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Clinical Study for UNECE U-168, an Enteral Nutritional Formula for Patients Receiving Long-Term Nasogastric Tube Feeding

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Abstract: The objective of this study was to examine the effect of UNECE U-168, an enteral nutrient formula on the nutritional status and renal or hepatic function. During November, 2009 to May, 2011, 30 participants (13 males and 17 females; average age 73.7±15.1 years) were recruited from five nursing homes in New Taipei City, Taiwan. All participants had been on nasogastric tube feeding for three months or more. For four weeks, UNECE U-168 (1500 Kcal) enteral nutritional formula was given to participants as part of their diet. Anthropometric and biochemical measurements were performed. Differences of the measurements before and the nutritional intervention were compared. After 4 weeks of UNECE U-168 enteral nutritional formula as diet, body weight and BMI were stable. Nutritional indicators including serum albumin and total protein levels were maintained at similar levels. Total triglyceride and low-density lipoprotein cholesterol levels had a significant decrease ($p<0.05$). Aspartate transferase, alanine transaminase and alkaline phosphatase showed normal values. In addition, creatinine and blood urea nitrogen levels were all within the normal range. UNECE U-168 enteral nutritional formula can maintain the nutritional status in diabetic patients and have no adverse effects on the hepatic and renal function.

Key words: Nasogastric tube feeding, enteral nutritional formula, UNECE U-168, malnutrition

INTRODUCTION

Since 1993, Taiwan has become "aged society" and the increasing aging population becomes a burden to the society (Yang *et al*., 2008). According the Nutrition and Health Survey in Taiwan (NAHSIT) between 2005-2008, the prevalence of chronic diseases remains high so there is a huge demand for long-term care assistance (Yeh *et al*., 2011). Research indicated approximately 40-85% of nursing home resident are malnourished or of high risks of malnutrition (DiMaria-Ghalili and Amella, 2005). Similarly in Taiwan, malnutrition is also common in elderly residents of nursing homes (Chang and Roberts, 2011). Malnutrition increases the risks of the occurrence and infection rates of bedsores (Davalos *et al*., 1996; Kane, 2003). Malnutrition could lead to infections, complications, reduced quality of life and mortality (Stange *et al*., 2013). Nutritional assessments of nasogastric feeding were mostly performed in the acute setting (Davies *et al*., 2002; Eckerwall *et al*., 2006; Norton *et al*., 1996; Park *et al*., 1992). A majority of patients receiving nasogastric feeding are bed-ridden with underlying chronic diseases. Very few reports have investigated the effect of nutritional supplement given in the form of nasogastric feeding. The supplement for total nasogastric feeding is designed in a way that energy and nutrient requirements are met. However, the conditions such as decreased arm muscle circumference, weight loss and hypoalbuminemia were reported in elderly bed-ridden patients fed with a total nasogastric diet (Okada *et al*., 2001). A suitable total nasogastric diet should at least maintain the nutritional status and anthropometry of the individual. Hence the aim of the study is to evaluate effects of UNECE U-168, a nutritional supplement designed for total nasogastric diet. In additional, the safety and tolerance were assessed by biochemical measurements and gastrointestinal tolerance.

MATERIALS AND METHODS

UNECE U-168 formulation: UNECE U-168 was specifically formulated for patients on nasogastric feeding and was consisted of 16% of protein, 34% of fat and 50% of carbohydrate. The ingredients of UNECE U-168 include, maltodextrin, canola oil powder, soybean protein, whey protein, sunflower oil powder, inulin, potassium citrate, calcium hydrogen phosphate, magnesium chloride, sodium chloride, *Enterococcus* spp., choline bitartrate, *Lactobacillus acidophilus*, *Bifidobacteria* spp., vanilla powder, L-Glutamine, L-Methionine, vitamin C, zinc gluconate, taurine, L-Carnitine, ferric pyrophosphate, yeast selenium, yeast chromium, yeast molybdenum, manganese gluconate, nicotinamide, calcium pantothenate, vitamin B_{12}, vitamin A, copper gluconate, vitamin B_6, vitamin B_2, vitamin B_1, vitamin D_3, Vitamin E, Vitamin K_1, folic acid, Biotin and potassium iodide.

