RESEARCH

# Quality improvement initiative to reduce adverse effects associated with parenteral nutrition overfeeding

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## ABSTRACT

**Objective** Parenteral nutrition (PN) overfeeding is a potential risk factor in the development of infections and other complications including hyperglycaemia, refeeding syndrome and liver dysfunction. This study was conducted to evaluate the impact of a quality improvement initiative to reduce PN overfeeding.

**Design** Retrospective cohort study of a quality improvement initiative.

**Setting** A health system comprised of two US Department of Veterans Affairs medical centres.

**Patients** Patients receiving PN.

**Interventions** Methods to reduce overfeeding included the use of standardised PN products with lower dextrose to amino acid ratios, reduced use of intravenous lipid emulsion (ILE), and use of adjusted body weights or guideline-recommended predictive equations for energy requirements.

**Main outcome measures** The primary outcome measures were the doses of kilocalories, amino acids and ILE in each cohort. The proportions of patients developing complications before and after the intervention were evaluated.

**Results** The mean maximum total daily kilocalorie dose was 30.2 kcal/kg/day in the preintervention group (n=86) vs 23.4 kcal/kg/day in the postintervention group (n=62) (p<0.001). More patients in the postintervention group received reduced ILE during the first week of PN therapy compared with the preintervention group (p<0.001). The mean maximum total daily amino acid dose in each group was not significantly different. Significantly fewer cases of central line-associated bloodstream infections, hyperglycaemia and liver dysfunction were observed in the postintervention group.

**Conclusions** A quality improvement initiative to reduce PN overfeeding was effective in reducing kilocalorie and ILE doses while maintaining similar amino acid doses. Observed complications were reduced following the intervention.

## INTRODUCTION

Parenteral nutrition (PN) is a necessary therapy for patients unable to receive adequate nutrition via the gastrointestinal tract. Despite this necessity, PN is associated with complications including central line-associated bloodstream infections (CLABSI).[1] The increased infectious risk associated with PN has been linked to the increased calories delivered in critically ill patients.[2 3] Hypocaloric PN appears to reduce the risk of infectious complications and is a recommended approach for reducing the risks associated with PN.[4–7] When provided in equicaloric doses, PN may have similar risk as enteral nutrition (EN).[8] Additionally, PN is associated with metabolic complications including hyperglycaemia, refeeding syndrome and liver dysfunction. Hyperglycaemia is the most common metabolic adverse effect of PN and is associated with negative clinical outcomes. Refeeding syndrome is primarily manifested by electrolyte abnormalities, most notably hypophosphataemia, which can have potentially life-threatening effects. PN-associated liver dysfunction may include hepatosteatosis and biliary disorders. Hepatosteatosis, evidenced by elevated serum alanine aminotransferase and aspartate aminotransferase levels, can potentially progress to liver failure. PN overfeeding increases the risk of hyperglycaemia, refeeding syndrome and hepatosteatosis.[9]

Limiting soy-based intravenous lipid emulsions (ILE) in the critically ill is a guideline-recommended approach to



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reducing complications from PN, as this was demonstrated to decrease PN complications including infections.[6 10] However, this recommendation is controversial as the results have not been replicated outside of one study involving critically ill trauma patients, and it has been hypothesised that overfeeding may have been the actual cause of the worsened complications in the trial patients receiving ILE. Protein is generally considered to be the most important macronutrient in the acutely ill population and restricting protein/amino acids is usually not recommended, although there is some evidence to suggest that even increased amino acid dosages may be associated with worsened outcomes.[11 12]

Within our health system, CLABSI remained a problem in patients receiving PN despite an extensive protocol to reduce central-line complications. CLABSI risk reduction typically focuses on catheter insertion and maintenance techniques.[13 14] In our institution, additional methods are in place that have been shown to reduce infectious complications with PN, including prescription by a nutrition support team (NST) and use of multichamber standardised PN products when possible.[15 16] As part of continuous quality assurance, complications associated with PN were tracked by the NST and reported locally. Overfeeding was identified as a potential modifiable risk factor in our practice. Although avoidance of overfeeding is commonly recommended to reduce complications with nutrition support, the definition of overfeeding is not well defined and many methods for calculating nutrition requirements exist.

