Aspects of protein metabolism in children in acute and chronic illness
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Effect of a nurse-driven feeding algorithm and the institution of a nutritional support team on energy and macronutrient intake in critically ill children

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ABSTRACT

**Background:** Critical care providers fail to meet patients’ nutritional demands particularly during the first days of stay on a pediatric intensive care unit (PICU).

**Objective:** We aimed to study if the introduction of a feeding algorithm combined with a nutritional support team (NST) can improve nutrition delivery in a PICU.

**Design:** In our PICU we compared the delivered percentages of goals for energy and macronutrients during the first 10 days of admission before and after the introduction of a feeding algorithm and NST. Patients with length of stay > 3 days and mechanical ventilation were included. The algorithm was based on early and aggressively incremental, nurse-driven enteral feeding with additional parenteral nutrition, if necessary. The NST reviewed and adjusted the nutrition regimens once a week and on demand.

**Results:** The percentages of enteral nutrition delivered on day 1 doubled from 40% to 78% ($p < 0.01$), and increased from 60% to 92% on day 2 ($p < 0.01$) without increase in adverse gastrointestinal events, compared to the control period. More than 85% of nutritional targets were reached on day 3 compared to on day 4 before the protocol.

**Conclusion:** The introduction of an early and aggressive, nurse-driven nutrition protocol, together with an NST, is an effective and safe tool to increase nutrition delivery on a PICU.
INTRODUCTION

There is a large body of evidence showing that intensive care patients are at risk of malnutrition during hospital stay (1, 2). Malnutrition is associated with higher nosocomial infection rates, increased length of stay (LOS), more ventilator days, hospital mortality, and stunted anthropometric measurements long after discharge (3–5). Approximately 20–50% of patients in a tertiary children’s hospital already have acute or chronic malnutrition on admission, and a stay on an intensive care unit then superimposes hospital malnutrition (6, 7). Critically ill children are at greater risk, as they have limited energy reserves and less muscle mass than adults (8–10).

Critical care providers are still failing to meet patients’ nutritional demands particularly during the first few days of intensive care stay. Studies have shown that 50% of patients in highly specialized pediatric intensive care units (PICU) reach estimated energy requirements as late as 7 days after admission (11–13). During PICU stay, up to 50% of cumulative energy and macronutrient deficits are caused in the first two days of admission (14).

Also in our PICU, we have observed that predefined goals for energy intake were reached as late as day 6 of hospital stay, and that energy was supplied mainly by fat and carbohydrates (15). Mean protein delivery stagnated at around 75% of the target, resulting in protein malnutrition in almost 85% of patient days (15). We found that in the absence of a feeding protocol, both delayed prescription and delivery of nutrition were important causes of malnourishment (15).

We hypothesize that introduction of a nurse-driven as opposed to physician-driven, feeding algorithm in addition to implementation of a nutrition support team (NST) would increase delivery of energy and macronutrients (carbohydrate, protein, and fat) relative to predefined targets in the first few days of PICU admission.

The aim of this study was to assess the delivery of energy and macronutrients during the first 10 days of PICU admission, after the introduction of a nurse-driven feeding algorithm combined with the implementation of an NST, and compare the results with a historical cohort.

SUBJECTS AND METHODS

In the setting of a 16-bed tertiary PICU, we performed an observational review of nutritional charts during the first 10 days of admission in the winter of 2010/11 (Group 2011) after the introduction of a feeding algorithm and NST. We compared these data with a cohort that we had studied during the winter of 2006/7 (Group 2007), prior to the introduction of the
feeding algorithm and NST. We chose a study design with historic controls, as with regard to feeding, aggressive early enteral nutrition (EN) demands a change in culture, which cannot be randomized. Moreover, a multi-centre design would have introduced many such different cultures. The endpoints were the delivered percentages of predefined goals of energy and macronutrients (fat, protein and carbohydrates). Optimal nutrition was defined as reaching > 85% of the predefined requirements for energy, protein, fat, and carbohydrate intake on each day of stay. Since we only reviewed patients’ medical charts and there was no experimental intervention, the Medical Ethics Board waived approval.

