino acids, lipids and energy, with greater weight gain in the group receiving individualized PN [6]. However, the difference in caloric intake and weight gain may not have been attributable to the administration of standard solutions per se, but to the more intensive monitoring assisted by pharmacists in the group receiving individualized PN. Some authors have suggested that individualized PN preparations are more optimal for the current more aggressive nutritional approach to PN in VLBW infants [7]. Yet, these authors admit that the currently available standardized PN admixtures with adequate nutritional composition should be considered as appropriate alternatives. This is in contrast to "historical" standardized PN solutions that did not meet all the nutritional requirements of neonates, and could have resulted in inadequate nutrition and poor growth if used for longer periods [2].

4. Standard parenteral solutions

R 13.1	**Standard PN solutions should generally be used over individualized PN solutions in the majority of pediatric and newborn patients, including VLBW premature infants (LOE 2 in premature infants and LOE 3 in children, RG 0, conditional recommendation for, strong consensus)**
R 13.2	**Individually tailored PN solution should generally be used when the nutritional requirements cannot be met by the available range of standard PN formulations (i.e. in very sick and metabolically unstable patients such as those with abnormal fluid and electrolyte losses; and in infants and children requiring PN for prolonged periods such as those with short bowel syndrome (LoE 2, RG B, strong recommendation for, strong consensus)**

A study comparing short term standard solution (fixed amino acid/glucose ratio) with a computer generated individualized prescription, taking enteral intake and additional fluids into account, did not find any differences in the weight gain of premature infants [8]. Furthermore, in a study that evaluated the use of standard PN solutions in a pediatric intensive care unit, it was found that standard PN orders could be used in the majority of the patients. These solutions were usually nutritionally adequate and the intake of most macronutrients and electrolytes was similar to

Table 1

Summary of studies on standardized and individualized PN in neonates, infants and children. Following the methodology of previous reviews [1,18,38]. Adapted for the pediatric population and updated − December 2014.

Author (year)	Patients	Intervention	Design	Results	Comments
LOE 1 + or 1++: Large randomized trials or systematic reviews with clear-cut results					
None					
LOE 1−: Small or large randomized trials or systematic reviews with uncertain results or flaws in study design					
Cade (1997) [8]	Premature infants − median GA 29 wks	STD (n = 25) vs. IND (n = 27). IND was computer-assisted regime	Prospective RCT	There were no differences in daily weight gain; biochemical stability (as indicated by plasma Na and P); or PN solution wastage	Both regimes prescribed electrolytes as per kg/day
Level 2+: Nonrandomized, contemporaneous controls					
