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Original Article

Changes in Blood Levels of Water-Soluble Vitamins in Patients Receiving Vitamin Supplementation with Peripheral Parenteral Nutrition after Gastrointestinal Surgery

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ABSTRACT

Background: We measured blood levels of water-soluble vitamins after gastrointestinal surgery.

Methods: Preoperative and postoperative blood levels of water-soluble vitamins were measured in 50 patients who had received postoperative peripheral parenteral nutrition (PPN), with or without vitamin supplementation, after gastrectomy or colectomy during 2010–2011.

Results: The participants were 34 men and 16 women (mean age, 69.4 years; range, 46–88 years). Among patients receiving PPN without vitamin supplementation, prolonged decreases in blood levels of water-soluble vitamins were observed immediately after surgery and thereafter. Vitamin C level was 8.33 μg/ml before surgery, 4.64 μg/ml immediately after surgery (before starting PPN), 3.89 μg/ml at the start of meal intake (3–5 days after starting PPN), and 5.20 μg/ml at the final observation (on the seventh day after switching to dietary intake only or at hospital discharge). Among patients receiving PPN with vitamin supplementation, mean vitamin C level in the multivitamin/vitamin C combination therapy groups was 7.49/8.31 μg/ml before surgery, 4.40/5.72 μg/ml immediately after surgery (before starting PPN), and 6.44/7.73 μg/ml at the start of meal intake. The blood level of homocysteine increased after the start of PPN without vitamin supplementation, but no such increase was observed in patients receiving PPN with vitamins. The blood level of lactic acid increased from the preoperative period to the immediate postoperative period in both groups and decreased from after the start of PPN to the start of meal intake. The decrease was greater in patients receiving PPN with vitamins.

Conclusions: Blood levels of water-soluble vitamins decreased after gastrointestinal surgery. Supplementation with water-soluble vitamins improved metabolic reactions in patients receiving PPN.

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KEYWORDS: gastrointestinal surgery, peripheral parenteral nutrition (PPN), water-soluble vitamin

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Thus far, 13 compounds have been classified as vitamins. Water-soluble vitamins are essential in nutrient metabolism and serve as coenzymes in complex interactions at various steps in glycolysis, amino acid metabolism, and lipid metabolism.[1] Some reports showed that patients for whom peripheral parenteral nutrition (PPN) was indicated had blood vitamin levels below reference ranges (so-called "latent vitamin deficiency"), due to pathologic conditions and/or poor nutritional status before starting PPN. Furthermore, these deficiencies persisted after PPN was started. Ozasa et al.[2] reported that blood levels of vitamins B_1, B_6, and C were below the lower limit of reference ranges in 79%, 71%, and 100% of patients, respectively, at 3 to 4 days after gastrectomy. These low vitamin levels persisted after PPN was terminated in patients not receiving supplementary vitamins. These results show that vitamin deficiencies may occur soon after surgery and persist for a considerable period of time. Fujiyama et al.[3] reported that patients for whom PPN was indicated tended to have low blood vitamin levels on admission. In particular, those with gastrointestinal diseases had low blood levels of vitamins B_1, B_2, B_6, B_{12}, and C and folic acid. The levels further decreased during and after PPN. However, some water-soluble vitamins were not measured in these reports, and the effects of water-soluble vitamins on nutrient metabolism were not examined. To better understand changes in both the blood levels of water-soluble vitamins during postoperative PPN administration and the nutritional and metabolic functions in which water-soluble vitamins are involved as coenzymes, we conducted a prospective clinical study of patients who had undergone gastrointestinal surgery.

Methods

The study was conducted from May 2010 through March 2011 in collaboration with the Surgical and Nutrition Departments of Toho University Ohashi Medical Center and Ajinomoto Pharmaceuticals Co., Ltd., (Tokyo). The study is currently being managed by AY Pharmaceuticals Co., Ltd., (Tokyo) a spin-off of the infusion and dialysis units of Ajinomoto Pharmaceuticals Co., Ltd. Before the study began, the protocol was reviewed and approved by the institutional review board (IRB) of Toho University Ohashi Medical Center (approval no. 22-3).