We sought to reduce overfeeding—specifically carbohydrate and fat—as a method to reduce adverse effects of PN. While this project was undertaken as a CLABSI reduction initiative, other complications from PN also had the potential to be reduced. Due to the generally accepted importance of amino acid provision, we sought to maintain the dosing of amino acids.

The primary outcome we sought to investigate was if reducing carbohydrate and lipid kilocalories could be accomplished while maintaining amino acid dosage. Secondarily, we sought to investigate if a decrease in CLABSI and metabolic complications was observed following these changes in prescribing practices.

## METHODS

The institution's guidelines for quality improvement studies was completed and approval was granted through local procedures. Informed consent was not required and patients' privacy and well-being were protected. The author did not have any real or potential conflicts of interest.

In our institution, PN therapy was coordinated by the NST, which included a registered dietitian, a clinical pharmacy specialist, and a collaborating physician available for oversight and clinical support. The NST attempted to adhere to established guidelines regarding appropriate indications for PN. As such, EN was typically recommended when feasible. As a consult-based service, the NST was responsible for provision and daily monitoring of all PNs. The clinical pharmacy specialist was responsible for writing the daily PN orders and progress notes. Computerised order entry was used for PN prescribing. The health system comprised two US Department of Veterans Affairs medical centres with a total of 560 acute and long-term care beds. The primary setting was an academic, tertiary medical centre that was part of the health system. Our practices regarding PN use and risk reduction strategies have been previously reported. In addition to the prescribing practices described in this report, an extensive vascular access device protocol is in place for appropriate insertion and maintenance, including but not limited to sterility measures, catheter dressing specifications, dedicated catheter lumen for PN and use of filters for PN solutions.[17 18] The primary champion of this project was the clinical pharmacy specialist of our institution's NST.

As previously discussed, we attempted to use multichamber standardised PN products when possible. The standard concentration most often used prior to this intervention was 25% dextrose and 5% amino acids. After reviewing the most common estimated nutritional goals in our patient population, a 15% dextrose and 5% amino acid formulation was added to the formulary.

Our initiative comprised three methods for reducing overfeeding. First, we aimed to reduce the ratio of dextrose to amino acid administration by using the newly added dextrose 15%/amino acid 5% multichamber standardised PN products. This allowed for maintaining amino acid provision while reducing the number of carbohydrate kilocalories. Second, we aimed to provide fewer lipid kilocalories by reducing the number or withholding ILE during the first week of PN therapy. When using body weight for nutritional estimates, we used the lesser of actual or ideal body weight. For obese patients, we incorporated the use of adjusted body weight, as well as the guideline-recommended Mifflin-St Jeor and Penn State predictive equations.[19] Goals following the intervention were to provide energy of 20–25 kcal/kg/day and amino acid dose of at least 0.8 g/kg/day based. This initiative was carried out by a small group of clinicians working on our NST.

We conducted a retrospective quality improvement cohort study comparing patients prior to the intervention with patients following the intervention. The study time frame was 6 years. The preintervention period was from 1 October 2011 to 30 September 2014. The postintervention group was from 1 October 2014 to 30 September 2017. All patients who received PN during the study time frame were included. No exclusion criteria were applied. The primary outcome

measures were the mean maximum daily kilocalorie dose, the mean maximum amino acid dose and the proportion of patients receiving a reduced ILE dose during the first week of PN therapy in each group. The secondary outcome measures were the proportion of CLABSI, hyperglycaemia, refeeding syndrome and liver dysfunction in each group. Kilocalorie doses were measured in kcal/kg/day with weight based on the lesser of ideal body weight or actual body weight. Amino acid doses were measured in g/kg/day with weight based on the lesser of ideal body weight or actual body weight. The US Centers for Disease Control and Prevention's definition of CLABSI was used, which includes laboratory confirmation of bloodstream infection, while a central line is in place, and not attributable to another site.[20] Hyperglycaemia was defined as a blood glucose of 180 mg/dL or greater. Refeeding syndrome was assessed by the development of its hallmark sign, severe hypophosphataemia, defined as a serum phosphate of 1.5 mg/dL or less.[21] Liver dysfunction was defined as an elevated aminotransferase level three times above the upper limit of normal. Proportions were determined as patients who developed each complication divided by the total number of patients receiving PN in the cohort. For statistical analysis of continuous data (mean energy and amino acid doses), a t-test was used; for nominal data (all other outcomes), Fisher's exact test was used. An alpha of 0.05 was selected for statistical significance.

