Original Article

Comparison of effectiveness, safety, and costs of standardized and customized parenteral nutrition support among gastric cancer patients after gastrectomy: a retrospective cohort study

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Background and Objectives: To compare the effectiveness, safety, and costs of commercial standardized multi-chamber bag and customized compounded total parenteral nutrition (TPN) among gastric cancer patients after gastrectomy. **Methods and Study Design:** A retrospective cohort study was conducted among 64 gastric cancer patients who underwent gastrectomy from 2014 to 2016 in a tertiary teaching hospital in Beijing, China. Patients were categorized into standardized (s-TPN) and customized TPN (c-TPN) groups based on their TPN order after gastrectomy. Patients were followed up until discharge. The effectiveness measures (body mass index (BMI) and albumin) and safety measures (liver and renal functions and electrolytes) were compared before TPN started and after TPN finished within and between the two groups. The length of hospital stay and costs were compared between the two groups. **Results:** There were no significant differences between the two groups in BMI preservation, metabolic complications, the length of hospital stay and costs, except that both total bilirubin (Tbil) and direct bilirubin (Dbil) were significantly higher in the s-TPN group than c-TPN (p<0.05). **Conclusions:** There were no significant differences in effectiveness and safety measures, the length of hospital stay and costs between s-TPN and c-TPN groups, except that s-TPN group was more likely to lead to parenteral nutrition-associated liver disease (PNALD). More studies are needed to confirm the findings of this study in other healthcare settings and study populations.

Key Words: parenteral nutrition, multi-chamber bag, clinical outcome, cost analysis, PNALD

INTRODUCTION

Commercial standardized multi-chamber bag (s-TPN) and customized compounded total parenteral nutrition (c-TPN) are two major types of TPN formulations and have been widely used around the world for more than two decades. It is important to compare these two types of TPN formulations regarding effectiveness, safety, and costs to optimize clinical decision-making in nutrition support.

Previous studies have shown that s-TPN formulations, i.e., multi-chamber bags (MCBs), are cheaper but as safe and effective as c-TPN in both childrenand adults.[1-9] However, MCBs may not be suitable for surgical and critically ill patients.[10] In very-low-birth-weight infants, the growth may be unsatisfactory if MCBs were used for nutrition support.[11] The amount of proteins in MCBs are lower, making it more difficult to meet patient's protein needs. Also, patients using MCBs are more likely to develop hyponatremia than those using c-TPN.[12]

Gastrectomy is an effective treatment option for gastric cancer, and patients with gastrectomy represent one of the largest populations receiving postoperative TPN. However, there are no published studies comparing the effectiveness, safety, and costs of s-TPN and c-TPN in gastric cancer patients after gastrectomy. Here we conducted a retrospective cohort study to further investigate the differences of effectiveness, safety, and costs between s-TPN and c-TPN in these patients.

MATERIALS AND METHODS

Study design and methods

This study was a retrospective cohort study. The effectiveness parameters, safety parameters, the length of

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Manuscript received 06 July 2017. Initial review completed 27 July 2017. Revision accepted 22 August 2017.
doi: 10.6133/apjcn.012018.03

hospital stay and costs were compared between s-TPN and c-TPN groups. We extracted the medical charts for patients who met inclusion and exclusion criteria and selected the admissions with gastrectomy as the observation periods. We followed up patients from the first day of postoperative parenteral nutrition (PN) support to discharge. Patient demographic characteristics were also extracted from admission, discharge and transfer (ADT) system of the hospital.

The effectiveness parameters included body mass index (BMI) and albumin. The safety parameters included liver function [alanine aminotransferase (ALT), total bilirubin (Tbil), direct bilirubin (Dbil)], kidney function [creatinine (Cr), urea nitrogen (Urea)], electrolytes (K, Na, Cl, Ca) and blood glucose (Glu). The costs parameters included total cost, total nutrition support cost, TPN drug cost, enteral nutrition (EN) drug cost. Total cost meant the total cost during the hospitalization. Total nutrition support cost included compounding cost, three-liter bags cost and other material costs.

Population

Patients aged 18-70 years, having gastrectomy due to gastric cancer, with preoperative BMI <30 kg/m^2, with postoperative PN ≥5 days and with normal baseline renal and hepatic functions at Peking Union Medical College Hospital (PUMCH) during Jan 2014-Jan 2016 were identified through electronic medical record system.

