A Systematic Review of Practice Surveys on Parenteral Nutrition for Preterm Infants\(^1\)–\(^3\)

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Abstract

Significant efforts have been made to improve the nutritional support of preterm infants in neonatal intensive care units (NICUs) to avoid cumulative nutritional deficits, reduce postnatal growth restriction, and promote optimal long-term development. The objective of this systematic review was to compare the characteristics and results of all surveys published in the past 10 y (2002–2012) that used a questionnaire to survey at least 2 NICUs receiving preterm infants with an intention to treat with parenteral nutrition (PN) and that reported information on at least 1 macronutrient. A total of 6 surveys were identified, which were conducted in the United States \((n = 2)\) or Europe \((n = 4)\). There was wide variability in the response rate \((23–100\%\)\), with a higher response rate in the smaller studies \((81–100\%\); 8–64 respondents) compared with the larger studies \((23–58\%; 296–809 respondents)\). Large differences were observed in the nutritional protocols both among the NICUs in the individual surveys and between surveys. PN was initiated on the first day of life \((DOL)\) by only 24–54\% of respondents \((4\) surveys) and within the second DOL by 67–94\% of respondents \((5\) surveys). Lipids were initiated before the third DOL for 46–96\% of respondents \((3\) surveys). The results of this systematic review suggest that continuous education is needed and that greater efforts are required to disseminate and implement guidelines. Repeated surveys are needed to highlight trends in clinical practices and level of compliance of NICUs with existing guidelines. J. Nutr. 143: 2061S–2065S, 2013.

Introduction

Clinical studies have shown that improving nutritional intake reduces the cumulative energy and protein deficit that may occur in preterm infants, promoting postnatal growth and improving neurodevelopmental outcomes \((1–6)\).

Clinical practice guidelines for the nutritional needs of preterm infants have been regularly revised over recent decades, leading to the development of the most recent guidelines on pediatric parenteral nutrition \((PN)\)\(^7\) in Europe from the European Society of Paediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Clinical Nutrition and Metabolism in 2005 \((7)\), and globally in the book entitled “Nutritional Needs of the Preterm Infant: Scientific Basis and Practical Guidelines” published in 2005 \((8)\).

Reports from neonatal intensive care units (NICUs) worldwide have shown that nutritional intake in preterm infants is inadequate \((9,10)\). The causes of this inadequate intake, particularly in the early neonatal phase, may be multifactorial and partly iatrogenic. It may depend not only on the infant’s metabolic capacities but also on the availability and safety of the solutions used, the type of venous access, the department’s usual practice, and the prescriber’s knowledge of the infant’s nutritional needs \((11)\).

Although the prescriber’s knowledge and compliance with PN guidelines is difficult to examine, several surveys have been conducted to determine the nutritional protocols and practices in preterm infants in NICUs. The objective of this systematic

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\(^5\) Abbreviations used: AA, amino acid; DOL, day of life; NICU, neonatal intensive care unit; PN, parenteral nutrition; VLBW, very low birth weight. 

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Of the 380 identified articles, we excluded 342 on the basis of a review of the title and abstract because they did not report any survey data. The full text of the remaining 7 articles was reviewed to determine whether the articles met the inclusion criteria. Eight articles did not meet our inclusion criteria (survey on enteral nutrition, survey on nutrition, survey on PN, use of a questionnaire, intention to treat, information on at least one macronutrient, neonatal units receiving preterm infants, and at least one study reported actual prescriptions, intention to treat, or PN). The exclusion criteria (survey on enteral nutrition, survey on nutrition, survey on PN, use of a questionnaire, intention to treat, information on at least one macronutrient, neonatal units receiving preterm infants, and at least one study reported actual prescriptions, intention to treat, or PN) were met for the remaining 2 articles. The following information was extracted from the articles and entered into a spreadsheet to allow direct comparison of the survey characteristics and results: year of survey, country, type of institution, type of infants (e.g., physicians), response rate, timing of initiation of nutrition evaluation, and the dosage used to assess compliance with the most recent nutritional protocols over time, and to evaluate adherence to guidelines. The characteristics and results from those included studies were included if they met all of the following criteria: survey on PN, use of a questionnaire, intention to treat, intention to report data for the use of at least 1 nutrient. Of the remaining 18 articles, 2 reported the same survey, but with additional data, and both articles were kept in the review. The characteristics of the evaluated surveys are provided in Table 1. Four of the surveys were published in separate articles, and both articles were kept in the systematic review.