Mutchie (1979) [5]	Pediatric hospital patients	STD solutions (n = 26) vs. IND (n = 26). IND was individualized by use of minicomputer and monitored by a pharmacist. Six patients in each group were neonates ≤35 days on PN only for 8−20 days	Nonrandomized contemporaneous controls	IND longer PN duration and rate of use (+31%), but lower costs (−44.10$ per TPN course). IND better weight gain (17 g/day vs. 4 g/day in STD) (p < 0.05) for the 6 neonates	Pharmacist monitoring of TPN only in IND group
Dice (1981) [6]	Premature infants − mean GA 31 wks	STD (1 formula) (n = 14) vs. IND (n = 14)	Nonrandomized contemporaneous controls (patients assigned alternatively to groups)	IND better weight gain (11.8 vs. 4.9 g/day) (p < 0.02) IND better intake of: (1) protein (2.2 vs. 1.9 g/kg/day) (p < 0.01); (2) Calories (62 vs. 52 kcal/kg/day) (p < 0.001); (3) Lipids (2.0 vs. 1.5 g/kg/day) (p < 0.001) But, in IND also greater costs	STD PN facility developed. IND both individualized and pharmacist-monitored
Krohn (2005) [9]	Pediatric ICU − ages 3 months to 18 years (n = 46). (Lack of demographic data)	STD (8 formulas) (226 prescriptions) (68%) vs. IND (111 prescriptions) (32%)	Observational study (8 months) based on record review. Descriptive results. No statistical analysis	54% of patients receiving STD PN required nutrient modifications Na, Ca and P lower but AA higher in IND vs. STD in patients <10 kg P not given in 20 of 57 IND PN More electrolytes imbalances in IND vs. STD (34% vs. 26%)	STD PN originally prepared in the hospital pharmacy, but modifications were performed by nurses under laminar flow hood on the ward. IND formulations were prepared by nurses under laminar flow hood on the ward area
Skouroliakou (2009) [13]	Preterm neonates (28−36 weeks) − mean GA − 33.9, mean BW − 2100 g − with respiratory failure	STD (computer-based) (n = 30) vs. IND (manually calculated by neonatologists) protocols	Nonrandomized contemporaneous controls (patients were pair-matched by GA and clinical condition)	STD protocols provided more: energy (111 vs. 89 kcal/kg/day) (p = 0.05); protein (AA 1.70 vs. 1.33 g/kg/day) (p = 0.023); and calcium (2.02 vs. 1.01 mEq/kg/day) (p < 0.001) Infants in STD group gained weight better during PN (+44 g) vs. IND (−53 g) (p = 0.002) At the end of PN, STD infants had some better CBC values (MCV & MPV)	Four STD protocols based on ASPEN guidelines (1993−7) prepared by automatic compounder supervised by pharmacist. IND manually calculated and prepared under pharmacist supervision
LOE 2−: Nonrandomized, historical controls					
Yeung (2003) [10]	Premature neonates GA < 33 wks	STD (2 formulas) (n = 27) (2000 −1) vs. IND (n = 31) (1999 −2000)	Retrospective observational study (nonrandomized historical controls)	Intake of protein better in STD in each of the days (2−7) and cumulative for the first week (13.6 vs. 9.6 g/kg/wk) (p < 0.05) STD received more Ca (1.25 vs. 0.95 mmol/kg) and P (1.25 vs. 0.95 mmol/kg) on days 4 −7 (p < 0.02), but less Mg Significant cost reduction STD 88 vs. IND 130 AUD per bag	STD PN commercially batched produced. IND prepared in the pharmacy
Lenclen (2006) [11]	Premature neonates GA < 32 wks	STD (3 formulas) (n = 20) (2003) vs. IND (n = 20) (2001)	Retrospective observational study (nonrandomized historical controls)	Intakes better in STD on Day 3: (1) AA (1.5 vs. 0.9 g/kg/day) (p = 0.0001); (2) CHO (10.7 vs. 9.6 g/kg/day) (p = 0.002); (3) Ca:P ratios better balanced (p = 0.0001)	STD PN prepared in sterile isolator in pharmacy. IND prepared by nursing staff under laminar airflow hood

