International Journal of Nutrition Sciences

Journal Home Page: ijns.sums.ac.ir

ORIGINAL ARTICLE

The Complications of Total Parenteral Nutrition and the Contributing Factors in Children in Tehran, Iran

Maryam Saeedi[1], Sadaf Mohajerani[2], Reihaneh Mohsenipour[3*]

1. Department of Neonatal Care Unit, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran
2. Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran
3. Growth and Development Research Center, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:
Total parenteral nutrition
TPN
Complications
Children
Iran

**Corresponding author:*
Reihaneh Mohsenipour, MD;
Growth and Development Research Center, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran.
Tel: +98 9123711560
Email: rmohsenipour@yahoo.com
Received: January 11, 2022
Revised: April 19, 2022
Accepted: April 27, 2022

ABSTRACT

Background: Total parenteral nutrition (TPN) is used to maintain the nutritional status of children in surgical wards which is essential not only for patients' recovery, but also for normal growth and development. Given the high prevalence of TPN in the surgical wards, the present study was designed to investigate the short-term complications of TPN and the factors affecting in children's medical center, in Tehran, Iran.

Methods: In a retrospective cross-sectional study, all records of patients who underwent TPN in surgery wards of the children's medical center of Tehran, Iran between 2017 and 2020 were enrolled. Demographic and baseline data including sex, age and also type of surgery, duration of TPN, TPN content, and short-term complications were analyzed.

Results: one hundred and forty-five children including 97 males (66.9%) and 48 females (33.1%) were enrolled. Female patients had a significantly higher rate of central line-associated bloodstream infections (CLABSI, p=0.03). The duration of TPN was significantly correlated with the incidence of glucose disturbances (p=0.012), metabolic acidosis (p=0.05), potassium disturbances (p=0.03), liver disorders (p=0.001), dehydration (p=0.002), and CLABSI (p=0.002). The age of the patients was also significantly associated with the prevalence of potassium disturbances (p<0.001), liver complications (p<0.001), and positive blood culture (p=0.001). TPN content was not significantly associated with complications.

Conclusion: Long-term TPN was shown to increase the risks of various metabolic diseases and CLABSI. Monitoring of electrolytes levels, liver function, and other health status aspects is necessary for the patient under prolonged TPN.

Please cite this article as: Saeedi M, Mohajerani S, Mohsenipour R. The Complications of Total Parenteral Nutrition and the Contributing Factors in Children in Tehran, Iran. Int J Nutr Sci. 2022;7(2):96-101. doi: 10.30476/IJNS.2022.94960.1183.

Introduction

Total parenteral nutrition (TPN) means maintaining proper nutritional status, normal weight, and positive intravenous nitrogen balance in patients who are unable to consume food through the gastrointestinal (GI) tract (1). In children who need surgery, especially malnourished ones, nutritional support not only preserves the organ's basic function, but

also meets other anabolic growth requirements (2). Carbohydrates are the main source of energy in nutrition and maintaining the appropriate intake of them during TPN is important considering the risks of hyper/hypoglycemia (3). Intravenous lipid emulsions are an indispensable part of parenteral nutrition as a noncarbohydrate source of energy that provides essential fatty acids and helps with the delivery of the lipid-soluble vitamins A, D, E, and K (4). Amino acid requirements are mainly determined by the rate of net protein synthesis (5), and TPN is important to provide the necessary calories and essential amino acids (6).

The use of central venous catheters and improvement in intravenous nutrition has increased the life span of patients undergoing surgery (7, 8). The importance of growth in children, also the gradual advancement in amino acid solutions, fat emulsions, vitamin supplements, and minerals has led to a significant increase in the efficacy of venous nutrition in children (2). The balance of electrolytes, especially sodium, potassium, calcium, and phosphorus must be carefully maintained (9). In some cases, TPN seemed to contribute to unfavorable results (8). TPN-related complications are divided into two main categories of metabolic and catheter-dependent complications, which can occur acutely or more commonly after prolonged use. Metabolic complications include hypo/hyperglycemia, metabolic acidosis, deficiency of fatty acids, deficiency of vitamins and trace minerals, electrolytes disturbances, cholestatic jaundice, and osteopenia (5, 9-13). Catheter-related complications include central line-associated bloodstream infection (CLABSI), hemothorax, pneumothorax, cardiac tamponade, air embolism, abscess, and thrombosis (10). Complications of the liver and biliary system are also among the most common and serious problems associated with TPN (8).