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Study participants: This clinical trial was approved by the Joint Institutional Review Board of Taipei Medical University. The study was conducted between the November of 2009 to the May of 2011. The participants must be greater than 20 years old, on nasogastric feeding for more than three months. The exclusion criteria are patients with a problematic nasogastric feeding, terminal cancer, hepatic encephalopathy, uremia due to renal failure, hepatic failure and those unable to receive nasogastric feeding. Patients were recruited from five nursing homes in the New Taipei City, Taiwan. All participants were provided with informed consent and the attending physician's agreement was obtained. 56 participants entered the trial, but only 30 completed the study including 13 males and 17 females. Their baseline characteristics are depicted in Table 1.

Study design: All information such as their clinical, medication histories including bed-bound length was also noted. Anthropometric measurements, blood pressure and medication histories were taken. The height was calculated by using the knee height methods, Male: 85.1+1.73*knee length -0.11*age; Female: 91.45+1053* knee length -0.16*age. The BMI was calculated as weight (kg)/height (m^2) (Chang *et al*., 1999), which was used as a reference for calculating the daily energy requirement.

The clinical study was designed as "time series study". Daily energy requirement was estimated by the same dietitian. Participants were given 54~65g of UNECE U-168 per meal (250-300 Kcal), six meals a day. The study comprised three phases: month 0 (observation period) during which patients maintained their usual diet; month 1 during which UNECE U-168 replaced 1500 Kcal of their usual diet daily and month 2 during which participants stopped taking UNECE U-168 and returned to the pre-study diet.

In each phase, venous blood was drawn after overnight fasting. Blood samples were centrifuged for 3,000 rpm for 10 min for plasma and serum separation. Biochemical measurements were performed by the department of laboratory Taipei Medical University Hospital. These included: total cholesterol (TC), triacylglycerol (TG), high-density lipoprotein cholesterol, (HDL-C), low-density lipoprotein cholesterol (LDL-C), blood urea nitrogen (BUN), creatinine (Cr); For hepatic function: aspartate transaminase (AST), alanine transaminase (ALT); nutritional parameter: total protein (TP), albumin (Alb), glycated hemoglobin (HbA1c), alkaline phosphatase (ALK-P), uric acid (UA). Blood count analysis: white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean cell hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet (PLT), mean platelet volume (MPV), % neutrophils (%NEUT), % lymphocyte (%LYM), % mononuclear cells (%MONO), % eosinophils (%EOS) and % basophiles (%BASO).

Statistical analysis: Statistical analysis was performed by using the statistics software SAS for Windows 9.01. The paired t-test was applied for difference between and after intervention and data were considered statistically significant if $p<0.05$.

RESULTS

Weight, blood pressure and defecation status: Participant characterization was summarized in Table 1. After one month of UNECE U-168 intervention, there was no significant change for weight, BMI, systolic and diastolic pressures were all within normal range. After one month of intervention, defecation frequencies were slightly increased ($p<0.05$) (Table 2).

Serum albumin and total protein levels as nutritional parameters: Serum albumin levels were maintained after one month of UNECE U-168 intervention at 3.6-3.7 g/dL. Albumin and total protein levels were stable (6.8±0.6, 6.7±0.6 and 6.9±0.5 g/dL) (Table 3).

Blood lipids levels: After one month of UNECE U-168 supplementation, total cholesterol levels were decreased (from 161.5±29.8 mg/dL to 154.4±27.4 mg/dL), but not statistically significant. Total triglyceride levels were significantly reduced from 119.8±43.1 mg/dL (month 0) to 97.4±38.1 mg/dL (month 1) ($p<0.05$). LDL-C levels were also significantly decreased from 92.8±22.0 mg/dL to 83.3±18.7 mg/dL ($p<0.05$) (Table 2).