### Results

#### Characteristics of the surveys included in the systematic review

<table>
<thead>
<tr>
<th>Survey</th>
<th>Year of study</th>
<th>Country</th>
<th>Type of institution</th>
<th>Type of questions</th>
<th>Type of infant</th>
<th>Method of administration</th>
<th>Number of units surveyed/contacted</th>
<th>Response rate</th>
<th>Position of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed et al. (12)</td>
<td>2002</td>
<td>UK</td>
<td>NICU with ≥6 intensive care cots</td>
<td>Open</td>
<td>VLBW</td>
<td>Phone</td>
<td>54/57</td>
<td>95</td>
<td>Physicians (specialist registrars)</td>
</tr>
<tr>
<td>Fleming et al. (13)</td>
<td>2005</td>
<td>Ireland</td>
<td>NICUs</td>
<td>Not described</td>
<td>VLBW</td>
<td>Mail</td>
<td>8/8 (29/32 physicians)</td>
<td>100 (91% of physicians)</td>
<td>Physicians</td>
</tr>
<tr>
<td>Grover et al. (14)</td>
<td>2005–2006</td>
<td>UK</td>
<td>Level III or II NICU with ≥5 intensive care cots</td>
<td>Not described</td>
<td>Not described</td>
<td>E-mail</td>
<td>52/64 (48 units analyzed)</td>
<td>81</td>
<td>Pharmacists</td>
</tr>
<tr>
<td>Hans et al. (16)</td>
<td>2006</td>
<td>USA</td>
<td>NICUs</td>
<td>Multiple-choice and open-ended</td>
<td>ELBW, VLBW, LBW</td>
<td>E-mail and mail</td>
<td>178/775 individuals</td>
<td>23</td>
<td>Physicians, dieticians, neonatal nurse practitioner</td>
</tr>
<tr>
<td>Lapillonne et al. (17,21)</td>
<td>2006</td>
<td>France</td>
<td>NICUs</td>
<td>Open</td>
<td>VLBW</td>
<td>Mail</td>
<td>172/296</td>
<td>58</td>
<td>Physicians</td>
</tr>
<tr>
<td>Kiefer et al. (15)</td>
<td>2007</td>
<td>USA</td>
<td>NICUs</td>
<td>Multiple-choice</td>
<td>ELBW (&lt;1000 g)</td>
<td>Mail</td>
<td>297/809</td>
<td>37</td>
<td>Physicians</td>
</tr>
</tbody>
</table>

1. ELBW: extremely low birth weight; LBW: low birth weight; NICU, neonatal intensive care unit; VLBW, very low birth weight.
2. Clinical case of a 28-wk VLBW infant (1.1 kg).
3. This survey was not entirely focused on nutrition and comprised 15 sections addressing clinical conditions commonly encountered during the management of VLBW infants, of which fluid, electrolytes, and nutrition were 1 section.
The objectives and the focus of the survey questionnaires also varied; 2 studies (13,15) reviewed current practice in the management of VLBW and extremely-low-birth-weight infants, which not only included questions on nutrition but also on other aspects of management, such as respiratory care. Two studies (12,14) reviewed current practices in PN administration and management, and 2 studies (16,17) compared current nutritional practices according to published recommendations.

Survey response and risk of bias. There was wide variability in the response rate for these surveys (23–100%). There was a higher response rate (81–100%) in the 3 smaller studies (8–64 respondents) compared with the response rate (23–58%) in the larger studies (296–809 respondents) (Table 1).

Nutritional outcomes. An overview of the results from each survey for the timing of initiation of PN (amino acids and lipids), target intakes of each nutrient, and the initial dosage is shown in Table 2.

Amino acids. All surveys documented the day of life (DOL) on which PN was initiated (introduction of amino acids) (Table 2). PN was initiated on the first DOL by 24–54% of respondents (4 surveys) and on the second DOL by 67–94% of respondents (5 surveys). One study in the United States (16) showed that the mean age of PN initiation in VLBW infants was 1.25 d, although some VLBW infants received PN as late as the fifth DOL. Of those surveys reporting the initial dose of amino acids, the dose ranged from 0.5 to 4 g/(kg · d). Knowledge of the target dose for amino acids was largely unknown in 1 study conducted in 2002 (12), and the target dose was known to be ≥3 g/(kg · d) by only 27% of respondents in 1 survey conducted in 2006 (14).

Lipids. Four surveys documented the DOL on which lipid emulsions were initiated (Table 2). Three surveys showed that lipids were initiated before the third DOL for 46–96% of respondents; they were initiated before the second DOL for 54% of respondents in 1 study (12). The initial dose was frequently between 0.5 and 1.0 g/(kg · d), except in 1 study in the United States (15) in which the dose was 2 g/(kg · d) for 8% of respondents. A target lipid dose of 3 to 4 g/(kg · d) was reported by 66% of respondents in 1 survey conducted in 2006 (14).

Common indications to stop or decrease lipids in PN were described in 3 studies (12,16,17). The most frequently cited indications were confirmed or suspected sepsis, increased liver enzymes, conjugated or unconjugated hyperbilirubinemia, low platelet count, disseminated intravascular coagulation, high TGs, and acidosis. However, the perception by physicians of these conditions as absolute or relative contraindications for lipid infusions varied dramatically within and between studies, making it impossible to identify a common pattern.