The CLABSI is a serious life-threatening complication of venous nutrition with an incidence of 2-29% and it is more common in children than in adults. Most infections are related to Gram-positive organisms and most commonly *Staphilococcus epidermis* (8, 14). Central venous catheter care is the most important factor in preventing infection (14). TPN is used extensively in surgical departments where children are at greater risk of complications due to nutritional requirements. This study investigated the short-term side effects of intravenous nutrition and its associated factors in hospitalized Iranian children.

Materials and Methods

In a retrospective cross-sectional study, all records of patients who underwent TPN in the Surgery Ward of the Children's Medical Center, Tehran, Iran, between 2017 and 2020 were evaluated. Patients with incomplete data in their medical records and those undergoing peripheral vein nutrition or home TPN were excluded from the study. Data on demographic characteristics, including age, sex, and also type of the surgery, TPN duration and its content, TPN-related complications such as metabolic and electrolyte balance disorders, hepatic and renal complications, catheter-related complications, and CLABSI were collected. Complications based on laboratory examinations results were defined as below: a) hypoglycemia: blood glucose ≤50 mg/dL, b) hyperglycemia: blood glucose ≥126 mg/dL, c) hypertriglyceridemia: triglyceride levels ≥160 mg/dL, d) metabolic acidosis (bicarbonate**)** HCO3 ≤18 meq/l and pH≤7.35, e) minerals deficiency (*phosphorus)* P≤3.5 mg/dL, (Magnesium) Mg≤1.6 mg/dL, (sodium) Na≤130 mg/dL (clinically significant hyponatremia), (calcium) Ca≤8 mg/dL, and (potassium) K≤ 3.5 mg/dL, f) (erythrocyte sedimentation rate) ESR values ≤20 mm/hr, and (C-reactive protein) CRP levels less than 6 mg/dL were defined as normal; g) normal (blood urea nitrogen) BUN was defined as 5-20 mg/dL and normal creatinine (Cr) as 0.3-0.7 mg/dL, and finally h) BUN/Cr≥ 20 and urine specific gravity (SG)≥ 1015 were considered as indicators of dehydration.

Patients were divided into two groups based on liver function status: a) the first group consisted of patients who presented with biliary atresia and had impaired liver function tests (LFT) from the beginning. Mean levels for these enzymes considered as aspartate transaminase (AST)=174.8 u/l, alanine transaminase (ALT)=119.6 u/l, bilirubin (Bill)=11 mg/dL, alkaline phosphatase **(**ALP**)**=796 iu/l, and gamma-glutamyl transpeptidase (GGT)=822 u/l in these patients; b) The second group was patients who have been fed intravenously due to other underlying diseases other than biliary atresia. Mean levels for liver enzymes considered as AST=30.2 u/l, ALT=15.1 u/l, Bill=2.2 mg/dL, ALK=381.5 iu/l and GGT=113 u/l in these patients. Any increase in LFT 1.5 times higher than the age-related normal range which was not due to medication, hemolysis, and other underlying issues was considered as impaired liver function.

In this study, all patients for 3 years were evaluated by the census method. The results for quantitative variables were expressed as mean and standard deviation (mean±SD) and qualitative categorical variables were expressed as percentages. A comparison between quantitative variables was done by ANOVA test or Kruskal-Wallis test for variables with the abnormal distribution. A comparison between quantitative variables was also

performed using the Pearson correlation coefficient and Spearman rank correlation tests. Statistical analysis was performed using SPSS software (Version 23, Chicago, IL, USA). The significance level was considered as a p value less than 0.05.