This study was carried out as a collaborative investigation with Toho University Ohashi Medical Center Surgery and Nutrition Department and AY Pharma Co., Ltd.

Participants

We recruited patients 20 years or older undergoing gastrectomy or colectomy requiring postoperative PPN. To ensure patient safety, we excluded patients with serious liver disorders, kidney disorders, or cardiac dysfunction, those with severe dysglycemia, severe electrolyte metabolism disorders, or clear symptoms of vitamin deficiency, and those whom the investigators considered as inappropriate for study inclusion. Centralized measurement of blood levels of water-soluble vitamins and nutritional and metabolic parameters was done at the Mitsubishi Chemical Medience Corporation. [presently known as LSI Medience Corp. (Tokyo)].

1. Informed consent

After distributing the informed consent form and all other information regarding participation in the study, voluntary informed consent was obtained from all patients.

Design

In the initial period of the study, we assessed patients who had undergone gastrointestinal surgery and received monotherapy with a vitamin B_1-containing PPN formulation (hereafter referred to as vitamin B_1 PPN). The protocol was then revised, and a multivitamin (multi-Vit) preparation (for patients who had undergone gastrectomy) or vitamin C (VC) preparation (for patients who had undergone colectomy) was used in combination with postoperative PPN. This revised protocol was also approved by the IRB.

Patients were randomly assigned to the PPN monotherapy group in the initial period of the study and to the PPN with vitamin combination therapy groups (hereinafter referred to as the multi-Vit and VC combination therapy groups) in the latter part of the study.

1. Treatment

As postoperative nutritional therapy, 500 to 1000 ml of vitamin B_1 PPN (Amigrand® intravenous infusion; Terumo Corp., Tokyo) and 500 to 1000 ml of an electrolyte preparation were administered daily from the day of, or day after, surgery until the day of, or day after, the first meal. The daily dose and start date of vitamin B_1 PPN administration, as well as the type, daily dose, and termination date of electrolyte preparation administration, were determined with regard to patient body size and condition. Combinations of other PPN formulations and enteral nutrition therapy or total parenteral nutrition formulations were prohibited. After revision of the protocol, the multi-Vit preparation (Vitaject® injection kit; Terumo Corp.) was used in combination with postoperative PPN for gastrectomy

Time point of examinations/observations*		Before operation	Immediately after operation		At the start of meal intake				At the final observation (at discharge)**		At the final observation (on the seventh day after switching to dietary intake only)			
Postoperative day (POD)		−14 to 0	Day of operation	1	2	3	4	5	6	7	…	11	12	13	14〜
Colectomy	PPN			○	○	○	← ◎ →								
	Electrolyte preparations	(○)	○	○	○	○	○	○	(○)	(○)	(○)	(○)	(○)	(○)	(○)
	Start of meal intake					← ○ → (semi-liquid diet)									
	Discharge									→ After POD 7					
Gastrectomy	PPN		(○)	○	○	○	○	← ◎ →							
	Electrolyte preparations	(○)	○	○	○	○	○	○	○	(○)	(○)	(○)	(○)	(○)	(○)
	Start of meal intake						← ○ → (liquid diet)								
	Discharge														→ After POD 14

Fig. 1 Schedule of treatments and examinations/observations

○: implemented (○): implemented if necessary based on the patient's condition, ◎: PPN was terminated on the day after the start of meal intake

*Time point of examination/observation: If the time point for examination/observation falls on a holiday, the time point was shifted to the day before or after the holiday.

**At the final observation (the time of discharge): In case the subject is discharged before the seventh day after switching to dietary intake only.

PPN: peripheral parenteral nutrition

cases, and the VC preparation (Vitacimin® injection; Takeda Pharmaceutical Co., Ltd., Osaka) was used in combination with postoperative PPN for colectomy cases. The start and completion dates of PPN administration, and the start of oral intake, were decided on the basis of preoperative and postoperative clinical pathways used in our hospital (Fig. 1).

2. End points

In accordance with the clinical pathway, examinations and observations were performed during the preoperative period (within 2 preoperative weeks), during the immediate postoperative period (on postoperative day 1), at the start of meal intake (before eating a meal on the day dietary intake was started), and at the final observation (7 days after switching to dietary intake only, or on the day of or before discharge, when the patient was discharged before the corresponding date) (Fig. 1). Examinations and observations of the VC combination therapy group were completed at the start of meal intake.