Subjects

In both cohorts, patients whose LOS was > 3 days and who were being mechanically ventilated were eligible for the study. Clinical patients from within our hospital who were referred to the PICU, and already receiving EN and/or parenteral nutrition (PN) were excluded. Preterm babies and neonates with very low birth weight were excluded from the study, since in our hospital they are admitted to a specialized neonatal ICU.

Recorded patient characteristics included age, gender, diagnosis on admission, predicted index of mortality (PIM2) (16), number of ventilator days and LOS.

Nutritional algorithm

Predicted energy expenditure (PEE) was calculated by the World Health Organization (WHO) equation (17), adjusted for illness factor, growth factor and energy absorption coefficient (18). According to Dutch national guidelines, fat intake was set at 50 energy-% (en%) for children ≤ 1 y, and 30 en% for children > 1 y, and also protein intake was age-dependent (0–1 y, 2.5 g/kg/d; > 1–4 yrs, 2 g/kg/d; and > 4 yrs, 1.5 g/kg/d) (18).

The feeding algorithm was based on early and aggressively incremental, nurse-driven enteral feeds (Figure 6.1). Typically, the attending physician initiated the protocol, which thereafter became nurse-driven, with potential intervention by the NST on the next working day. In the absence of contraindications, EN was started as continuous drip feeding via a gastric or duodenal feeding tube as soon as possible, but usually within 24 hrs of admission, at a rate of 25% of the age-dependent target that had been prescribed by an attending physician. The EN consisted of commercially available, ready-made solutions, divided into four age categories: < 1 y, 1–6 yrs, 6–12 yrs, and > 12 yrs. Both hydrolyzed and lactose-free variants were available for all age groups.
Gastric retention was measured every 4 hrs. If the residual volume was less than the worth of 2 hrs feeding, nutritional intake was increased by 25%, until the prescribed target was reached. If there was a large amount of gastric residue, enteral feeding was stopped for 1 h. If gastric retention persisted, EN was either not increased or stopped depending on clinical assessment, and PN was started in order to reach nutritional goals. The choice of additional PN was limited to five standardized, age-dependent, ready-made solutions. In these cases, the NST was consulted on the next week day.

Diarrhea was defined as three or more liquid stools per day. The total intake of energy and macronutrients was calculated from EN, PN and glucose infusions for a minimum of 3 and a maximum of 10 days.

**Figure 6.1** Feeding algorithm. EN, enteral nutrition; PN, parenteral nutrition; GI, gastro-intestinal.
Nutritional support team

Once a week, and on demand, the NST, consisting of a pediatrician-intensivist, a nurse practitioner, and a clinical dietician, reviewed the nutritional regimen of all patients, and advised the attending clinicians. Examples of interventions by the NST were: adjustment of composition of EN and/or PN in accordance with nutritional goals or clinical and biochemical variables, providing extra information by indirect calorimetry and/or body impedance assay, if indicated, and solving logistical problems in the ordering and supply of EN or PN. Therefore, we considered the combination of a feeding algorithm and the introduction of an NST as one intervention, and did not design the study in such way to ascribe outcome measures to either one of them.

Statistical analysis

The baseline patient characteristics of each group were compared using the Mann-Whitney U test for numerical data, and the Pearson Chi-squared test for categorical data. The percentages of patients in each group that received feeding on consecutive days were compared using the unpaired t test. If Levene’s test for normal distribution of data was positive, the corrected outcome was used. In all statistical tests a p-value of < 0.05 was considered to be statistically significant. Statistical analysis was performed with PASW Statistics for Windows (version 18.0, SPSS Inc., Chicago, Illinois, USA).

RESULTS

During the study 84 patients were enrolled in Group 2007 and 87 in Group 2011. The groups were comparable with regard to age, weight, gender, LOS on the PICU and ventilator days (Table 6.1). Group 2011 was more severely ill than group 2007, shown by a higher predicted index of mortality (-3.52 [-4.35 to -1.96] and -4.15 [-5.13 to -3.06] in Groups 2007 and 2011, respectively, p < 0.01), and the use of muscular blocking medication (13.8% and 28.6%, respectively, p < 0.01). In both groups, the inclusion criteria of LOS > 3 days and mechanical ventilation led to the exclusion of simpler cases (e.g. recovery on PICU after relatively minor surgical procedures), and hence to higher mortality (7.1% and 8.0%, respectively, p = 0.82) than our usual PICU mortality rate of less than 5% (19). The median age in both winter cohorts is lower than our normal annual population (4.7 and 6.6 mos, respectively, compared with the normal 31.2 mos). This was probably due to overrepresentation of babies who needed mechanical ventilation for respiratory infections (19). Post-hoc analysis showed that in 2011
there were more admissions with RSV (respiratory syncytial virus) bronchiolitis than in 2007. This accounted for a higher incidence of respiratory diagnoses, and relative more sepsis/post surgical cases in Group 2007. Statistical analysis showed no correlation of diagnosis groups with differences in outcome parameters (data not shown).