Results

One hundred and forty-five children including 97 males (66.9%) and 48 females (33.1%) were enrolled in the study. The mean age of the patients was 10.7±22.8 months. The mean TPN duration was 10.3±8.9 days (min=2 and max=50 days). The frequency and percentage of different underlying diseases and TPN contents were listed in Table 1 and 2. The frequency and percentage of TPN complications were presented in Table 3. The gender of patients was significantly correlated with CLABSI (p=0.03) and elevated ESR (p=0.05) and the prevalence of both of them was higher in female patients. There was no significant relationship between the gender of patients and glucose disturbances, hypertriglyceridemia, metabolic acidosis, trace minerals disorders, intravenous catheter-related complications, liver enzymes disorders, renal complications, and CRP levels.

The prevalence of CLABSI was significantly correlated with the type of surgery (p=0.008). Patients with the imperforated anus (50%), diaphragmatic hernia (50%), and GI atresia (40%) had the highest prevalence of CLABSI. All patients with biliary atresia, imperforated anus, and diaphragmatic hernia as well as a significant percentage of Hirschsprung's patients (87.5%), malrotation (857%), esophageal atresia (87.5%), gastrointestinal atresia (75%), and gastrointestinal obstruction (375%) had LFT changes. The type of surgery was not considerably correlated with glucose disturbances, hypertriglyceridemia, metabolic acidosis, trace minerals disorders, intravenous catheter-related complications, renal complications, and CRP levels.

There was no significant relationship between the TPN content and glucose disturbances, hypertriglyceridemia, metabolic acidosis, trace minerals disorders, intravenous catheter-related complications, liver enzymes disorders, renal complications, CLABSI, and CRP levels. Also, the prevalence of LFTs disorders in patients receiving intralipid was not significantly different from other patients (p=0.6). The rate of CLABSI in patients of lower ages was significantly higher than in older ones (p=0.01). Potassium level disturbances were significantly correlated with the age of patients and the mean age was significantly higher in those with hypokalemia and lower in those with hyperkalemia (26.42 vs. 0.9 months) (p<0.001). There was a

Table 1: The leading causes of surgeries needed TPN during the hospital admission.

Variable	N (%)
Hirschsprung's disease	62 (42.8)
Imperforated anus	2 (1.4)
Pancreatitis	1 (0.7)
Biliary atresia	17 (11.7)
Esophageal atresia	16 (11.0)
Malrotation	15 (10.3)
Obstruction	12 (8.3)
Gastrointestinal atresia	15 (10.3)
Meconium ileus	2 (1.4)
Diaphragmatic hernia	2 (1.4)
Midgut volvulus	1 (0.7)

Table 2: Type and frequency of TPN contents in patients needed TPN during hospital admission.

Variable		N (%)
TPN content	All	78 (53.7)
	All without B-complex, Calcium	4 (2.7)
	All without B-complex, pediatrace, glycophose	3 (2.1)
	All without magnesium, pediatrace, glycophose	4 (2.8)
	All without pediatrace, glycophose	2 (1.4)
	All without pediatrace, magnesium, glycophose, calcium	2 (1.4)
	All without B-complex, magnesium	1 (0.7)
	All without glycophose	1 (0.7)
	All without intralipid, glycophose	2 (1.4)
	All without intralipid,	18 (12.4)
	All without intralipid, aminofusion, vitamin C	1 (0.7)
	All without pediatrace	2 (1.4)
	All without B-complex	7 (4.8)
	All without pediatrace, B-complex	10 (6.9)
	All without intralipid, pediatrace	6 (4.1)
	All without magnesium, pediatrace	4 (2.8)

All means TPN with following content: Dextrose serum, B complex, Vitamin C, Calcium, Glycophose, Pediatrace, Magnesium, Intralipid, Aminofusion.

Table 3: Type and frequency of TPN-related complications in patients needed TPN during hospital admission.