1) Blood levels of water-soluble vitamins

At each time point for examination and observation, blood levels of vitamins B_1, B_2, B_6, B_{12}, and C, folic acid, nicotinic acid, pantothenic acid, and biotin were measured. Only VC levels were measured in the VC combination therapy group.

2) Nutritional indices

At each time point of examination/observation, prealbumin, transferrin, and retinol-binding protein levels were measured.

3) Metabolic indices

At each time point for examination/observation, homocysteine and lactic acid levels were measured.

4) Nutrient uptake status

Eating rate was measured from the start of oral intake until the final observation day. Energy (kcal), protein, and water-soluble vitamin (excluding biotin) intakes were calculated based on the Standard Tables of Food Composition in Japan.[4]

Statistical analysis

Statistical analysis was performed by our collaborator, Ajinomoto Pharmaceuticals Co., Ltd. The software package SAS (version 9.13; SAS Institute Japan Ltd., Tokyo) was used to calculate summary statistical data [including means, standard deviation (SD) s, and medians] of blood levels of water-soluble vitamins and nutritional and metabolic indices, as well as differences in means by the inde-

Table 1 Demographic characteristics of the patients

	Postoperative treatment		
	PPN mono	Multi-Vit comb	VC comb
Sample size	32	8	10
Men (cases)	21	7	6
Women (cases)	11	1	4
Age, mean (range), (years)	70.7 (53–88)	65.9 (46–84)	67.8 (57–79)
Underlying disease (cases)	Cecal cancer: 1 Colon cancer: 12 Rectal cancer: 7 Stomach cancer (early): 6 Stomach cancer (progressive): 6	Stomach cancer (early): 4 Stomach cancer (progressive): 4	Cecal cancer: 1 Colon cancer: 7 Rectal cancer: 2

PPN: peripheral parenteral nutrition, mono: monotherapy; multi-Vit: multivitamin, comb: combination therapy, VC: vitamin C

Table 2 Duration and mean daily dose of PPN formulation/vitamin preparation

	Postoperative treatment		
	PPN mono	Multi-Vit comb	VC comb
Sample size	32	8	10
Mean duration of PPN (days)	5.6	6.1	3.4
Mean dose of vitamin B_1 PPN formulation (ml)	849.3	720.2	987.5
Multivitamin preparation (kit)[1]	-	0.9	-
Vitamin C preparation (ampules)[1]	-	-	1.9

PPN: peripheral parenteral nutrition, mono: monotherapy, multi-Vit: multivitamin, comb: combination therapy, VC: vitamin C
[1]No. of kits or ampules per day during PPN

pendent *t*-test between patients receiving PPN monotherapy and those receiving multi-Vit combination therapy. Microsoft Excel 97–2003 (Microsoft Corp., Redmond, WA, USA) was used for other aggregate calculations. Nutritional intake status was evaluated by measuring eating rate and mean intakes of energy, proteins, and water-soluble vitamins in relation to resection area/postoperative treatment.

Results

The participants were 34 men and 16 women (mean age, 69.4 years; range, 46–88 years): 32 patients in the PPN monotherapy group, 8 in the multi-Vit combination therapy group, and 10 in the VC combination therapy group. Table 1 shows sample sizes and demographic data for each group. Table 2 shows PPN duration (days), mean daily dose for vitamin B_1 PPN and the concomitant vitamin preparation for each group. Table 3 shows the blood levels of water-soluble vitamins for each group, according to time point of examination and observation.

Changes in blood levels of water-soluble vitamins from the preoperative period to immediate postoperative period

Blood levels of vitamins B_6 and C, folic acid, nicotinic acid, pantothenic acid, and biotin decreased from the preoperative period to the immediate postoperative period in all groups. In particular, levels of vitamins B_6 and C markedly decreased during this period, to below the lower limit of the reference ranges, in the PPN monotherapy and multi-Vit combination therapy groups (Fig. 2).