This was an observational study in which no randomisation or control other than historical was used. This study design was implemented because the intervention was made through clinical practice and quality improvement initiatives.

## RESULTS

A total of 148 patients were included in this study. There were 86 patients in the preintervention group and 62 in the postintervention group. The median age was 65 years in the preintervention group and 66 years in the postintervention group. All patients were over 18 years of age. Eighty-two patients (95.3%) in the preintervention group and 60 patients (96.8%) in the postintervention group were men. The mean body mass index was 25.1 kg/m$^2$ in the preintervention group and 27.8 kg/m$^2$ in the postintervention group. In the preintervention group, 49 patients (57%) had the intensive care unit (ICU) as their highest level of care, while 37 patients (43%) had general acute care or intermediate care as their highest level of care. In the postintervention group, 39 patients (62.9%) had ICU as their highest level of care, while 23 patients (37.1%) had general acute care or intermediate care as their highest level of care. The median duration of PN therapy in the preintervention group was 11 days compared with 7 days in the postintervention group.

In the preintervention group, the mean maximum total daily kilocalorie dose was 30.2 kcal/kg/day. In the postintervention group, the mean maximum total daily kilocalorie dose was 23.4 kcal/kg/day. The difference in kilocalorie dose in the postintervention group was significantly lower than the preintervention group ($p<0.001$). In the preintervention group, 48 patients (55.8%) received ≥30 kcal/kg/day. In the postintervention group, 14 patients (22.6%) received ≥30 kcal/kg/day. The proportion of patients receiving ≥30 kcal/kg/day was significantly less in the postintervention group ($p=0.009$).

The preintervention group's mean maximum total daily amino acid dose was 1.09 g/kg/day. The postintervention group's mean maximum total daily amino acid dose was 1.02 g/kg/day. The amino acid dose in each group was not significantly different ($p=0.141$).

In the preintervention group, 85 of the 86 patients (98.8%) received ILE from the start of PN therapy and received more than 100 g of ILE during the first week of therapy. In the postintervention group, 16 patients (25.8%) received ILE from the start of PN therapy, 17 patients (27.4%) received a reduced dose of ILE during the first week of PN therapy, and 29 patients (46.8%) did not receive ILE during the first week of PN therapy. A significantly larger proportion of patients in the postintervention group received a reduced ILE dose during the first week of PN therapy compared with the preintervention group ($p<0.001$).

Eleven patients (12.8%) developed CLABSI in the preintervention group. Of the patients who developed CLABSI, five patients (45.5%) received more than 35 kcal/kg/day and an additional three patients (27.3%) received 30–35 kcal/kg/day. There were no cases of CLABSI in the postintervention group. The proportion of patients who developed CLABSI was significantly lower in the postintervention group than in the preintervention group ($p<0.003$). The micro-organisms identified as the causative CLABSI pathogen were *Klebsiella pneumonia* (four cases), Methicillin-resistant *Staphylococcus aureus* (two cases), coagulase-negative *Staphylococcus* sp (one case), *Enterococcus faecalis* (one case), *Enterobacter cloacae* (one case), *Stenotrophomonas maltophilia* (one case) and *Candida* sp (one case).

There was no significant difference in the proportion of patients who experienced severe hypophosphataemia, consistent with refeeding syndrome. In the preintervention group, two patients (2.3%) developed severe hypophosphataemia compared with one patient (1.6%) in the postintervention group ($p=1$). In the preintervention group, 13 patients (15.1%) developed liver dysfunction compared with two patients (3.2%) in the postintervention group. This difference was statistically significant ($p=0.025$). In the preintervention group, 64 patients (74.4%) developed hyperglycaemia compared with 34 patients (54.8%) in the postintervention group. This difference was statistically significant ($p=0.015$). The outcome results are summarised in table 1.