We excluded patients whose regimen did not comply with the Chinese Society for Parenteral and Enteral Nutrition (CSPEN) Guidelines for adult perioperative nutrition support[13] to control for confounding. Furthermore, patients with immunodeficiency, with hypersensitivity to PN, having used both standardized and customized TPN during admission, or without complete data were also excluded.

Statistical analysis

We compared pre- and post- TPN nutrition status and lab values to evaluate the effectiveness and safety of TPN for the s-TPN group and c-TPN group, respectively. We also compared the change of the nutrition status and lab values, length of hospital stay and costs between the two groups.

All continuous variables were performed with Normal Distribution Test and Homogeneity of Variance Test. Paired t-test (if normally distributed) or Wilcoxon signed ranks test (if not normally distributed) was used to make within-group comparisons. Independent t-test (if normally distributed) or Mann-Whitney U test (if not normally distributed) was used to do between-group comparisons. A p value <0.05 was considered statistically significant.

All analyses were performed using SPSS, Version 22 (SPSS Inc, Chicago, IL).

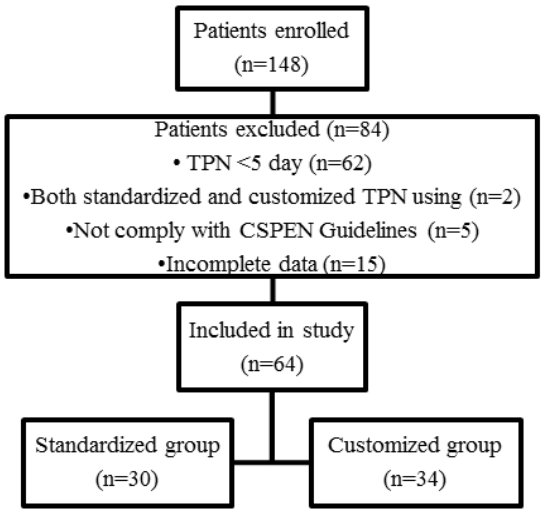

Figure 1. Patient enrolled, exclusion and distribution.

RESULTS

We included 30 patients in the s-TPN group and 34 patients in the c-TPN group in this study (Figure 1). The baseline characteristics were shown in Table 1. Patient demographic characteristics (age, gender, BMI) and clinical characteristics (NRS2002, Alb, ALT, Tbil, Dbil, Cr, Urea, Glu, K^+, Na^+, Cl^- and Ca^{2+}) between s-TPN and c-

Table 1. Demographic and clinical characteristics at baseline

	S-TPN (n=30)	C-TPN (n=34)	p value
Age (y)	59±15	59±10	0.990†
Gender (F %)	5(17%)	13(38%)	0.057‡
BMI (kg/m^2)	23.28±3.08	22.62±2.98	0.385†
NRS2002	3±1	4±1	0.360§
ALB (g/L)	35±6	34±5	0.366†
ALT (U/L)	55±90	37±34	0.459§
Tbil (μmol/L)	14.3±8	12.6±4.5	0.835§
Dbil (μmol/L)	4.4±2.4	3.8±1.2	0.726§
Cr (μmol/L)	74±20	73±41	0.087§
Urea (mmol/L)	5.31±1.9	4.73±1.82	0.174§
Glu (mmol/L)	6.8±2.1	6.6±1.4	0.459†
K (mmol/L)	4.1±0.3	4.1±0.4	0.856†
Na (mmol/L)	140±3	140±3	0.977†
Cl (mmol/L)	106±2	105±3	0.359†
Ca (mmol/L)	2.12±0.14	2.09±0.1	0.317†

BMI: body mass index; NRS2002: nutritional risk screening 2002; ALB: albumin; ALT: alanine transaminase; Tbil: total bilirubin; Dbil: direct bilirubin; Cr: creatinine; Glu: glucose; K: potassium; Na: sodium; Cl: chloride; Ca: calcium.
†Independent t-test.
‡Chi-square test.
§Mann-Whitney U test.

TPN groups were similar.

The main TPN components of the two groups were as follow: amino acid was 60.38±6.35 and 60.38±6.35; fat emulsion was 63.97±6.26 and 59.76±5.11; dextrose was 134.39±13.36 and 200.51±36.26 in S-TPN and C-TPN. All the MCB used in this study were Kabiven Peripheral 1.92L and Kabiven Peripheral 1.44L. Type of lipids, type of amino acids and dextrose were calculated based on this brand.

