How standardised are paediatric parenteral nutrition formulations in Europe?

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ABSTRACT

Background: Standardisation of parenteral nutrition (PN) formulae has several advantages in terms of safety and cost-efficiency, but individualised PN is still widely used for infants and neonates because their needs vary considerably.

Study objectives: To assess how standardisation of paediatric PN is managed in hospitals in Europe.

Method: A prospective survey was conducted in six European countries. A structured four-page questionnaire was forwarded to pharmacists in teaching and non-teaching hospitals in Belgium, France, Germany, Spain, Switzerland and the UK.

Results: Pharmacists in 51 hospitals replied; 22 hospitals (43%) use standard PN, mostly prepared in the pharmacy and principally used in neonatal patients. Addition of micronutrients to standard PN bags before administration occurred in 80% of the hospitals. Standard formulae are often dedicated to a specific use, e.g. first day of life in premature newborns, and composition of ingredients is mostly based on usual practice and prescribers’ knowledge. Twelve (24%) hospitals have a specific formula for the first day of life of premature newborns; however, there is great variation in their composition. None of these mixtures has an amino acid content that corresponds to the latest recommendations.

Conclusion: This survey suggests that standard PN is not widely used in paediatrics. Standard PN does not preclude additions just before administration, with the risks, e.g. errors, microbial contamination, related to this practice.

KEYWORDS

Neonatal, paediatrics, parenteral nutrition, standard

INTRODUCTION

The process of producing paediatric parenteral nutrition (PN) formulations is complex and can fail at any step from prescription to administration [1]. Standardising the PN process can be performed at different stages: by using standard protocols or sophisticated software that alert the prescriber directly and that can be connected to an automatic compounder at the pharmacy, or by producing standard formulations delivered in volumes tailored to the needs of individual patients or ready-to-use PN. Standardisation reduces prescribing and compounding time, limits the risk of errors and rationalises the production process [2, 3]. The American Society of Parenteral and Enteral Nutrition (ASPEN) encourages standardisation to reduce variation and promote uniformity [4]. Ready-to-use standard PN (i.e. without any additions after preparation) offers many advantages by reducing the risk of microbial contamination and compounding errors, and by facilitating initiation of PN as soon as it is needed, without any delay, because it will be available in the ward’s stock.

Despite these advantages, standardisation of paediatric PN is not well established in Europe. Considerable differences in compounding practice were observed in five European countries in a study investigating prescribing, compounding and administration practice with regard to PN, as well as the use of pre-prepared batch-manufactured standard PN [5]. About 43% of hospitals use a standardised PN process (standardisation at any stage of the process), mostly for neonates, whereas the others only use PN that is prepared for each patient [5].

In fact, different clinical and compounding problems are encountered in standardisation of PN for infants and neonates. The requirements in volume and nutrients vary greatly depending on age and weight. European guidelines on
paediatric PN published in 2005 provide recommendations for each nutrient, but the range is very broad for the same groups of patients [6]. Clinical status evaluation and physician experience and knowledge remain decisive factors when PN is prescribed. Moreover, compounding an admixture of PN with long-term stability is difficult, because of the instability of vitamins and lipid emulsion [7].

Some authors estimate that up to two-thirds of feeds could be covered by a standard PN formula in neonatal and paediatric intensive care units [8, 9]. In addition, another study found that standard PN for babies born very prematurely improves their nutritional intake during the first week of life compared with PN dispensed on an individual basis because the standard formula provides more energy and amino acids [10].

The present study describes a survey carried out in six countries to evaluate how standardisation of paediatric nutrition formulations is managed in European hospitals. Clinical and pharmaceutical practice regarding neonatal and paediatric standard PN were investigated; information was compiled about the composition of the different formulations. It is hoped that the results will help Geneva University Hospitals to elaborate a future strategy involving the development of standard PN.

**METHOD**

The survey was carried out in six European countries: Belgium, France, Germany, Spain, Switzerland and the UK. A questionnaire was developed and sent to lead pharmacists at hospitals in each country. These hospital pharmacists then forwarded the questionnaires to other hospital pharmacists throughout their countries who are involved in paediatric PN. The survey was conducted for three months from February to April 2007. The questionnaire was divided into three sections: general information about the hospital, information about PN (number per year, place of preparation and type of patients) and information about their standard PN process (number of formulations and their composition).

A descriptive analysis of the data was performed. Results are expressed as mean ± standard deviation. Geneva University Hospitals were not included in the survey.

**RESULTS**

Responses to the questionnaire were received from 51 hospitals: nine in Belgium, 14 in France, 12 in Germany, six in Spain, eight in Switzerland and two in the UK. Teaching (n = 28) and non-teaching hospitals (n = 23) were equally represented.

Twenty-two (43%) hospitals use standard PN, out of which 12 (24%) exclusively use standard PN; the remainder combine standard PN and PN specially prepared for individual patients. The general consumption of PN for all hospitals is more than 160,000 PN bags per year and standard PN represents 29% of the total amount. As shown in Figure 1, neonatal units are the major user of PN, with 56% of all PN, from which 40% are standard formulations.