Changes in blood levels of water-soluble vitamins after the immediate postoperative period in the PPN monotherapy group

In the PPN monotherapy groups, decreased blood levels of vitamins B_6 and C, folic acid, nicotinic acid, pantothenic acid, and biotin in the immediate postoperative period did not recover to preoperative levels during the period after PPN was started until the final observation. In particular, levels of vitamins B_6 and C did not recover even after the start of meal intake and remained low until the final obser-

Table 3 Blood levels of water-soluble vitamins

Postoperative treatment		Before surgery		Immediately after surgery		At start of meal intake		At final observation	
		Sample size	Mean ± SD	Sample size	Mean ± SD	Sample size	Mean ± SD	Sample size	Mean ± SD
Vitamin B_1 (μg/dl)	PPN mono	31	3.83 ± 0.88	30	3.94 ± 1.02	31	3.64 ± 0.76	32	3.63 ± 0.85
	multi-Vit comb	8	3.78 ± 0.68	8	4.23 ± 0.94	8	4.16 ± 0.99	8	4.24 ± 0.83*
Vitamin B_2 (μg/dl)	PPN mono	31	18.76 ± 2.96	30	18.59 ± 4.24	31	17.39 ± 3.25	32	18.54 ± 4.28
	multi-Vit comb	8	20.76 ± 2.53 *	8	20.73 ± 3.81	8	23.51 ± 3.63**	8	23.23 ± 3.89**
Vitamin B_6 (ng/ml)	PPN mono	32	7.62 ± 6.46	31	3.93 ± 2.81	31	3.22 ± 1.75	32	4.18 ± 2.74
	multi-Vit comb	8	6.80 ± 2.14	8	4.78 ± 2.32	8	10.11 ± 1.20**	8	7.73 ± 2.58**
Vitamin B_{12} (pg/ml)	PPN mono	32	559.6 ± 346.7	31	521.0 ± 330.8	31	606.1 ± 319.1	32	769.5 ± 424.6
	multi-Vit comb	8	297.5 ± 97.4**	8	326.3 ± 135.2	8	544.4 ± 226.5	8	615.0 ± 375.7
Vitamin C (μg/ml)	PPN mono	32	8.33 ± 3.13	31	4.64 ± 1.86	31	3.89 ± 1.95	32	5.20 ± 3.47
	multi-Vit comb	8	7.49 ± 3.00	8	4.40 ± 1.59	8	6.44 ± 2.18**	8	7.76 ± 3.30*
	VC comb	10	8.31 ± 2.07	10	5.72 ± 1.44	10	7.73 ± 1.84	-	-
Folic acid (ng/ml)	PPN mono	32	6.88 ± 2.69	31	4.02 ± 1.78	31	4.59 ± 1.94	32	5.79 ± 2.30
	multi-Vit comb	8	6.56 ± 2.46	8	4.88 ± 2.39	8	7.91 ± 2.39**	8	8.93 ± 2.87**
Nicotinic acid (μg/ml)	PPN mono	32	5.79 ± 0.75	30	5.26 ± 0.78	30	5.03 ± 0.63	31	5.38 ± 0.95
	multi-Vit comb	8	6.16 ± 0.96	8	5.49 ± 0.62	8	5.20 ± 0.61	8	5.60 ± 0.51
Pantothenic acid (ng/ml)	PPN mono	32	77.82 ± 33.72	31	70.60 ± 33.26	31	67.71 ± 30.22	32	77.45 ± 69.40
	multi-Vit comb	8	63.79 ± 16.24	8	60.25 ± 17.75	8	81.25 ± 30.77	8	90.79 ± 28.61
Biotin (ng/ml)	PPN mono	32	0.77 ± 0.21	31	0.46 ± 0.16	31	0.53 ± 0.21	32	0.62 ± 0.24
	multi-Vit comb	8	1.11 ± 0.16**	8	0.54 ± 0.09	8	0.89 ± 0.39**	8	0.97 ± 0.30**

PPN: peripheral parenteral nutrition, mono: monotherapy, multi-Vit: multivitamin, comb: combination therapy, VC: vitamin C
*independent *t*-test, $p < 0.1$; **independent *t*-test, $p < 0.05$

vation. Levels of vitamins B_1 and B_2 tended to decrease from the preoperative period until the start of meal intake. No marked decrease in vitamin B_{12} level was observed.