**Table 1** Results

| | Preintervention (n=86) | Postintervention (n=62) | P values |
|---|---|---|---|
| Energy (kcal/kg/day) | | | |
| Mean | 30.2 | 23.4 | <0.001 |
| ≥30, n (%) | 48 (55.8) | 14 (22.6) | 0.009 |
| Amino acids (g/kg/day) | 1.09 | 1.02 | 0.141 |
| Withheld/reduced ILE during the first week of PN, n (%) | 1 (1.2) | 46 (74.2) | <0.001 |
| CLABSI, n (%) | 11 (12.8) | 0 (0) | 0.003 |
| Refeeding syndrome, n (%) | 2 (2.3) | 1 (1.6) | 1 |
| Liver dysfunction, n (%) | 13 (15.1) | 2 (3.2) | 0.025 |
| Hyperglycaemia, n (%) | 64 (74.4) | 34 (54.8) | 0.015 |

CLABSI, central line-associated bloodstream infections; ILE, intravenous lipid emulsion; PN, parenteral nutrition.

## DISCUSSION

This study demonstrates that a significant reduction in kilocalorie provision can be made without significant reduction in amino acid delivery. We were able to improve PN provision by making simple changes to our formulary and prescribing practices. We also observed significantly fewer cases of CLABSI, hyperglycaemia and liver dysfunction following the intervention; however, causation of these outcomes cannot be determined by the intervention and may have occurred independently.

Most, but not all, patients who developed CLABSI were receiving a high caloric intake, defined as more than 30 kcal/kg/day. Some patients developed CLABSI despite lack of overfeeding, suggesting that other factors played a role in the development of this complication. All patients who developed CLABSI received ILE from the start of treatment. The shorter median duration of PN may be a potential explanation of the decrease in CLABSI. It is also notable that fewer patients received PN in the postintervention group. Potential differences between groups that were not specifically evaluated include catheter insertion/maintenance techniques, non-PN kilocalories, hyperglycaemia management and patient comorbidities; these could have been factors in the lower proportion of CLABSI in the postintervention group.

There was no observed significant difference in refeeding syndrome between the preintervention and postintervention groups. This could be explained by the definition of refeeding syndrome chosen, which was an absolute serum phosphate value of less than 1.5 mg/dL. While the definition of refeeding syndrome is not exact, it also has been suggested that a change in serum phosphate level be used for diagnosis as opposed to an absolute value.[22] Electrolyte composition of PN formulations was not compared; thus, it is unknown if patients in the preintervention cohort required higher doses of electrolytes in PN to avoid severe hypophosphataemia. Additionally, the higher doses of ILE in the preintervention group could have had a preventative effect on the occurrence of refeeding syndrome. While more patients in the preintervention group developed hyperglycaemia, blood glucose management was not evaluated. Thus, it is unknown if effective treatment of hyperglycaemia might have mitigated this complication. The association between each complication and the development of further adverse effects was not evaluated.

As a retrospective study, this study is limited by potential biases inherent to the study design. Since this study was conducted at a single centre, with few clinicians involved, external validity is low. Generalisability to other settings or patient populations may not be possible. Potential confounding variables may have occurred during the study time frame which make the intervention appear to have had larger impact.

## CONCLUSION

The results of this study are consistent with previous data showing improved quality of PN management with NSTs. Reducing kilocalorie administration and overfeeding while maintaining amino acid delivery is an important intervention. Additionally, the fewer observed adverse effects of PN in the postintervention group is consistent with previous findings on overfeeding. The results of this study support the provision of PN by NSTs and prescribing methods designed to reduce PN overfeeding. Prospective, randomised controlled trials are needed to determine the appropriate PN doses for optimal safety and efficacy.

### Significance of this study

**What is already known on this topic**

- Parenteral nutrition (PN) is often a necessary treatment, but it is associated with infectious and metabolic complications.
- Overfeeding with PN increases the risks for complications.

**What this study adds**

- A nutrition support team's quality improvement initiative reduced PN overfeeding while maintaining amino acid provision.
- Observed complications were decreased following the intervention.

**How might it impact on clinical practice in the foreseeable future**

- These findings may assist practitioners in reducing PN overfeeding and its associated risks.

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