The percentage of patients who received nutrition in any form (EN, PN, or combination) during the first five days of admission was significantly higher after the introduction of a feeding algorithm and NST (*Figure 6.2*). A higher percentage of enterally fed patients was solely accountable for this increase, with a trend towards less use of PN (*Table 6.2*). In Group 2011, compared with Group 2007, the percentages of EN on day 1 almost doubled from 40% to 78% (**p** < 0.01), and increased from 60% to 92% on day 2 (**p** < 0.01), respectively. In Group 2011 70% of patients had started nutrition within 12 hrs of admission, of which more than half in the first 6 hrs (*Figure 6.3*).

### Table 6.1 Patient characteristics

|                      | Group 2007 | Group 2011 | **p-value**
|----------------------|------------|------------|-------------
| Children (n)         | 84         | 87         | 0.89        
| Male (%)             | 54         | 63         | 0.89        
| Age (months)         | 4.7 (0.9 to 18.9) | 6.6 (0.9 to 30.13) | 0.50        
| Weight on admission (kg) | 6.1 (3.6 to 11.8) | 7.2 (3.8 to 14.0) | 0.26        
| SDS WFA on admission | -0.81 (-2.29 to 0.34) | -0.51 (-1.43 to 1.69) | 0.08        
| PIM2 score           | -3.52 (-4.35 to -1.96) | -4.15 (-5.13 to -3.06) | < 0.01      
| Observation days total (n) | 679         | 559        |             
| Observation days (d) | 7.5 (6.0 to 10.0) | 6.0 (4.0 to 9.0) | < 0.01      
| Length of stay PICU (d) | 8 (6 to 13) | 8 (6 to 13) | 0.54        
| Ventilator days (d) | 6.8 (4.0 to 10.3) | 6.5 (4.6 to 10.1) | 0.96        
| Primary diagnosis (%) |           |            |             
| Respiratory          | 48.8       | 67.8       | 0.01        
| Circulatory/sepsis   | 23.8       | 14.9       | 0.14        
| Post surgical        | 17.9       | 9.2        | 0.10        
| Trauma               | 1.2        | 1.1        | 0.98        
| Neurology/trauma     | 8.3        | 6.9        | 0.72        
| Supportive care (%)  |           |            |             
| Vasopressive medication | 23.4     | 19.7       | 0.19        
| Pain medication      | 91.7       | 91.8       | 0.99        
| Sedation             | 91.7       | 91.8       | 0.99        
| Muscular blockade    | 13.8       | 28.6       | < 0.01      
| Mortality (%)        | 7.1        | 8.0        | 0.82        

*a* Values given as median (interquartile range), unless otherwise noted. SDS, standard deviation score; WFA, weight for age; PIM2, predicted index of mortality 2; PICU, pediatric intensive care unit. *b* Pearson’s Chi-squared test. *c* Mann-Whitney U test.
The aggressively incremental nutritional algorithm did not lead to increased incidence of adverse gastrointestinal effects. We observed less vomiting in Group 2011 than in Group 2007 (2.1% and 0.7%, respectively, \( p = 0.05 \)), and saw no differences in the occurrence of diarrhea or gastric residue between groups (Table 6.3).