Table 1 (*continued*)

Author (year)	Patients	Intervention	Design	Results	Comments
Smolkin (2010) [7]	Premature VLBW (BW ≤ 1500 g) neonates	STD (n = 70 cohort in 2000–1) vs. INS (n = 70 cohort in 2006–7). (5 STD formulations)	Retrospective observational study (GA-matched historic controls)	Cumulative intake of AA at first week better in STD (13.6 vs. 11.1 g/kg/wk (p = 0.0003) IND group showed significantly greater daily weight gain during NICU stay (23.76 vs. 20.27 g/day) (p < 0.0001). IND group showed significantly greater weight gain SDS (standard deviation scores) at 1st week (p = 0.036) and over the 1st month of life (p = 0.0004); and had higher discharge weights (2627 vs. 2434 g) (p = 0.001) and discharge weight SDS (p = 0.012). IND had also better FOC SDS at discharge (p = 0.006) IND infants received higher mean daily caloric intakes (75 vs. 53 kcal/kg/day) (p < 0.0001), as well as higher mean daily protein, glucose and fat intakes (p < 0.0001 for all intakes) compared to STD PN IND had significantly shorter durations of exclusive PN (5.6 vs. 7.9 days) (p = 0.007) and needed less electrolyte corrections (p = 0.003)	IND infants had significantly lower mean BW All intakes (energy, AA, CHO and fat) were significantly lower with STD formulations. STD data reflects nutritional practices 6 years earlier. Authors admit that IND PN was in accordance with the current more aggressive nutritional approach to VLBW infants, and that STD PN with adequate compositions (as opposed to their STD formulations) may offer appropriate alternative to IND PN in VLBW
Iacobelli (2010) [12]	Premature neonates GA < 33 wks	STD (n = 67 cohort in 2006–7) vs. IND (n = 40 cohort in 2006). (8 STD formulations for days 1–7)	Prospective observational study (non-randomized historic controls)	STD group received during the 1st wk of life significantly more: energy (64 vs. 56 kcal/kg/day) (p < 0.001); AA (2.2 vs. 1.8 g/kg/day) (p < 0.001); glucose (10.4 vs. 9.8 g/kg/day) (p < 0.01); lipids (1.7 vs. 1.3 g/kg/day) (p < 0.001); Na (1.48 vs. 0.93 mmol/kg/day); and less volume/water (125 vs. 131 ml/kg/day) (p < 0.05) compared to IND. Nonoliguric hyperkalemia was significantly less frequent in STD compared to IND (2.9% vs. 20.0%) Weight loss (% of BW) at DOL # 7 was significantly reduced in STD (4.2%) vs. IND (7.7%)	IND prescriptions prepared with the help of computer system. STD orders based on ESPEN/ESPGHAN guidelines 2005. STD bags prepared by a commercial manufacturer
Caba Porras (2010) [14]	Children > 1 yr, or > 10 kg; Mean age 6.8 yrs (1–14), weight 26.6 kg (9–50) (From 2006 to 2008)	N = 47 children, 539 units of PN STD (83%): n = 39, 437 units IND: n = 8, 102 units	Retrospective observational	STD: Total energy requirements reached within 1–3 days using 1–3 types of formulas. Only 4% (22) modified with easily feasible changes: volume increase (16), glucose lowering (3), K increase (3) IND: The same trends, but caloric intake lower than 33% of recommended	STD PN meet nutritional requirements in most patients with adaptability and versatility to morbidity. STD eased prescription-validation and preparation and improved efficiency
Doublet (2013) [15]	Newborns admitted to NICU on DOL#1 and required TPN	3500 PN prescriptions evaluated	Retrospective observational study comparing two one-year periods before and after move from individualized to standardized formulations	The TPN goals for newborns in the first 2 wks of life (as defined and written in the NICU policy) were better full filled with STD PN compared to IND (44.0% vs. 9.4% of the prescriptions). Differences appeared as early as DOL#3 and remained during the first 15 days on PN	Goals defined by TPN goals for newborn of this university hospital unit
Bolisetty (2014) [39]	Preterm neonates GA < 32 wks N = 153 divided into pre (N = 68) & post-consensus (N = 85) groups	New STD PN formulations implemented in July 2011 [17]	Before-after intervention study	New consensus STD PN solutions provided better protein intake in the first 7 days and were associated with greater weight gain in the first 4 weeks Post-consensus group in comparison to pre-consensus cohort: • Commenced PN earlier (6 vs. 11 h, p = 0.005);	Before and after study, old vs. new STD solutions, in a small population (n = 153) Comparison to either IND PN solutions and/or each NICU's own STD PN solutions Some of the results might have been attributed to the change in