PN is mainly prepared in the hospital pharmacy (78%). Six hospitals (12%) indicated that PN bags are prepared in the wards and five (10%) that production is subcontracted to an outside manufacturer.

The preparations for standard PN are mostly formulated based on knowledge and usual hospital practice (80% of hospitals). Literature data are used in 50% of the cases and only two hospitals base their formulations on a retrospective analysis of their own prescriptions.

On average 3.2 ± 2.5 (minimum one, maximum 12) standard PN formulations are available per hospital. Around two-thirds of these formulations are dedicated to neonatal use. Some of them are formulated for a specific use. For example, 12 hospitals have a standard PN for the first day of life of premature newborns. While all formulations contain glucose and calcium, variations exist in the type of nutrients and their concentrations (see Figure 2). Glucose concentration is quite similar in all formulations (from 8–12%) except one (18%). Amino acid content varies greatly (from 0.85–2.4%), with two formulations having none. The same variation is observed for electrolytes.

Specific formulations for day 2 (n = 6) and day 3 (n = 5) after birth, for peripheral administration (n = 2) or for the last day of PN (n = 1) are available in some hospitals.

![Figure 1: Distribution of individualised and standard parenteral nutrition in the 51 hospitals](image)
PN formulations are standardised in Western Europe. However, interpretation of the data is limited by the method used to send out the questionnaire. Results could have differed in hospitals not included in this survey and in other countries.

The number of standard PN formulations in each hospital shows a high variability, because formulations are often dedicated to a specific use, e.g. for the first day of life of premature newborns. One important finding is that formulations dedicated to similar patients have a large variability in their composition. Some formulations contain only one electrolyte (calcium) whereas others include up to six different ones. The mode of preparation of the formulations, mostly based on usual practice, and the broad recommendations for preterm neonates given by the European associations (minimum 1.5 g/kg/day, maximum 4 g/kg/day) [6] can explain this diversity. It is now well established that premature newborns require and tolerate high amounts of amino acids from the first day of life (2.5–3.5 g/kg/day) [12] as recommended by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN) in 2005 [6]. Nevertheless, the concentration of amino acids in the majority of these standard PN formulations is not in accordance with these recommendations. More formulations conforming with such recommendations with regard to amino acid content could have been expected because the survey took place two years after publication of the European recommendations. The same fact was noticed in the French survey where 30% of standard PN dedicated to neonatal units contained no amino acids. Efforts should be made by ESPGHAN and ESPEN to disseminate the recommendations more widely and to convince prescribers to follow them.

Most of the standard PN bags are not fully ready-to-use. Vitamins, trace elements and other micronutrients are frequently added to the bags. Before administration, one-third of additions are made in the pharmacy, the other two-thirds in the wards. These additions need to be made because patient requirements differ from standard electrolyte concentrations. Other last-minute additions, such as vitamins and trace elements, permit an improved stability. When performed in the ward environment, these

### DISCUSSION

Although the present survey is based on voluntary answers, the results are very similar to a previous survey [5]. About 43% of hospitals use standard PN mainly prepared by the hospital pharmacy and only 29% of all PN bags produced per year are standard PN, mostly for neonates. Similarly, a recent study evaluating the frequency of use of standard PN in neonatal units in France found that 45.4% of all PN for premature newborns are standard PN [11] compared with 40% in the present study.

The results presented here for 51 hospitals in six European countries probably provide a good picture of how paediatric PN formulations are standardised in Western Europe. However, interpretation of the data is limited by the method used to send out the questionnaire. Results could have differed in hospitals not included in this survey and in other countries.

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### Table 1: Standardisation of micro-nutrients in standard parenteral nutrition (n = 22)

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Already in PN bags</th>
<th>Added at the pharmacy</th>
<th>Added in wards</th>
<th>No answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrolytes</td>
<td>22</td>
<td>6 (if needed)</td>
<td>2 (if needed)</td>
<td></td>
</tr>
<tr>
<td>Vitamins</td>
<td>2</td>
<td>5*</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Trace elements</td>
<td>6</td>
<td>4</td>
<td>11</td>
<td>1</td>
</tr>
</tbody>
</table>

*Three hospitals indicated that vitamins are added to lipids.
procedures could increase the risk of error and microbial contamination.

The authors of the present study believe that ready-to-use PN, without any addition of nutrients in the wards, should be the gold standard for standard PN in terms of safety and cost-effectiveness. It could decrease the risk of error during the prescribing and preparation stages and reduce the workload at the pharmacy and in the wards. However, even in the most recent French study, it was observed that additions to PN bags of macro- and micronutrients are very common: 40–83% (depending on the formula) of standard PN need additives.

Because there is evidence that a standardised PN process has advantages in terms of efficiency, economy and clinical appropriateness compared with PN tailored for individual patients, the ASPEN recommendations encourage a standardised process for PN management. However ASPEN recommendations point out that availability of specially formulated PN for individual patients with complex requirements is also necessary [4].

**CONCLUSION**

Each hospital should have ready-to-use standard PN with formulations conforming to the most recent literature data. PN tailored for individual patients remains necessary when there are complex requirements and should be prepared in the hospital pharmacy by using a safe process, including electronic prescription, connected to an automated preparation system.

**REFERENCES**