Changes in blood levels of water-soluble vitamins after the immediate postoperative period in the multi-Vit and VC combination therapy groups

Decreased blood levels of vitamins B_6 and C, folic acid, pantothenic acid, and biotin during the immediate postoperative period improved after the start of PPN combined with multi-Vit preparations. At the final observation, levels of vitamins B_6 and C, folic acid, and pantothenic acid recovered to preoperative levels, and the blood level of biotin improved, although it did not recover to the preoperative level. The same trend was noted for change in blood VC level in the VC combination therapy group. The blood levels of the other vitamins were improved by concomitant use of the multi-Vit and VC preparations. After the start of PPN, at the start of meal intake, and at the final observation, blood levels of vitamins B_2, B_6, and C, folic acid, and biotin were significantly higher in the multi-Vit combination therapy groups than in the PPN monotherapy group.

Nutrition-related indices (prealbumin, transferrin, and retinol-binding protein)

Table 4 shows the analysis of prealbumin, transferrin, and retinol-binding protein levels, by group and time point of examination and observation. Prealbumin, transferrin, and retinol-binding protein levels decreased below reference ranges from the preoperative period to the immediate postoperative period in all groups, and further decreased after the start of PPN. All indices tended to improve after the start of meal intake but had not recovered to preoperative levels at the final observation. After the start of meal intake, prealbumin and transferrin levels were slightly higher in the multi-Vit combination therapy group than in the PPN monotherapy group, but the difference was not significant.

Metabolic indices (homocysteine and lactic acid)

Table 5 shows the analysis of homocysteine and lactic acid levels, by group and time point of examination and observation. In the PPN monotherapy group, homocysteine

