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BRIEF ARTICLE

Hypocaloric peripheral parenteral nutrition with lipid emulsion in postoperative gastrointestinal cancer patients

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Abstract

AIM: To investigate the use of lipid emulsion substituting for glucose in postoperative hypocaloric peripheral parenteral nutrition (HPPN).

METHODS: This prospective, randomized study was conducted on 20 postoperative gastrointestinal cancer patients. They were randomized and equally divided into interventional group and control group, and both were administered isocaloric and isonitrogenous diets with for lipid emulsion substituting for partial glucose loads in the interventional group.

RESULTS: Nutritional parameters and biochemical data were compared between the two groups before and after 6-d of HPPN. Most investigated variables showed no significant changes after administration of HPPN with lipid emulsion. However, the postoperative triglyceride level was significantly lower in the interventional group than in the control group ($P < 0.05$). In comparison with lipid emulsion, glucose administration resulted in less decrease in postoperative prealbumin level ($P < 0.05$).

CONCLUSION: In addition to supplementing with essential fatty acid, it seems that HPPN with lipid emulsion is well-tolerated and beneficial to postoperative gastrointestinal cancer patients.

Key words: Hypocaloric peripheral parenteral nutrition; Lipid emulsion; Dextrose

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INTRODUCTION

Parenteral nutrition has been accepted as an effective means of nutritional supplementation for malnourished patients or those ordered to fast for a period of time. However, parenteral nutritional support often requires access *via* the central venous route, which sometimes leads to technical complications such as pneumothorax or hemothorax on insertion of central venous catheter, and subsequent catheter-related infection. In clinical practice, patients undergoing surgery for gastrointestinal (GI) tract cancer only need a brief period of fast, to wait for flatus passage and confirm recovering peristaltic function of the bowel. Total parenteral nutrition is indicated for patients having nothing *per os* or without normal enteral function over one week. Therefore, for those patients evaluated as well-nourished before operation, the short-term hypocaloric parenteral nutrition is more appropriate than total central parenteral nutrition postoperatively.

Hypocaloric peripheral parenteral nutrition (HPPN) appears to be indicated in patients without malnourishment who are planning to undergo a short-term fast following surgery. HPPN is a method using lower glucose loads mixed with soluble alternatives *via* the peripheral venous route to avoid the complications of hypermetabolism, hyperglycemia and the use of central venous catheters in stressed patients[1,2]. Currently, HPPN (15-20 kcal/kg per day) has been a trend for managing postoperative patients in a situation of moderate malnutrition and short-term fast[3]. Our current study was designed as a prospective, randomized clinical trial to explore the effects of short-term HPPN using lipid emulsion for patients with GI cancers following surgery.

MATERIALS AND METHODS

Patients

This prospective, randomized study was conducted on 20 patients (8 males and 12 females) between the ages of 33 and 80 years old. All of the patients underwent elective resection for GI cancer at the Department of Surgery of Kaohsiung Medical University Hospital. Patients with underlying diseases, such as hepatic failure, renal failure, dyslipidemia, shock, and congestive heart failure, and patients with any metabolic disorder associated with impaired nitrogen utilization were excluded from this study. The including criteria for our patients are per the following features: (1) GI cancer patients receiving elective resection; (2) Preoperative serum albumin level ≥ 3.0 g/dL; and (3) Blood loss < 500 mL in operation and no need of blood transfusion. Written informed consent was obtained from all subjects and/or guardians for the use of their blood samples. Sample acquisition and subsequent use were also approved by the institutional review board of the Kaohsiung Medical University Hospital. The patients were randomly divided into two groups with isocaloric and isonitrogenous solution (Table 1). In the interventional group, 10 patients were given 120 g of carbohydrate (Taita No.5®, Otsuka Pharmaceuticals, Taipei, Taiwan), 40 g of amino acids (Amiparen® 10% solution, Otsuka Pharmaceuticals, Osaka, Japan) and 40 g of fatty acid (Intralipid®, Fresenius Kabi Pharmacia AB, German). In the control group, 10 patients were given 220 g of carbohydrate and 40 g of amino acids (Amiparen®) and no fat emulsion. The initial blood samples were drawn one day before surgery. The peripheral infusion of parenteral nutrition was administered immediately for 6 d postoperatively.

Table 1 Isocaloric and isonitrogenous constituents of the two groups

	Interventional group	Control group
[1]Taita No.5® (400 mL/bot)	3 bot/d	4 bot/d
[2]Amiparen® (400 mL/bot)	1 bot/d	1 bot/d
[3]Intralipid® (100 mL/bot)	2 bot/d	
50% glucose (20 mL/amp)		6 amp/d
Total volume (mL)	1800	2120
Total calories (kcal)	1040	1040

[1]Taita No.5® (10% glucose), Taiwan Otsuka Pharmaceutical Co., Ltd; [2]Amiparen® (10% crystalline amino acid), Japan Otsuka Pharmaceutical Co., Ltd; [3]Intralipid® (20% fatty acid), Fresenius Kabi Pharmaceutical Co., Ltd.