				• Had higher protein intake on days 1–7 (up to 3.55 vs. 2.35 g/kg/day, p < 0.001); • Had higher caloric intake on days 1–3 (p = 0.03); • Had less daily fluid intake on days 3–7 (p = 0.02); • Had reduced duration of lipid therapy (p = 0.01); • Had a significantly greater weight gain in the first 4 weeks (p = 0.003). Protein intake on DOL#1 was below the consensus goal of 2 g/kg/day Safety – OK	PN practices dictated by the new consensus guidelines More SGA infants in post-consensus group (with twice more SGA infants in the "Before" group) Effect of enteral and PN nutrition pooled together, along with limitations related to the lack of complete enteral and PN intake data from birth to discharge to determine any improvements or variation between the cohorts Significant increase of protein and energy intake without real clinical benefit
LoE 3: Case series, uncontrolled studies, surveys					
Devlieger (1993) [40]	VLBW Neonates (≤1500 g)	STD (a single PN formulation with fixed amount of nutrients in four dilutions with water to a fluid load of 90, 110, 130 or 170 ml/kg/day). Multivitamins and fat emulsions given separately	Observational	Weight gain similar to the normal fetal weight gain in utero. STD presents advantages in terms of safety, availability, ease of application, and lower production costs. No significant complications recorded	No comparison to control patients on IND PN
Beercroft (1999) [4]	Neonates – Median GA 29 wks, median BW 1080 g	148 IND PN prescriptions over 4-wks period were compared to computer-recommended STD protocols	Observational	82% of PN prescriptions deviated from protocol (in relation to nutrients: CHO 61%, AA 7%, fat 0, Na 52%, K 9%, P 53% and Ca 24%); But only 44% of these changes were prompted by abnormal lab results (Na13%, K 53%, Ca 4%, P 69%) Authors estimated that up to 2/3 of PN orders could be given as a range of STD PN solutions	Only comparison of IND vs. STD PN formulations recommended via a single specific computer program. Authors conclude that a higher proportion of PN solutions could be standardized if the computer regimes were modified to reflect current practices in the NICU
Bethune (2001) [2]	Neonates, infants and children	Comparison of STD PN formulations to recommended intakes (in neonates and infants 2 leading university hospitals' standards; and in children 2 commercially available standards)	Survey of STD PN solutions in the UK	With adequate nutritional monitoring commercially available STD can be used safely for children > 1 yr for short periods if biochemical deficiencies corrected by addition of electrolytes No commercially available STD for PN in neonates and infants, commonly resulting in inadequate provision of nutrition to these patients with potentially serious consequences	Recommendations: Increase training in PN compounding and clinical nutrition Preparation of commercially available, licensed STD bags suitable for neonates and infants, as well as next-day service for IND formulations from a small number of specialist centers for those in need
Lapillonne (2009) [41]	National survey in France in 296 neonatal departments	STD PN were used in 66% of units and accounted for 45% of PN prescriptions. Significantly more in Level II than Level III (68% vs. 24%) (p < 0.0001)	Survey	13 of the 40 STD PN solutions for neonates did not contain AA The addition of macro- and/or micronutrients was very frequent	Great heterogeneity in PN practices Large number of STD PN solutions were not appropriate for the nutrition of full-term and/or preterm infants
Rigo (2013) [16]	1. Single center – cohort of VLBW neonates – Mean GA 28.5 wks, mean BW 1005 g 2. Multi-center (phase III) non-comparative study of preterm (<37 wks) neonates – Mean GA 31.2 wks, mean BW 1382 g	Binary premixed RTU STD PN solution from pharmacy hospital (n = 102) Commercially premixed 3-chamber STD PN bag (n = 97)	Observational	1. Nutritional intake was in line with the most recent updated recommendations for AA and energy intakes (2.5 and 45 on Day 1 increasing to > 3.5 g/kg/day and >100 kcal/kg/day at the end of the 1st week). Postnatal weight loss ≤6% limited to 1st 3 days with mean return to BW by 7 days	Cumulative nutritional deficit and postnatal growth restriction can be abolished, even in ELBW infants, by using STD premixed RTU PN solutions STD PN formulations give answer to the need for well-

Table 1 (continued)

Author (year)	Patients	Intervention	Design	Results	Comments
				2.10 infants required additional AA in the 1st 2 days. & infants received additional glucose. 65 required additional electrolytes (Mainly Na) and minerals. Mean protein & energy were in the range of recommendations. Weight gain during PN was positive especially in those included early, close to birth	balanced PN with high AA from the 1st day of life in VLBW infants Commercial premixed 3-chamber STD PN bags (with possibility to activate also the lipid component in the same bag) are easy to use, practical for handling and well-accepted by nurses, pharmacists and neonatologists, compared to RTU compounded bags and tailored premixes without any serious adverse events
McCarthy (2016) [42]	VLBW infants	Over 5 months all IND PN prescriptions for VLBW infants ≤ 31 weeks from DOL#2 on were compared to the STD appropriate for use on the day in question	Observational	VLBW infants prescribed IND PN received significantly more AA (28%), glucose (6%), energy (11%) and calcium (8%) from the aqueous phase of PN than they would have received if given a similar volume of STD PN. These benefits were seen over all the days for which PN was administered	Modifications of the STD PN formulations that have been used for comparison to IND PN in this study would probably result in better STD PN formulations that could change the conclusions of this study
Kriessl (2016) [43]	VLBW (≤1500 g) preterm infants (N = 71)	Observational study	Comparison of IND (using the new prescription software catoPAN, Cato Software Solutions) vs. STD (Numeta, "ready-to-use" triple-chamber container, Baxter) PN prescriptions	Protein intake in STD PN was significantly lower than in IND prescribed PN solutions, and below the recommendations for daily supply during the first days of life Energy intake was significantly higher with Numeta, but energy, carbohydrate, and fat intakes were satisfying The protein-energy relation in Numeta is not well balanced Numeta provided inadequate high intake of electrolytes for the first day of life and also during the transition phase Numeta as a STD commercial PN save human resources (shorter preparation time), but bags of this STD PN cost higher than STD	Single center Small sample: 374 prescriptions in a small population (n = 71) Most prescriptions studied were for preterm infants with BW > 1000 g (n = 333) (BW ≤ 1000 g [n = 41]) The conclusion of the authors was that Numeta is an alternative to IND PN in infants with BW > 1000 g and an enteral feeding volume of approximately $^1/_3$ of the total daily intake