![Figure 6.2 Percentages of patients receiving nutrition in 2007 and 2011. EN, enteral nutrition; PN, parenteral nutrition; Combi, combination of EN and PN; 07, Group 2007; 11, Group 2011. Asterixes indicating statistically significant difference between groups.](image)

**Table 6.2** Daily percentages of patients receiving nutrition with relative contribution of EN and PN during the first 5 days of admission

<table>
<thead>
<tr>
<th>Day</th>
<th>Total 2007</th>
<th>Total 2011</th>
<th>( p )-value*</th>
<th>EN 2007</th>
<th>EN 2011</th>
<th>( p )-value</th>
<th>PN 2007</th>
<th>PN 2011</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46.2</td>
<td>86.2</td>
<td>&lt; 0.01</td>
<td>39.8</td>
<td>78.2</td>
<td>&lt; 0.01</td>
<td>6.5</td>
<td>6.1</td>
<td>0.84</td>
</tr>
<tr>
<td>2</td>
<td>72.5</td>
<td>98.9</td>
<td>&lt; 0.01</td>
<td>60.4</td>
<td>92.0</td>
<td>&lt; 0.01</td>
<td>8.8</td>
<td>6.9</td>
<td>0.64</td>
</tr>
<tr>
<td>3</td>
<td>90.0</td>
<td>100</td>
<td>&lt; 0.01</td>
<td>74.4</td>
<td>90.8</td>
<td>&lt; 0.01</td>
<td>14.4</td>
<td>6.9</td>
<td>0.11</td>
</tr>
<tr>
<td>4</td>
<td>91.9</td>
<td>98.7</td>
<td>0.04</td>
<td>74.4</td>
<td>91.0</td>
<td>&lt; 0.01</td>
<td>14.0</td>
<td>6.4</td>
<td>0.11</td>
</tr>
<tr>
<td>5</td>
<td>93.8</td>
<td>100</td>
<td>0.04</td>
<td>76.3</td>
<td>91.0</td>
<td>0.02</td>
<td>15.0</td>
<td>3.1</td>
<td>0.02</td>
</tr>
</tbody>
</table>

EN, enteral nutrition; PN, parenteral nutrition. *Pearson’s Chi-squared test.
Energy intake was more rapidly increased during the first days of admission in Group 2011 than in Group 2007, with more than 85% of the mean energy goal reached on day 3 of admission in Group 2011, compared with day 4 in Group 2007 (Figure 6.4A). Over consecutive days there was a slightly lower energy intake in Group 2011 than in Group 2007. During the 10-d study period we observed the same pattern in fat intake as in energy intake (Figure 6.4C). During the first two days of stay there was a higher carbohydrate intake in Group 2011 than in Group 2007 (Figure 6.4B). During the first five days of stay, protein intake was significantly higher in Group 2011 than in Group 2007 (Figure 6.4D). The goal for protein intake was not fully reached in either of the groups, with maximum protein intake stagnating at about 85% of the target from day 6 onward in Group 2011.

Table 6.3 Adverse effects of enteral nutrition

<table>
<thead>
<tr>
<th></th>
<th>Group 2007 (n = 679)</th>
<th>Group 2011 (n = 559)</th>
<th>p-valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>14 (2.1)</td>
<td>4 (0.7)</td>
<td>0.05</td>
</tr>
<tr>
<td>Diarrhea*</td>
<td>5 (0.8)</td>
<td>8 (1.4)</td>
<td>0.29</td>
</tr>
<tr>
<td>Gastric residual</td>
<td>28 (4.1)</td>
<td>35 (6.3)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*aValues given as number of observation days on which event occurred, with percentages between brackets. bPearson’s Chi squared test. cPatients with infectious diarrhea as primary diagnosis on admission were not included.

Figure 6.3 Percentages of patients receiving nutrition within 6, 12, 18, 24 or > 24 hrs after admission in group 2007 (A) and group 2011 (B).
We found no differences in clinical outcome parameters (length of ICU stay, ventilator days, and mortality) between the groups.