Nutritional assessment, including body weight, anthropometry, serum proteins (prealbumin, transferrin and albumin) and nitrogen balance, were determined one day prior to surgery and on post-operative day 7. In addition, hematological and biochemical parameters, including complete blood count, total lymphocyte count, electrolytes, total bilirubin, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, creatinine, triglyceride, cholesterol, glucose, insulin and c-peptide, were also measured. The frequency of thrombophlebitis by peripheral parenteral nutrition was also recorded.

Statistical analysis

All of the continuous data were expressed as mean ± SE. Laboratory data before the administration of HPPN showed no statistical differences between the two study groups, and were regarded as baseline. Statistical analyses were performed using the Statistical Package for the Social Sciences Version 11.5 software (SPSS, Inc., Chicago, IL). The independent Student's *t*-test was used to compare the differences between continuous variables in postoperative measurements between the two groups. All of the nominal data were tested with either Fischer's exact test or the chi-square test. A P value of less than 0.05 was considered to be statistically significant.

RESULTS

Patient demographic data are listed in Table 2. There were no differences in age, gender, preoperative diagnosis and frequency of postoperative complications between the two groups. The study parameter values at baseline, one day before surgery, and after 6 d of peripheral parenteral infusion (day 7) are shown in Tables 3 and 4.

Except for triglyceride, all of the hematological and biochemical parameters exhibited no statistical significance in terms of differences between the preoperative

Table 2 Demographic data and postoperative complications in the two groups

Parameter	Interventional group n = 10	Control group n = 10	P
Gender			NS
Male/Female	5/5	3/7	
Age (years ± SE)	58.9 ± 2.9	67.2 ± 3.6	NS
Primary lesion			NS
Colon cancer	7	6	
Gastric cancer	3	4	
Complication			NS
Thrombophlebitis	3	4	
Fever	1	1	
Wound infection	1	1	
Pneumonia	1	0	

Table 4 Anthropometry and various nutritional parameters before and after operation between the two groups

Variables	Pre-operative	Post-operative	P
Body weight (kg)			NS
Intervention group	56.9 ± 3.6	55.6 ± 3.9	
Control group	54.8 ± 3.0	52.2 ± 2.7	
Triceps skin fold (cm)			NS
Intervention group	12.9 ± 2.0	13.3 ± 2.0	
Control group	13.4 ± 2.2	13.5 ± 2.1	
Mid-arm circumference (cm)			NS
Intervention group	25.1 ± 1.2	24.3 ± 1.1	
Control group	24.4 ± 0.8	24.2 ± 0.9	
Prealbumin (mg/dL)			< 0.05
Intervention group	22.0 ± 1.9	17.7 ± 1.6	
Control group	21.4 ± 2.3	19.9 ± 1.2	
Transferrin (mg/dL)			NS
Intervention group	254.4 ± 21.0	186.2 ± 18.2	
Control group	224.8 ± 10.8	173.4 ± 12.5	
Albumin (gm/dL)			NS
Intervention group	4.0 ± 0.1	3.5 ± 0.1	
Control group	3.9 ± 0.1	3.4 ± 0.1	
Nitrogen balance			NS
Intervention group	-5.5 ± 1.4	-6.5 ± 1.3	
Control group	-5.6 ± 1.3	-6.4 ± 1.4	

and postoperative data between the two groups (all P > 0.05, Table 3). Postoperative triglyceride level in the interventional group was significantly lower than the control group (P < 0.05, Table 3). There were no significant differences in anthropometry, transferrin, albumin level, and nitrogen balance postoperatively between the two groups. However, postoperative prealbumin level showed a significant decrease in the interventional group compared with the control group (P < 0.05, Table 4).