AA = amino acids; BW = birth-weight; CHO = carbohydrates; DOL = day of life; ELBW = extremely-low-birth-weight (BW ≤ 1000 g); FOC = fronto-occipital circumference (head circumference); GA = gestational age; ICU = intensive care unit; IND = individualized; NICU = neonatal ICU; PN = parenteral nutrition; RCT = randomized controlled study; RTU = ready to use; SDS = standard score deviations; STD = standardized; TPN = total PN; VLBW = very-low-birth-weight (BW ≤ 1500 g).

those from individually prescribed PN [9]. In fact, calcium and phosphate intakes were better with standard PN compared to the individualized PN, and electrolyte imbalances occurred less frequently [9]. Another study retrospectively evaluated the difference in nutrient intakes and biochemical responses in premature infants who received standardized versus individualized PN between days 2–7 of life. In that study, there was no clinical advantage or improved biochemical control with individualized PN regimes [10]. An increase in protein intake was observed in the standardized PN group, accompanied by proportional increases in the intakes of glucose, electrolytes and acetate. It was also found that in infants who were on standardized PN, the cumulative deficit in protein intake by the end of the first week was 35% less compared to those who were on the individualized regimes. Infants on standardized PN also had higher intakes of calcium and phosphate, resulting in less cumulative deficits and better bone mineralization [10]. Lenclen et al. also showed that in premature infants standardized PN formulations provided higher early intakes of amino acids and glucose, and better calcium phosphate ratio during the first week of life, while maintaining the same biochemical parameters [11]. More recently, studies in preterm infants have shown that PN using standardized formulations resulted in better intakes of protein, energy, glucose and calcium with less water intake and decreased incidence of significant electrolyte disturbances [12,13]. Furthermore, nutritional goals of preterm infants and children could be successfully met using standardized PN formulations [14–16]. Recently, the Australasian Neonatal Parenteral Nutrition Consensus Group agreed that standardized PN offers advantages over routine individualized PN in terms of providing adequate nutrition for the majority of neonates in neonatal intensive care units without significant alteration in biochemical responses, and with the potential for reduced cost and prescription error. These conclusions are based on five different ready-to-use binary solutions for preterm infants and one for term neonates [17].

Based on the above, it is suggested that a standardization strategy should be considered as part of the approach for improving quality control and good professional practice for the preparation of PN solutions. Batch-produced standardized PN bags can be readily available as ward stock in neonatal intensive care units, thus allowing initiation of PN immediately after the delivery of a premature infant [16]. Overall, readily available standardized PN solutions are advantageous compared to individualized prescriptions, by providing higher nutrient intakes that are associated with better weight gain and less nutritional deficits [18]. Commercially prepared standard PN bags decrease the risk of ordering errors, as well as the risk of compounding errors in the hospital pharmacy that has to deal with many different PN prescriptions on a daily basis. Large-scale commercial production of standard PN bags can be further facilitated by using automated compounding technology that can assure better pharmaceutical control of the physicochemical stability and compatibility of PN admixtures. This can decrease the risk of potentially adverse outcomes from infusion of incompatible nutrient admixtures (e.g. precipitated calcium phosphate) [19–21]. Large-scale commercial production of standard PN bags can also offer better aseptic manufacturing conditions than the average hospital pharmacy, thus decreasing the risk of PN-associated infections [2]. Commercially batch-produced standardized PN bags may also reduce the large costs of individualized PN production [22]. The need to add the parenteral multi-vitamins to the standard PN bag shortly before infusion is a limitation that requires proper handling to assure aseptic conditions and avoid errors. Also, the inclusion of various trace elements may shorten the shelf life of the standard bag.

5. Computer assisted prescribing

R 13.3	Computerized prescription, whether standardized or individualized, should be used in the ordering process of PN when possible (LoE 2+, RG B, strong recommendation for, strong consensus)

PN is an intravenous medication, with more than 50 ingredients and additives, and as such is liable to medication errors, especially in pediatric patients where all the calculations are weight-based [23]. The ordering process is time consuming, necessitates knowledge and experience, and involves the risk of fatal errors [23,24]. Development of an optimal PN order form, including age and weight-specific nutrient requirements with guidelines for advancing substrates may help the clinician especially if inexperienced, facilitating PN prescription and decreasing prescribing errors [25,26]. Computerized prescription may aid in maintaining stability and compatibility of PN solutions, which are safety issues of great concern [23]. The most significant pharmaceutical issues involve the stability of intravenous lipid emulsions and the compatibility of calcium and phosphate salts to avoid precipitates. The existence of a hospital nutrition support team, well-established communication channels between the prescribing clinicians and the pharmacy team dedicated to PN preparation, and the use of compounding devices decrease these risks, but does not abolish them [19–21,27].