S-TPN group received higher levels of amino acids, fat emulsions, calcium, magnesium, and phosphorus, while lower levels of dextrose, sodium, and potassium, compared to the c-TPN group. Also, the composition of fat emulsions was significantly different between the two groups. S-TPN group used more long-chain fat emulsions, but c-TPN group used more medium/long-chain emulsions, structured fat emulsions, and ω-3 fish oil.

Effectiveness and safety of TPN support

TPN support was effective in preserving BMI and Alb after gastrectomy (Table 2). The pre- and post-TPN BMI and Alb were similar in s-TPN and c-TPN groups (the deltas were not significantly different from zero).Also the pre- and post-TPN lab values were similar as well.

We also compared the pre- and post-TPN differences between the two groups. We found both Tbil and Dbil increased in the s-TPN group, and the increase was significantly greater than the c-TPN group. Increased Tbil were 6.74±12.18 μmol/L and -0.77±4.77 μmol/L respectively (p=0.002). Increased Dbil were 4.86±7.75 μmol/L and 0.41±1.93 μmol/L respectively (p=0.002). Both post-TPN Tbil (21.08±15.89 μmol/L) and Dbil (9.21±8.5 μmol/L) in S-TPN group almost reached or exceeded the upper limit (reference range: TBil 5.1-21.2 μmol/L; DBil 0.0-6.8 μmol/L). Other lab values were not significantly elevated in both groups (ALT, Cr, Urea and Glucose, K, Na, Cl and Ca) and no between-group differences were detected.

Length of hospital stay and cost analysis

The lengths of postoperation to discharge were not significantly different between the two groups. S-TPN had slightly longer TPN support (8±3 days) than c-TPN group (7±5 days), and S-TPN group had a significantly shorter length of hospital stay (19±12 days) versus c-TPN group (24±13 days) may because of longer preoperative stay.

There were no significant differences in total cost, total nutrition support cost, TPN drug cost and EN drug cost between the two groups (Table 3).

DISCUSSION

In this study, we found significantly elevated Tbil and Dbil levels in the s-TPN group after TPN supported. Other measures of effectiveness, safety, the length of hospital stay and costs were show no significant differences in between two groups.

The s-TPN group, significantly elevated in Tbil and Dbil levels, was suggested cholestasis of parenteral nutrition-associated liver disease (PNALD). PNALD is defined as a decrease in bile flow, independent of mechanical obstruction in patients receiving prolonged PN and with no other underlying cause of liver disease, It is also referred to as PN-associated cholestasis (PNAC).[14] Recent studies found that fasting, extended duration of PN, soybean oil (contain phytosterols) may play important roles in the pathogenesis of PNALD.[15-17] In the s-TPN group, 100% of the patients received soybean-based long-chain fat emulsion. The higher level of long-chain fat emulsions may increase the risk of cholestasis. Meanwhile, the fish oil in the c-TPN group may be protective against PNALD.[18,19] Also, the amount of macronutrients may be another reason. The amino acids and fat emulsion are more in s-TPN, and Dextrose is more in c-TPN.

We found there was no significant difference in post-operative hospital stay between the groups, and TPN duration was slightly longer in the s-TPN group than in the c-TPN group. The 1-day difference, however, may not have clinical significance. Our study was in line with previous research that the length of hospital stay was not significantly different between customized and standardized PN in an acute care setting.[12]

As mentioned earlier, the dominant views regarding the cost of s-TPN and c-TPN support were that c-TPN have cost-saving advantages than s-TPN. But there is also an opposite opinion that considering fixed cost (depreciation, maintenance, filters and testing of laminar flow cabinets and manpower), s-TPN might be cheaper in hospitals with at least 15 patients requiring PN support per day.[20] In our study, as we did not consider workforce cost, clean room, and laminar flow cabinets' maintenance cost, we didn't find statistically significant difference in the total costs. If we counted those costs in, the c-TPN group might have higher costs than the s-TPN group. On the other hand, it should be noted that as ω-3 fish oil injection was much costly than other fat emulsions, and the 94.1% of the c-TPN group contained ω-3 fish oil while this component was absent in the s-TPN group at all. Patients in c-TPN may have benefited from ω-3 fish oil because they had better liver functions.

This study has strengths. First, based on our knowledge this is the first study to compare standardized and customized PN support among Asian people. Second, this study was the first study focus on gastric cancer patients after gastrectomy. The results may help surgeons to make a decision on PN support in these patients. Third, to explore the costs of standardized and customized PN support in development country could provide better decision support to health insurance policy.