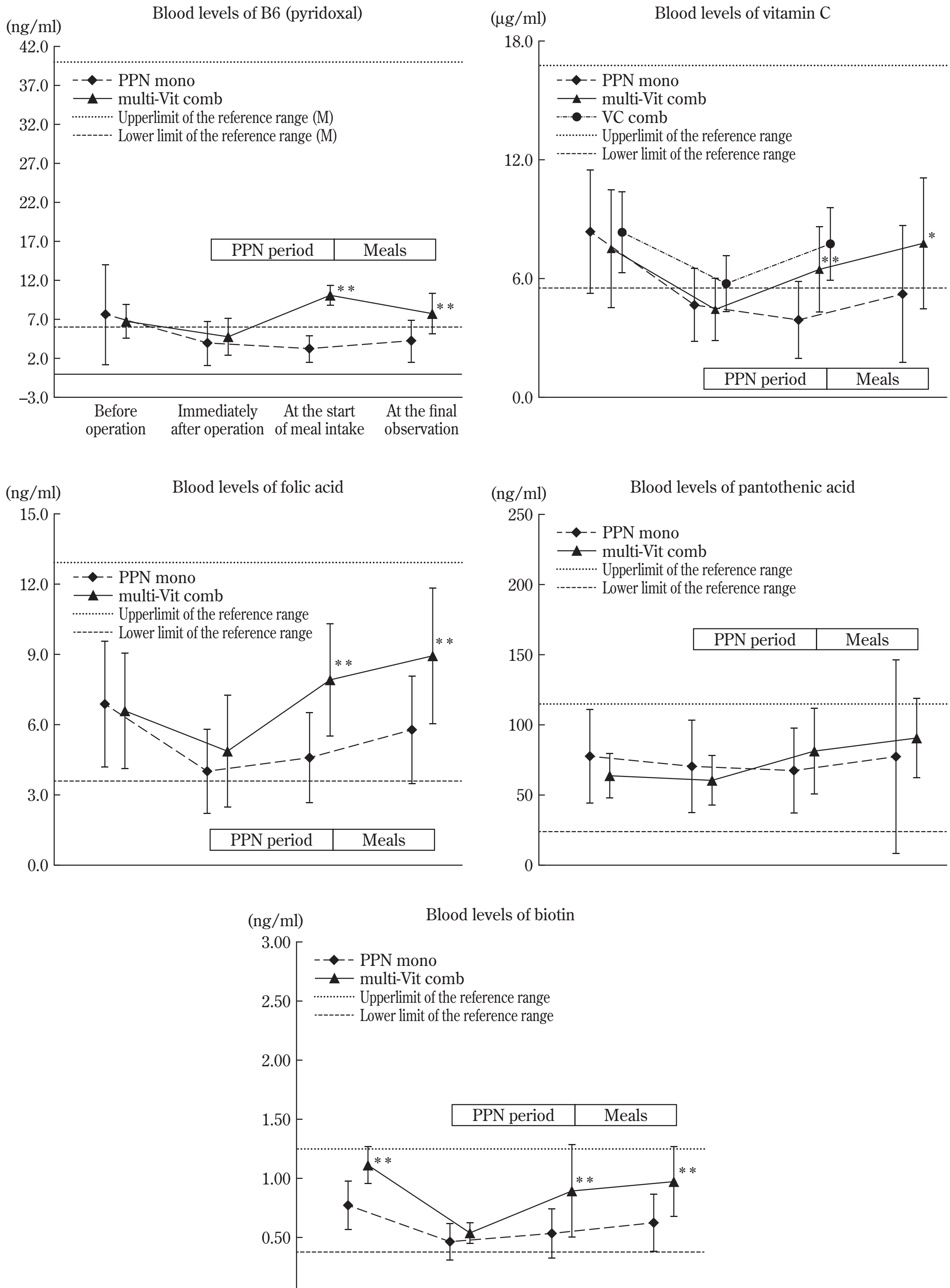

Fig. 2 Changes in blood levels of water-soluble vitamins

PPN: peripheral parenteral nutrition, mono: monotherapy, multi-Vit: multivitamin, comb: combination, VC: vitamin C

Table 4 Blood levels of nutritional indices

Postoperative treatment		Before operation		Immediately after operation		At start of meal intake		At final observation	
		Sample size	Mean ± SD	Sample size	Mean ± SD	Sample size	Mean ± SD	Sample size	Mean ± SD
PA (mg/dl)	PPN mono	32	25.29 ± 6.71	31	17.61 ± 5.13	31	13.70 ± 4.24	32	16.49 ± 6.47
	Multi-Vit comb	8	27.98 ± 7.15	8	18.28 ± 2.59	8	12.69 ± 2.46	8	18.03 ± 4.36
Tf (mg/dl)	PPN mono	32	238.5 ± 50.7	31	176.7 ± 38.8	31	169.8 ± 32.5	32	195.7 ± 45.8
	Multi-Vit comb	8	240.0 ± 39.3	8	178.5 ± 26.4	8	166.9 ± 22.6	8	203.1 ± 41.6
RBP (mg/dl)	PPN mono	32	4.20 ± 1.31	31	2.54 ± 0.95	31	2.38 ± 0.83	32	2.88 ± 1.55
	Multi-Vit comb	8	3.68 ± 0.66	8	2.08 ± 0.29	8	1.89 ± 0.44	8	2.38 ± 0.49

PPN: peripheral parenteral nutrition, mono: monotherapy, multi-Vit: multivitamin, comb: combination therapy, VC: vitamin C, PA: prealbumin, Tf: transferrin, RBP: retino binding protein, SD: standard deviation

Table 5 Blood levels of metabolic indices

Postoperative treatment		Before operation		Immediately after operation		At start of meal intake		At final observation	
		Sample size	Mean ± SD	Sample size	Mean ± SD	Sample size	Mean ± SD	Sample size	Mean ± SD
Homocysteine (mmol/ml)	PPN mono	32	10.67 ± 3.18	31	7.19 ± 2.95	31	12.01 ± 4.14	32	11.90 ± 4.74
	Multi-Vit comb	8	11.05 ± 3.37	8	9.31 ± 9.11	8	9.03 ± 2.95*	8	9.81 ± 3.05
Lactic acid (mg/dl)	PPN mono	32	9.68 ± 4.21	31	12.32 ± 5.30	31	7.89 ± 3.88	32	7.98 ± 3.20
	Multi-Vit comb	7	8.36 ± 2.26	8	16.23 ± 10.63	8	6.23 ± 2.08	8	9.59 ± 3.66