Recent technology has enabled the development of advanced computerized PN ordering systems where the software is based on guidelines [28]. Such computerized nutritional software provides a low cost and easy to use method for correctly calculating nutrient dosages. Indeed, the use of a computerized prescription results in better growth and better biochemical control in newborn studies [23]. In addition, electronic ordering systems can still allow individualization of PN prescription, thus improving biochemical control and decreasing wastage. Computer assisted PN prescribing programs are a valuable educational tool for the junior clinician who is not experienced in clinical nutrition. These tools also facilitate communication between the prescribing clinical team and the pharmacy department [4]. Computer programs for ordering PN are widely used [23,24,29]. One such program reduced the time needed to calculate a nutrition plan from a mean of 7.1 min to 2.4 min, with errors in calculation being corrected interactively and reduced from 56% to 22% [24]. In another study it was found that automating the process of writing and delivering PN orders saved time and resulted in improved nutrient content of the PN solutions [30]. The time required to write and deliver PN orders was significantly lower using computer rather than manual methods (1.4 ± 0.2 vs. 4.5 ± 0.5 min; $P = 0.0001$), and the use of computer ordering lead to significant improvements in weight gain [31] and the nutrient composition of the PN for energy, protein, calcium, and phosphate [23,32]. In addition, alkaline phosphatase concentrations improved. This helped achieve caloric and protein intake goals earlier and improved mineral status in premature infants compared with the manual method of ordering [30]. Available programs can rapidly generate a nutrition plan with reduced likelihood of providing excessive glucose and energy [33].

However, in practice it has not been possible to confirm all the proposed advantages of individualized computer-assisted prescriptions in premature infants [8]. A possible disadvantage of a computer-based prescription program is that it might encourage trivial adjustments in PN prescriptions, based on laboratory results that in clinical practice are irrelevant [4]. Based on these

observations, it was suggested that a higher proportion of PN could be standardized, if modified to reflect the practice guidelines.

6. All-in-one multi-chamber standardized PN solutions

When standardizing PN solutions, the stock solutions may be two in one (proteins and dextrose while lipids are given separately) or all in one (bag containing protein dextrose and lipids). A recent study evaluated four all-in-one (AIO) standard pediatric PN solutions and found that their use was feasible and safe, although some may require electrolyte changes and a few patients still require individualized PN, especially for longer periods [34]. Other recent studies evaluated the efficacy, safety, flexibility, and ease of use of an industrially manufactured ready-to-use multi-chamber PN bag system containing three sterilized macro-nutrient solution chambers (for amino acids, glucose and optional lipid bag activation system) specially designed for administration not only to children [35] but also to preterm infants [16,18,36]. This technologically advanced multi-chamber PN bag system was easy-to-use, guaranteed sterility and longer shelf life, and provided well-balanced and safe nutritional support. Nutritional intakes and weight gain were within the recent PN recommendations for preterm infants.

7. Conclusions

Computer assisted prescribing software for PN should become readily available, as these programs can save time, decrease prescription and compounding errors, and improve the quality of nutritional care. Such computerized programs should guide the physician to the most adequate standardized solution and optimize the use of individualized solutions. The combination of computerized prescription and the use of multi-chamber PN bags may enhance the ability to rely on standardized PN with minimal usage of individualized prescriptions. Computerized prescription, whether standardized or individualized, should be used in the ordering process of PN where possible.

Standard PN solutions can be used safely in most pediatric and newborn patients, including VLBW premature infants, certainly for the short periods (up to 2–3 weeks) needed for most infants [18,37]. Standard PN solutions should generally be chosen over individualized PN solutions in the majority of pediatric and newborn patients, including VLBW premature infants.

A range of standard regimens to suit different clinical conditions should always be available. Adequate monitoring of the metabolic and nutritional status of an infant on standardized PN should be assured, and the most suitable available standard PN formulation for the infant's condition should be ordered at least once daily. Individually tailored PN solution should generally be used when the nutritional needs cannot be met by the available range of standard PN formulations (i.e. in very sick and metabolically unstable patients (such as those with abnormal fluid and electrolyte losses); and in infants and children requiring PN for prolonged periods (such as those with short bowel syndrome)). Uncritical use of standard formulations in such patients, particularly over longer periods of time, may be less than optimal for growth and development.

Conflict of interest

None declared.

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