Table 3 Routine blood and biochemical data before and after operation between the two groups

Variables	Pre-operative	Post-operative	P
White blood cells (/μL)			NS
Intervention group	5667.0 ± 767.5	6564.0 ± 665.3	
Control group	6222.0 ± 579.4	6675.0 ± 704.4	
Hemoglobin (g/dL)			NS
Intervention group	11.9 ± 0.3	11.4 ± 0.3	
Control group	11.8 ± 0.6	11.7 ± 0.5	
Hematocrit (%)			NS
Intervention group	35.8 ± 0.7	34.1 ± 1.1	
Control group	35.7 ± 1.5	34.6 ± 1.5	
Total lymphocyte count (/μL)			NS
Intervention group	1596.3 ± 215.1	1177.8 ± 150.9	
Control group	1485.9 ± 166.0	1174.9 ± 98.8	
Triglyceride (mg/dL)			< 0.05
Intervention group	102.2 ± 8.3	89.0 ± 13.1	
Control group	105.1 ± 18.9	109.6 ± 9.7	
Cholesterol (mg/dL)			NS
Intervention group	155.0 ± 6.7	143.6 ± 8.5	
Control group	170.3 ± 11.7	150.8 ± 11.0	
Blood urea nitrogen (mg/dL)			NS
Intervention group	9.7 ± 1.1	13.2 ± 0.9	
Control group	11.9 ± 2.3	13.9 ± 1.4	
Creatinine (mg/dL)			NS
Intervention group	0.9 ± 0.1	0.7 ± 0.1	
Control group	1.0 ± 0.1	0.8 ± 0.1	
Aspartate aminotransferase (IU/L)			NS
Intervention group	13.2 ± 2.4	14.0 ± 1.6	
Control group	12.2 ± 1.8	13.4 ± 1.8	
Alanine aminotransferase (IU/L)			NS
Intervention group	6.1 ± 1.3	9.5 ± 1.3	
Control group	6.6 ± 1.0	10.2 ± 1.4	
Total bilirubin (mg/dL)			NS
Intervention group	0.5 ± 0.08	0.4 ± 0.05	
Control group	0.5 ± 0.08	0.4 ± 0.04	
Glucose (gm/dL)			NS
Intervention group	86.9 ± 3.8	122.1 ± 10.8	
Control group	88.7 ± 4.9	119.7 ± 9.8	
Insulin (IU/mL)			NS
Intervention group	8.3 ± 1.2	18.1 ± 2.7	
Control group	9.8 ± 2.7	20.1 ± 3.8	
C-peptide (ng/dL)			NS
Intervention group	1.8 ± 0.5	4.3 ± 0.6	
Control group	1.8 ± 0.5	4.9 ± 1.0	
Na (mmol/L)			NS
Intervention group	139.6 ± 0.7	136.3 ± 1.2	
Control group	139.3 ± 1.1	137.2 ± 1.1	
K (mmol/L)			NS
Intervention group	4.2 ± 0.2	3.8 ± 0.2	
Control group	4.0 ± 0.1	3.8 ± 0.1	
Cl (mmol/L)			NS
Intervention group	105.3 ± 0.6	102.4 ± 1.3	
Control group	106.0 ± 0.9	101.9 ± 0.8	

NS: Not significant.

DISCUSSION

Surgical trauma induces a catabolic response with hypermetabolism and insulin-resistant hyperglycemia[3]. Traditionally, postoperative parenteral nutrition with full calories and high glucose loads results in deteriorating hyperglycemia, hyperosmolar state, increased carbon dioxide generation[4], and net fat synthesis- deposition when the capacity of oxidation is overwhelmed. Thus physicians often have had to prescribe additional insulin to control hyperglycemia. The result of this is forced glucose oxidation and forced lipogenesis, both of which necessitate considerable physiologic effort leading to iatrogenic hypermetabolism. These metabolic alternations have been associated with increased morbidity and mortality in the early and late postoperative periods[5]. Thus, in a randomized controlled study of postoperative patients under intensive care, normoglycemia was achieved by aggressive control with infusion of sufficient insulin to overcome insulin resistance. By this treatment, morbidity and mortality were substantially decreased[6].

Hepatic triglyceride synthesis and secretion of very-low-density lipoprotein (VLDL) are related to the availability of carbohydrate or free fatty acid substrate[7,8]. Consequently, patients receiving parenteral nutrition frequently present significant hypertriglyceridemia[9]. However, the difference in mean triglycerides between post- and pre-operative levels in our interventional group is significantly lower than the control group (Table 3). This suggests that infusion of 20% Intralipid® antagonized the hypertriglyceridemic effect of intravenous glucose by altering the balance between hepatic VLDL synthesis and intravascular VLDL catabolism.