Complication	N (%)
Hypoglycemia	16 (11.0)
Hyperglycemia	17 (11.7)
Hypertriglyceridemia	2 (1.4)
Metabolic acidosis	5 (3.4)
Magnesium deficiency	10 (6.9)
Phosphate deficiency	8 (5.5)
Hyponatremia	12 (8.3)
Hypernatremia	3 (2.1)
Hypocalcemia	22 (15.2)
Hypercalcemia	9 (6.2)
Hypokalemia	13 (9)
Hyperkalemia	7 (4.8)
Impaired at least one liver function test in 15 patients with biliary atresia	13 (88.2)
Impaired at least one liver function test in 128 patients without biliary atresia	39 (30.5)
(Blood urea nitrogen) BUN≥20 mg/dl	4 (2.8)
(Blood urea nitrogen/creatinine) BUN/Cr≥20	42 (29)
(Urine specific gravity) SG≥1020	9 (6.2)
Dehydration	9 (6.2)
(Erythrocyte sedimentation rate) ESR≥20 mm/h	15 (10.3)
(C-reactive protein) CRP≥6mg/dl	39 (26.89)
Positive blood culture	15 (10.3)
Central venous line complication	6 (4.1)

significant relationship between age and hepatic complications, with the mean age of LFT patients being significantly lower (4 vs. 15 months) (p=0.001).

The age of patients was not considerably correlated with glucose disturbances, hypertriglyceridemia, metabolic acidosis, trace minerals disorders, intravenous catheter-related complications, sodium and calcium disturbances, and rate of dehydration. The duration of TPN was significantly longer in people with glucose disturbances (p=0.012). The duration of TPN was positively correlated with the incidence of metabolic acidosis (p=0.05), mineral disorders (p=0.002), CLABSI (p=0.002), hyperkalemia (p=0.03), liver function disorders (p=0.002), and dehydration (p=0.02). There was no significant relationship between the duration of TPN and hypertriglyceridemia, intravenous catheter-related complications, trace minerals disorders, and sodium and potassium disturbances.

Discussion

Maintaining the nutritional status of children in the surgical wards is essential not only for the recovery of patients, but also for growth and development (2). The importance of growth in children has led to significant advances in total parenteral nutrition. Although TPN, like other therapeutic modalities, can be associated with complications that are sometimes life-threatening, most studies on the use of TPN and its complications have been conducted in adults (15). In the present study, over 3 years, short-term complications of intravenous feeding were evaluated in 145 patients. The mean period of TPN in patients was 10.3 days.

The child's developing brain is more susceptible to hypoglycemia which can result in permanent damages (16). Furthermore, young age is a risk factor for developing hypoglycemia, especially when the child is ill (17). In the studied patients, glucose disturbances were the most common complication, with the prevalence of 16 (11%) hypoglycemia, 17 (11.7%) hyperglycemia, and 3 (2.1%) of both disorders. The prevalence of this complication was almost in line with the results of a similar study (10). The incidence of glucose disturbances had a significant relationship with the duration of TPN (p=0.012). Five patients (3.4%) developed acid-base disorders in the course of the disease, which was less prevalent than in other similar study (10). The duration of TPN was significantly associated with acid-base disturbances (p=0.05), although this complication may also be due to the underlying disease of the patient that caused acidosis.

The prevalence of electrolyte abnormalities in this study was lower than that of Mantegazza *et al.*'s (10), in which the most common electrolyte complications were hyperphosphatemia, hypermagnesemia, and hypercalcemia. The inclusion of patients undergoing chemotherapy and possibly tumor lysis syndrome and malnourished patients in the abovementioned study may lead to different results from our ones. On the other hand, most of the complications associated with these electrolytes in the present study were in the form of hypomagnesemia and hypophosphatemia; therefore, it seems that adjusting a standard solution according to the needs of the Iranian population and regular monitoring of electrolyte levels would be effective in reducing these complications.