Glucose and calories. The current practice for PN (glucose and calories) in NICUs responding to the surveys was detailed in several studies (14,17,18) (Table 3). In an e-mail survey of pharmacists performed in the United Kingdom between 2005 and 2006 (14), the median initial and target doses of glucose were 5.9 and 14.1 g/(kg · d), respectively. The median initial amount of calories initiated was 25.6 kcal/(kg · d), with a median target of 95.2 kcal/(kg · d).

Discussion
The results of individual surveys have previously demonstrated that the knowledge and clinical practices of the respondents for

<table>
<thead>
<tr>
<th>Survey</th>
<th>Target intakes of each nutrient</th>
<th>Initial dose of lipids</th>
<th>Target for lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed et al. (12)</td>
<td>N/A</td>
<td>N/A</td>
<td>Median dose: 3</td>
</tr>
<tr>
<td>Fleming et al. (13)</td>
<td>N/A</td>
<td>N/A</td>
<td>Median dose: 1</td>
</tr>
<tr>
<td>Grover et al. (14)</td>
<td>Median dose: 0.5</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Hans et al. (15)</td>
<td>Median dose: 2</td>
<td>N/A</td>
<td>Median dose: 3</td>
</tr>
<tr>
<td>Lapillonne et al. (17,18)</td>
<td>Median dose: 1</td>
<td>N/A</td>
<td>Median dose: 3</td>
</tr>
<tr>
<td>Kiefer et al. (15)</td>
<td>Median dose: 2 (66% of respondents)</td>
<td>N/A</td>
<td>Median dose: 3</td>
</tr>
</tbody>
</table>

AA, amino acid; DOL, day of life; ELBW, extremely low birth weight; LBW, low birth weight; N/A, not available; VLBW, very low birth weight.
the nutritional support of preterm infants varied greatly among NICUs. The results from this systematic review further support this finding by demonstrating that variations also exist between surveys and countries.

The methodologic limitations of using surveys for the assessment of nutritional protocols have been previously discussed in detail (17), and it should be reiterated that these surveys reflect the intention to treat of the personnel from the NICU who respond to the survey and may not reflect the actual clinical practice within the unit. Nevertheless, intention to treat reflects one of the first steps of the dissemination of guidelines and thus provides insight on compliance to guidelines.

The most recent European and U.S. guidelines recommended a change in PN practice, specifying that amino acids should be initiated earlier, on the first DOL with a minimum intake of 1.5–2 g/(kg·d) and a maximum intake of 4.0 g/(kg·d) [3.2–3.8 g/(kg·d) for VLBW infants] (7,8,19). Therefore, it is not surprising that the results from those surveys conducted before the publication of these guidelines demonstrate a failure to comply with these recommendations. However, the results from surveys conducted after the publication of these guidelines still demonstrate that the recommended timing and dose of amino acids are frequently not met. Furthermore, a survey performed in Poland in 2007 (20) showed that PN was not used for the care of preterm infants in approximately half of the 302 units that were surveyed.

Current guidelines recommend that lipid administration be initiated between the first and second DOL (7,8), and a recent systematic review of the literature has demonstrated that initiation of lipids within the first 2 DOL in VLBW infants is safe and well tolerated (21). The timing of initiation of lipid infusion to VLBW infants has previously been reported to vary widely among different NICUs (17). The results from this systematic review confirm that the timing of lipid administration also varies between surveys to a scale that is even larger than that for amino acids. It was also found that there was a lack of consensus between surveys on the contraindications for lipids and/or indication for stopping lipids, reflecting the lack of scientific data and absence of clear guidance on this topic.

In summary, although the level of compliance with current guidelines is still unclear, the results of this systematic review suggest that continuous education is needed and that greater efforts are required to disseminate and implement them. The limited or delayed availability of individualized PN solutions (17), as well as difficulties in ordering individualized PN (3), have previously been identified as reasons for noncompliance with guidelines. Repeating these surveys is needed to determine how much treatment variation in routine clinical practice may still exist, to assess the level of compliance of NICUs with existing clinical practice guidelines, and to highlight trends in clinical practices over time. Larger surveys that include several countries may also help to compare variations in practice between countries and to determine the factors that may promote or restrict implementation of guidelines at a national level. Given the need for continuous monitoring, it would be of value for scientific societies (particularly those that publish guidelines) to develop web-based standard reporting systems that determine the actual compliance of in-house protocols with guidelines. In the case of nutrition for preterm infants, a limited number of questions on access to PN and the dose of nutrients given would be sufficient to provide insight on the implementation of guidelines at a local level.

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Literature Cited