Several biochemical mechanisms for such an effect can be considered[9]. Isocaloric substitution of 20% Intralipid® for glucose could blunt carbohydrate-induced hepatic triglyceride synthesis not only by reducing the daily input of carbohydrate substrate but also by adding an exogenous triglyceride, which in itself can inhibit hepatic triglyceride synthesis[10]. Another possible mechanism relates to the inhibitory effect of insulin on triglyceride hydrolysis and fatty acid release from adipose tissues. Acute hyperinsulinemia induced by parenteral glucose suppressed the release of free fatty acids from peripheral adipose stores[11]. Because hepatic utilization of free fatty acids is regulated solely by their ambient serum concentration, this in turn would lead to a reduction in hepatic triglyceride synthesis and VLDL secretion[8]. Finally, Taskinen *et al*[12] demonstrated that infusion of glucose plus Intralipid® causes a 1.5-fold greater induction of adipose tissue lipoprotein lipase activity than infusion of glucose alone. This enzyme plays a central role in peripheral VLDL catabolism and hence increased activity would lead to enhanced clearance of VLDL and a decrease in triglyceride levels[13]. The factors regulating VLDL synthesis and clearance are in a delicate balance and the effect of combined glucose and lipid regimens on serum triglycerides may ultimately depend on many variables such as the total daily caloric load, the percent of total calories infused as lipid component, the nutritional status of the patients, or even the daily timing of the infusions[14].

Protein sparing is the major goal of nutritional support, which may be affected by the fuel source of glucose or lipid. The nitrogen sparing effects of glucose and lipid have been addressed in several reports with conflicting results. Some studies have found glucose achieves better nitrogen retention than lipids[15-17], but usually there is no benefit of one fuel source over the other[18-20]. A review of the literature by Iapichino *et al*[21], attempted to consider the potential confounding factors, and then compare the effects of glucose alone with the glucose-fat mixed system upon protein metabolism. In 40 groups of catabolic patients, a satisfactory nitrogen balance result was more frequently observed with a glucose system (17 of 19 studies) than with a mixed system (12 of 21 studies).

The nitrogen balance showed no significant change between our two parenteral nutritional groups with isocalories and isonitrogen (Table 4), which indicated lipid emulsion and glucose have similar nitrogen sparing effects after a 6-d study period. When compared to the glucose-lipid mixed interventional group, prealbumin was significantly higher in the glucose-based control group after 6 d of parenteral nutrition (Table 4). Prealbumin underwent significant change in our study because of its short half-life (2-3 d), and it showed a somewhat favorable nitrogen retention effect of glucose rather than lipid. However, the traditional nutritional indicators such as albumin level showed no significant change between the two groups (Table 4).

The amino acid supplement (Amiparen®) used in our study contains abundant branched-chain amino acids, which provide a substrate for producing alanine and glutamine, and also prevent amino acid loss from muscle breakdown. It is therefore reasonable to hypothesise that amino acid supplements maintain and/or increase the plasma glutamine concentration and prevent plasma and muscle depletion in the immediate postoperative fasting period. It has been shown that postoperative supply of amino acids improves protein synthesis and decreases early protein catabolism[22]. Consequently, HPPN is a nutritional support regimen based on amino acids, with a lower energy supply in the form of glucose or other alternatives such as lipid emulsion and glycerol[1]. Its purpose is not to turn the negative nitrogen balance of these patients with postoperative injury into a positive balance, but rather to prevent a greater degree of protein breakdown during the postoperative period of fasting[23,24].

In summary, we conclude that HPPN with lipid emulsion is well-tolerated for providing nutritional support in the immediate postoperative period. It thus appears to be appropriate to replace hypercaloric loads which are still used routinely in many postoperative patients. Although HPPN with lipid emulsion is well-tolerated and beneficial to postoperative gastrointestinal cancer patients, further large-scale population-based data sets validated under multicenter settings are needed.

COMMENTS

Background

Hypocaloric peripheral parenteral nutrition (HPPN) is appropriate for patients with moderate nutrition who are prepared to have a short-term period of fast. HPPN is designated to contain lower glucose loads supplemented with soluble alternatives *via* the peripheral venous route to avoid the complications of hyperglycemia and the use of central venous catheters.

Research frontiers

There are conflicting opinions regarding the use of different alternatives substituting for glucose in such an amino acids-based HPPN. The study is designed as a prospective, randomized clinical trial to compare the effects of lipid emulsion substituting for glucose in HPPN for postoperative gastrointestinal (GI) cancer patients.

Innovations and breakthroughs

The study demonstrates that HPPN supplemented with lipid emulsion is advisable to replace conventional hypercaloric (hyperglycemic) loads *via* the central venous route in postoperative patients necessitating short-term of nutritional support.

Applications

HPPN (15-20 kcal/kg per day) supplemented with lipid emulsion is well-suited for providing short-term nutritional support for GI cancer patients following surgery.

Terminology

HPPN is also termed as median caloric peripheral parenteral nutrition, and the daily caloric supply is about 15-20 kcal/kg.

Peer review

The authors conducted a prospective, randomized controlled study of HPPN with lipid emulsion *vs* dextrose in postoperative GI cancer patients, and demonstrated that HPPN with lipid emulsion is well-tolerated for these patients.

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