**DISCUSSION**

In this study we have demonstrated that the introduction of an early enteral, nurse-driven nutritional algorithm and implementation of an NST are effective and safe measures that significantly increase the nutritional intake of critically ill children, especially during the first few days of stay on a PICU.
A large international, observational survey, including 158 ICUs and 2946 mechanically ventilated adult patients, has shown that one third of ICUs failed to initiate EN during the first 48 hrs of admission, and that for more than one third of the time patients did not receive any EN, resulting in overall 60% delivery of prescribed calories and protein (20). Major barriers to adequate nutrition that play an important role in ICU malnutrition include fluid restriction, particularly in septic and cardiac surgical patients, interruptions of nutrition regime due to intensive care procedures, and intestinal intolerance in multi-organ dysfunction syndrome (MODS) (12). Despite this, we were able to feed a higher percentage of patients in the protocol group during the first five days of admission, with the greatest effect on days 1 and 2, on comparison with the controls with lower PIM2 scores (Figure 6.2). In Group 2011, more than 70% of all children received their first feed within 12 hrs of admission, with 44% within the first 6 hrs (Figure 6.3B), compared with 43% and 25% in Group 2007 (Figure 6.3A). These higher percentages are in concert with the results of a study by Tume et al following the introduction of an early goal nutritional algorithm on their PICU (21). In a cohort of critically ill children, by implementing a nutritional protocol, Petrillo-Albarano et al also reached the goal for energy intake earlier than in a retrospective group, but with a higher incidence of gastro-intestinal adverse events (22). Lambe et al reported no differences in cumulative energy and protein deficits in critically ill children before and after the introduction of an NST, but their nutritional intervention programme was limited to a weekly meeting of 1 h (23). In general, feeding protocols can improve nutritional practices in a PICU provided that introduction is monitored regularly (24).

In our study, the higher intake of nutrition observed was solely attributable to increased EN, without an increase in adverse effects (Tables 6.2 and 6.3). Due to the study design, we could not determine if this effect was caused by the nutritional algorithm or the NST or both. A very recently published study showed that the sequential introduction of a bottom-up feeding guideline and a clinical dietician (1 y later) both improved nutritional support in critically ill adults, and that the latter was related to early introduction and route of feeding, and achievement of improved early energy balance (25). Other studies also report that nutritional protocols increase delivery of EN. In a retrospective study, Gurgueira et al observed an increase of EN from 25% to 67% with a decrease to 0% of PN, with the strongest correlation to the introduction of a NST. Briassoulis et al achieved a positive energy and nitrogen balance in 2/3 of critically ill children after 5 days of PICU stay, using an aggressive early EN algorithm (26).

Our study demonstrates that on increased feeding, there was a significantly higher cumulative intake of energy and macronutrients, most notably protein, throughout the entire observation period (Figure 6.4). During the observation periods in 2007 and 2011 we did not reach the...
predefined goals for protein intake, according to the Dutch guidelines (18). However, since the recommendations for protein intake in infants are higher in the Dutch guideline than the recommendations of the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) for injured children 0–2 yrs (27), the achieved protein intake at 85% of the Dutch target was within the A.S.P.E.N. range for the majority of our patients. In critically ill children, as in adults, negative protein balance with loss of lean body mass is associated with longer stay on a PICU, and an important risk factor for mortality and long-term morbidity (5, 9, 28). We speculate that commercially available feeding formulae contain too few protein calories per milliliter to meet patients’ demands, even with the addition of extra protein powder within practical limits, without overfeeding with too many calories and/or fluids.

We did not observe effects of early EN on clinically relevant outcome parameters, such as ventilator days, LOS, and PICU mortality. The study was not powered to detect changes in these secondary outcome parameters. One limitation of our study is that we did not measure body composition by performing body impedance assay and spectrometry on admission and discharge to detect effects of our feeding protocol. However, during PICU stay, up to 50% of cumulative energy and macronutrient deficits are caused in the first two days of admission (14). Therefore it is plausible that early start and aggressive increase of delivery of energy and macronutrients during the first few days of stay on PICU may mitigate cumulative deficits, and improve biometric measures and clinical outcome.

The effect of successful early EN on the clinical outcome of both pediatric and adult intensive care patients is still a subject of debate (29–33). The ESPEN expert committee on EN in critically ill patients, however favors the view that critically ill patients, who are hemodynamically stable and have a functioning gastrointestinal tract, should be fed early (< 24 hrs), if possible, using an appropriate amount of feed (34). A Cochrane review to assess the impact of EN and PN on clinically important outcomes for critically ill children was able to identify only one study (protocol) that was relevant to the research question (35). The conclusion of this review was that there is an urgent need for well designed prospective research aimed at clinically relevant outcome parameters, both short-term and long-term, of the increased delivery of nutrition to critically ill children, as a result of nutrition algorithms and/or NSTs. The set-up of our study, with a nurse-driven bedside algorithm and an NST, could serve as a basis for such a trial.
REFERENCES