Among electrolyte abnormalities, there was a significant relationship between the patient's potassium level and the age (p<0.001), with a higher mean age in the group with hypokalemia. Potassium abnormalities were also significantly correlated with TPN duration (p=0.03). It seems that the occurrence of hyperkalemia in people with longer TPN duration should be monitored accurately. Liver disorders were evaluated in two groups of patients with and without biliary atresia at the beginning, separately. In previous studies, different definitions of the prevalence of liver disorders ranged from

7.4% to 84% (10, 18). In this study, 88.2% of patients with biliary atresia had at least one impaired LFT parameter, and in other patients, this rate was 30.2%. The incidence of liver disorders in both groups was not significantly correlated with TPN content.

The incidence of liver disorders was significantly correlated to the type of surgery. In patients with biliary atresia, as expected, liver dysfunction was initially observed, and Hirschsprung's and gastrointestinal atresia patients had a higher prevalence of these disorders after biliary atresia. However, because of the smaller number of patients in other types of surgeries, a larger sample size study is recommended for accurate comparison. The duration of TPN was also significantly correlated with the incidence of liver disorders. Liver dysfunction and intestinal failure have been reported as complications of prolonged TPN (18, 19). So it is necessary to discontinue the TPN, according to indication, as soon as possible. There was also a significant relationship between the incidence of complications and the patient's age; therefore, it is more likely to occur in younger people.

Of the 145 patients studied, only 4 (2.8%) had BUN above 20 mg/dl and 9 (6.3%) had dehydration. The incidence of dehydration was significantly associated with the duration of TPN. Dehydration is also mentioned as a complication of prolonged home parenteral nutrition (20); therefore, further studies concerning patients' weight and glomerular filtration rate (GFR) calculation are needed to evaluate renal complications. The CLABSI occurred in 15 cases (10.3%) which were significantly associated with TPN duration. The prevalence of CLABSI was also reported to be higher in patients with longer hospitalization in (intensive care unit) ICU wards in the United States and prolonged TPN patients in Turkey (21, 22). The most common organisms in the microbial culture were *S. epidermis* and subsequently Gram-negative species. There was a significant relationship between the rate of CLABSI and the type of surgery, and the age of patients too. The present study was limited by the retrospective design in which those cases with incomplete data were excluded from the study.

Conclusion

Prolonged total parenteral nutrition in children, especially in lower-aged ones can cause different life-threatening complications such as metabolic, electrolytes, and organ-related disorders. Therefore, all TPN recipients require close monitoring of their metabolic and clinical status to prompt responses to situations that need adjustments in the TPN regimen.

Acknowledgment

The authors would like to thank our institution for their support.

Conflict of Interest

None declared.

References

1 Wheble GA, Knight WR, Khan OA. Enteral vs total parenteral nutrition following major upper gastrointestinal surgery. *Int J Surg*. 2012;10:194-7. DOI: 10.1016/j.ijsu.2012.02.015. PMID: 22414681.

2 Koletzko B, Goulet O, Hunt J, et al. 1. Guidelines on paediatric parenteral nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr*. 2005;41:S1-S4. DOI: 10.1097/01.mpg.0000181841.07090.f4. PMID: 16254497.

3 Mesotten D, Joosten K, van Kempen A, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Carbohydrates. *Clin Nutr*. 2018;37:2337-43. DOI: 10.1016/j.clnu.2018.06.947. PMID: 30037708.

4 Lapillonne A, Mis NF, Goulet O, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids. *Clin Nutr*. 2018;37:2324-36. DOI: 10.1016/j.clnu.2018.06.946. PMID: 30143306.

5 Van Goudoever JB, Carnielli V, Darmaun D, de Pipaon MS, Braegger C, Bronsky J, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Amino acids. *Clin Nutr*. 2018;37:2315-23. DOI: 10.1016/j.clnu.2018.06.945. PMID: 30100107.

6 Arsenault D, Brenn M, Kim S, et al. ASPEN Clinical Guidelines: Hyperglycemia and hypoglycemia in the neonate receiving parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 2012;36:81-95. DOI: 10.1177/0148607111418980. PMID: 22179520.