This study also has limitations. First, the follow-up time was short. We did not follow up patients after discharge; thus, long-term outcomes and costs were not evaluated. Second, the study was conducted in a tertiary teaching hospital in China, and the results may not be generalizable to other healthcare settings. We may need more studies to compare these two PN support strategies.

There were no significant differences in BMI preservation, metabolic parameters and costs between the s-TPN group and c-TPN group, except that s-TPN group was more likely to lead to PANLD. We suggest that c-TPN should be used in the patients with cholestasis. More studies are needed to confirm the findings of this study in other healthcare settings and study populations.

Table 2. Clinical parameters pre- and post-TPN support

	S-TPN				C-TPN				D	
	Pre-TPN	Post-TPN	D1	*p*	Pre-TPN	Post-TPN	D2	*p*	D2-D1	*p*
BMI	23.28±3.08	22.18±2.78	-1.11±1.06	0.000[†]	22.62±2.98	21.72±2.85	-0.90±0.98	0.000[a]	0.21	0.416[§]
ALB	35.3±6.3	32.1±4	-3.1±7	0.020[†]	34±4.8	33.3±4.3	-0.7±6.2	0.494[a]	2.4	0.151[§]
ALT	54.6±89.5	37.1±28.4	-17.5±86.1	0.579[‡]	36.8±33.7	26±16.7	-10.8±33.6	0.049[b]	6.7	0.667[¶]
Tbil	14.33±7.96	21.08±15.89	6.74±12.18	0.004[‡]	12.61±4.54	11.85±4.58	-0.77±4.77	0.355[a]	-7.51	0.002[¶]
Dbil	4.35±2.36	9.21±8.5	4.86±7.75	0.000[‡]	3.82±1.15	4.22±1.95	0.41±1.93	0.228[b]	-4.45	0.002[¶]
Cr	74.2±19.6	68.5±15.5	-5.7±11.8	0.037[‡]	73.1±41	72±59	-1.1±20.4	0.011[b]	4.6	0.936[¶]
Urea	5.311±1.902	6.164±1.917	0.853±2.434	0.065[†]	4.726±1.819	5.597±1.874	0.871±1.68	0.005[a]	0.018	0.973[§]
Glu	7.06±2.64	6.77±2.09	-0.29±2.72	0.657[‡]	7.15±1.9	6.6±1.35	-0.55±2.21	0.270[b]	-0.26	0.866[¶]
K	4.09±0.34	4.06±0.37	-0.04±0.48	0.677[†]	4.08±0.39	4.05±0.38	-0.03±0.53	0.774[a]	0.01	0.936[§]
Na	139.6±2.6	137.8±2.4	-1.8±3	0.003[†]	139.6±3.4	138.9±3.2	-0.6±3.9	0.336[a]	1.2	0.194[§]
Cl	106±2.5	103.7±3	-2.3±3	0.000[†]	105.4±2.9	104.6±3.6	-0.8±4.2	0.257[a]	1.5	0.112[§]
Ca	2.119±0.14	2.126±0.121	0.007±0.165	0.544[‡]	2.088±0.103	2.150±0.107	0.062±0.122	0.005[a]	0.055	0.099[¶]

BMI: body mass index; ALB: albumin; ALT: alanine transaminase; Tbil: total bilirubin; Dbil: direct bilirubin; Cr: creatinine; Glu: glucose; K: potassium; Na: sodium; Cl: chloride; Ca: calcium.
[†]Paired t-test.
[‡]Wilcoxon signed ranks test.
[§]Independent t-test.
[¶]Mann-Whitney U test.

Table 3. Length of stay and cost analysis

	S-TPN (n=30)	C-TPN (n=34)	*p* value†
Length of hospitalization (d)	19±12	24±13	0.029
Length of postoperative hospitalization (d)	14±10	14±11	0.749
TPN duration (d)	8±3	7±5	0.002
Total cost (RMB)	47,961.31±21,059.16	50,916.42±18,857.46	0.216
Total nutrition support cost (RMB)	5,131.42±2,510.67	5,506.13±4,417.74	0.306
TPN drug cost (RMB)	5,031.46±2,418.73	5,385.99±4,382.91	0.925
EN drug cost (RMB)	120.19±242.27	120.14±217.7	0.987

TPN: total parenteral nutrition; EN: enteral nutrition.
†Mann-Whitney U test.

AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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