PPN: peripheral parenteral nutrition, mono: monotherapy, multi-Vit: multivitamin, comb: combination therapy, VC: vitamin C, SD: standard deviation

*independent *t*-test, $p < 0.1$

Table 6 Mean eating rate and mean intakes of energy, protein, and vitamins

Postoperative treatment	Sample size	Eating rate (%)	Energy intake (kcal)	Protein intake (g)	B_1 intake (mg)	B_2 intake (mg)	B_6 intake (mg)	B_{12} intake (μg)	C intake (mg)	Folic acid intake (μg)	Niacin intake (mg)	Pantothenic acid intake (mg)
PPN mono	31	57.1	904.0	38.4	0.58	0.70	0.86	2.21	89.71	210.83	8.72	3.49
Multi-Vit comb	8	51.5	706.2	31.9	0.64	0.75	1.02	2.48	124.60	222.76	8.24	3.31

PPN: peripheral parenteral nutrition, mono: monotherapy, multi-Vit: multivitamin, comb: combination therapy

level was higher after the start of PPN, but no increase was observed in the multi-Vit combination therapy group.

Lactic acid level increased from the preoperative period to the immediate postoperative period in all groups, and decreased from after the start of PPN to the start of meal intake. In the multi-Vit combination therapy group, the increase from the preoperative to the immediate postoperative period was greater than that in the PPN monotherapy groups, but the level decreased to the same level as that observed in the PPN monotherapy groups from after the start of PPN to the start of meal intake, which indicates a greater decrease. The extent of the change in lactic acid level from immediately after surgery to the start of meal intake was -10.00 mg/dl in the multi-Vit combination therapy group and -4.39 mg/dl in the PPN monotherapy group ($p < 0.05$ by the independent *t*-test).

Nutritional intake

Table 6 shows mean eating rate and daily intakes of energy, protein, and vitamins from the time a diet was started until the final observation in each group. The mean eating rate was slightly higher in the multi-Vit combination therapy group than in the PPN monotherapy group. Among the gastrectomy and colectomy patients, the eating rate was highest when oral intake was started, or immediately after that, and decreased thereafter.

Discussion

The Practical Guidelines for Parenteral and Enteral Nutrition established by the Japanese Society for Parenteral and Enteral Nutrition (JSPEN)[5,6] emphasize the importance of nutritional management. Adequate nutritional support helps maintain good health and proper maintenance of body constituents that enable normal body functions. Patients with increased energy demands, increased protein catabolism, low nutrient availability, or tissue or organ damage are at high risk of worsening malnutrition, which is a risk factor for tissue and organ dysfunction, delayed wound healing, infectious complications, healing abnormalities, and exacerbation of underlying diseases. Postoperative patients, including those who have undergone gastrointestinal surgery, have a high risk of worsening malnutrition due to surgical stress and therefore need adequate nutritional therapies to maintain their body functions, promote proper wound healing, and reduce the risk of complications, including infections.

With regard to concomitant use of vitamins with parenteral nutrition, the American Medical Association (AMA)/Food and Drug Administration (FDA) guidelines on multi-Vit administration during parenteral nutrition (1975 and 2000)[7,8] and the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N) guidelines on parenteral and enteral nutrition (2002)[9] recommend that vitamins should be administered to patients receiving parenteral nutrition with limited oral intake, because vitamins are essential nutrients that are involved in metabolic pathways as coenzymes and cofactors. Water-soluble vitamins are necessary for nutrient metabolism and serve as coenzymes in complex interactions at various steps in glycolysis, amino acid metabolism, and lipid metabolism. Water-soluble vitamins also interact as coenzymes in their generation and activation.[1] Because these vitamins are water soluble, their absorption and metabolism rates are fast; hence, they are rapidly excreted in urine. As a result, water-soluble vitamin deficiency tends to manifest early, and surgical stress, infections, and wounds lead to enhanced metabolic reactions and promote excretion of various vitamins, which can easily result in vitamin shortages.[10] Recently, studies in Japan found that patients who had undergone gastrointestinal surgery and patients with internal diseases had diminished blood levels of water-soluble vitamins.[2,3] However, studies have not assessed all nine water-soluble vitamins or examined the effect of water-soluble vitamins on nutrient metabolism.