7 Herman R, Btaiche I, Teitelbaum DH. Nutrition support in the pediatric surgical patient. *Surg Clin North Am*. 2011;91:511-41. DOI: 10.1016/j.suc.2011.02.008. PMID: 21621694.

8 Worthington PH, Gilbert KA. Parenteral nutrition: risks, complications, and management. *J Infus Nurs*. 2012;35:52-64. DOI: 10.1097/NAN.0b013e31823b98ef. PMID: 22222292.

9 Jochum F, Moltu SJ, Senterre T, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric

parenteral nutrition: Fluid and electrolytes. *Clin Nutr.* 2018;37:2344-53. DOI: 10.1016/j.clnu.2018.06.948. PMID: 30064846.

10 Mantegazza C, Landy N, Zuccotti G, et al. Indications and complications of inpatient parenteral nutrition prescribed to children in a large tertiary referral hospital. *Ital J Pediatr.* 2018;44:66. DOI: 10.1186/s13052-018-0505-x. PMID: 29880053.

11 Domellöf M, Szitanyi P, Simchowitz V, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Iron and trace minerals. *Clin Nutr.* 2018;37:2354-9. DOI: 10.1016/j.clnu.2018.06.949. PMID: 30078716.

12 Mihatsch W, Fewtrell M, Goulet O, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Calcium, phosphorus, and magnesium. *Clin Nutr.* 2018;37:2360-5. DOI: 10.1016/j.clnu.2018.06.950. PMID: 30097365.

13 Bronsky J, Campoy C, Braegger C, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Vitamins. *Clin Nutr.* 2018;37:2366-78. DOI: 10.1016/j.clnu.2018.06.951. PMID: 30100105.

14 Johnson T, Sexton E. Managing children and adolescents on parenteral nutrition: challenges for the nutritional support team. *Proc Nutr Soc.* 2006;65:217-21. DOI: 10.1079/pns2006502. PMID: 16923305.

15 Agudelo GM, Giraldo NA, Aguilar NL, et al. Incidence of nutritional support complications in patient hospitalized in wards. multicentric study. *Colomb Med (Cali).* 2012;43:147-53. DOI: 10.25100/cm.v43i2.830 . PMID: 24893056.

16 Verbruggen SC, de Betue CT, Schierbeek H, Chacko S, van Adrichem LN, Verhoeven J, et al. Reducing glucose infusion safely prevents hyperglycemia in post-surgical children. *Clin Nutr.* 2011;30:786-92. DOI: 10.1016/j.clnu.2011.05.011. PMID: 21719165.

17 Joosten K, Verbruggen SC, Verhoeven JJ. Glycaemic control in paediatric critical care. *Lancet.* 2009;373:1423-4. DOI: 10.1016/S0140-6736(09)60814-X. PMID: 19394523.

18 Cober MP, Teitelbaum DH. Prevention of parenteral nutrition-associated liver disease: lipid minimization. *Curr Opin Organ Transplant.* 2010;15:330-3. DOI: 10.1097/MOT.0b013e328338c2da. PMID: 20386446.

19 Andorsky DJ, Lund DP, Lillehei CW, et al. Nutritional and other postoperative management of neonates with short bowel syndrome correlates with clinical outcomes. *J Pediatr.* 2001;139:27-33. DOI: 10.1067/mpd.2001.114481. PMID: 11445790.

20 Dreesen M, Foulon V, Vanhaecht K, et al. Development of quality of care interventions for adult patients on home parenteral nutrition (HPN) with a benign underlying disease using a two-round Delphi approach. *Clin Nutr.* 2013;32:59-64. DOI: 10.1016/j.clnu.2012.05.006. PMID: 22658235.

21 Control CfD, Prevention. Vital signs: central line-associated bloodstream infections—the United States; 2001, 2008, and 2009. 2011.

22 Yilmaz G, Koksal I, Aydin K, et al. Risk factors of catheter-related bloodstream infections in parenteral nutrition catheterization. *JPEN J Parenter Enteral Nutr.* 2007;31:284-7. DOI: 10.1177/0148607107031004284. PMID: 17595436.