To better understand changes in both the blood levels of water-soluble vitamins during postoperative PPN administration and the nutritional and metabolic functions in which water-soluble vitamins are involved as coenzymes, we conducted a prospective clinical study of patients undergoing gastrointestinal surgery. Blood levels of water-soluble vitamins clearly decreased from the preoperative period to the immediate postoperative period. We believe that because preoperative assessment was performed immediately before surgery, consumption or increased demand of water-soluble vitamins in the body due to surgical stress itself led to decreases in blood levels of water-soluble vitamins.

In the groups that received the vitamin B_1 PPN formulation as monotherapy without concomitant use of the multi-Vit/VC preparations after the postoperative period, the decreased blood levels in the immediate postoperative period remained low after the start of oral intake and termination of PPN until the final observation. This result was consistent with the findings of Ozasa et al.[2] and Fujiyama et al.[3], who examined blood levels of several water-soluble vitamins during PPN. In the multi-Vit and VC combination therapy groups, levels of water-soluble vitamins, except vitamin B_6, improved in the immediate postoperative period and remained conctant after the start of oral intake and termination of PPN. This suggests that the decrease in water-soluble vitamins immediately after surgery persists even after the start of meal intake, unless separate water-soluble vitamin supplementation is provided. In addition, blood levels improved in the groups that received vitamin B_1 PPN with concomitant use of the multi-Vit/VC preparations. These levels were maintained or further improved at the time of final observation, except for vitamin B_6, after termination of administration of the multi-Vit/VC preparations. These findings suggest this regimen was almost able to compensate for the decrease in water-soluble vitamins resulting from consumption or increased demand for water-soluble vitamins due to surgical stress. We have thus newly shown that water-soluble vitamins have a similar tendency.

Levels of the nutritional indices prealbumin, transferrin, and retinol-binding protein were markedly lower at the immediate postoperative examinations/observations, decreased even further after the start of PPN, and did not recover to preoperative levels by the final observation, which suggests a prolonged decrease in nutritional status. After the start of meal intake, prealbumin and transferrin levels were slightly higher in patients receiving concomitant multi-Vit than in those not receiving concomitant multi-Vit; however, this finding may be a result of slightly higher eating rates in the former group.

Homocysteine and lactic acid were examined as metabolic indices. Homocysteine is a metabolic intermediate of L-methionine, and vitamins B_6 and B_{12} and folic acid are involved in its metabolism. Thus, we assessed changes in this metabolic index in which water-soluble vitamins are involved. In patients receiving vitamin B_1 PPN, homocysteine levels were lower after the start of meal intake in patients receiving concomitant multi-Vit but not in those who did not receive concomitant multi-Vit. Homocysteine metabolism appears to have been interrupted by a shortage of the water-soluble vitamins involved in metabolism after surgery and to have recovered after supplementation with water-soluble vitamins. In addition, blood levels of lactic acid—the metabolism of which involves vitamin B_1—increased immediately after surgery and had decreased to preoperative levels at the start of meal intake in both groups, *i.e.*, with vitamin B_1 PPN monotherapy and concomitant use of multi-Vit. However, the degree of improvement was greater in patients receiving concomitant multi-Vit; thus, changes in blood levels appear to reflect the amount of vitamin B_1.

Conclusion

This study revealed prolonged decreases in nutritional indices and blood levels of water-soluble vitamins after gastrointestinal surgery. Levels improved with concomitant use of vitamins and postoperative PPN, and these improvements persisted after termination of this regimen. Concomitant use of vitamins also appeared to improve metabolic indices, namely, homocysteine and lactic acid. These results suggest that maintaining sufficient levels of water-soluble vitamins as coenzymes enhances metabolic reactions. However, postoperative decreases in nutritional indices did not improve. Further studies with a larger number of patients and a longer study duration are warranted in order to elucidate the effects of deficiencies in water-soluble vitamins and vitamin supplementation on nutritional status.

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