Biochemical indicators for renal, hepatic and cardiac function: No significant difference was observed for the AST, ALP and ALK-P levels, which all within normal values. No significant difference was found for BUN, Cr and UA concentration.

Table 1: Baseline characteristics of the patients in the UNECE U-168 clinical trial

	All	Male	Female
Case (n)	30	13	17
Percentage	100	43	57
Age (year)	73.7±15.1	68.2±16.3	77.9±13.1
Body height (cm)	157.3±7.9	163.2±6.2	152.8±5.9
Body weight (kg)	52.9±8.4	52.7±10.4	53.1±6.9
BMI (kg/m^2)	21.3±3.4	19.6±3.4	22.6±2.8
History of disease			
CVA (n)	11	7	4
Hypertension (n)	13	4	9
Dementia (n)	5	2	3
Pneumonia (n)	5	3	2

Body height was calculated using the knee length by applying the calculation: for males: 85.1+1.73* -0.11*age; for females:91.45+1.53* knee length -0.16 *Age (Chang *et al*., 1999). CVA, cerebral vascular accident; DM: *Diabetes mellitus*

Table 2: Measurements of body weight, BMI, blood pressure and defecation status

	Month 0	Month 1	Month 2
Body weight (kg)	52.9±8.4	52.8±8.1	53.9±7.5
BMI (kg/m^2)	21.3±3.4	21.4±3.4	21.8±3.2
SBP (mm/Hg)	125.5±18.2	129.2±14.6	131.4±18.7
DBP (mm/Hg)	75.0±10.8	79.3±8.2†	77.5±7.8
Feces frequency (times/day)	0.5±0.2	0.6±0.3†	0.6±0.5

Data are expressed as Mean±SD.

†Paired t-test showed the comparison between month 1 and month 0. $p<0.05$.

Abbreviations: BW, body weight; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure

Table 3: Biochemical measurements

	Normal range	Month 0	Month 1	Month 2
Alb	3.5-5.2 g/dL	3.7±0.4	3.6±0.3	3.7±0.3
TP	6.6-8.7 g/dL	6.8±0.6	6.7±0.6	6.9±0.5
BUN	6-20 mg/dL	15.5±4.0	15.1±4.4	12.6±5.0
Cr	0.5-1.2 mg/dL	0.6±0.2	0.6±0.2	0.6±0.2
UA	2.5-7.0 mg/dL	4.3±1.1	4.6±1.2	4.6±1.2
TC	<200 mg/dL	161.5±29.8	154.4±27.4	166.9±31.1
TG	<200 mg/dL	119.8±43.1	97.4±38.1†	105.5±43.0
HDL-C	>35 mg/dL	54.4±15.4	53.5±14.4	54.3±15.5
LDL-C	<160 mg/dL	92.8±22.0	83.3±18.7†	95.2±23.8
ALK-P	40-129 IU/L	100.0±30.1	104.5±33.7	95.1±25.7
AST	<37 U/L	25.4±9.8	24.3±6.9	24.0±8.9
ALT	<41 IU/L	21.8±7.8	19.0±6.7	20.2±8.1
HbA1c	4.0-6.0%	6.1±0.6	6.0±0.3	6.0±0.4

Data are expressed as Mean±SD.

Abbreviations: Alb, Albumin, TP: Total protein, BUN: Blood nitrogen urea, Cr: Creatinine, UA: Uric acid, TC: Total cholesterol, TG: Triacylglycerol, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, ALK-P: Alkaline phosphatase, AST: Aspartate transferase, ALT: Alanine transaminase, HbA1c: Glycated hemoglobin. †Paired t-test showed the comparison between month 1 and month 0 ($p<0.05$)

Table 4: Blood cell count

	Normal range	Month 0	Month 1	Month 2
TRF	202-336 mg/dL	241.3±50.6	248.2±56.3	249.6±56.5
PA	18-38 mg/dL	24.9±5.2	22.7±5.5†	23.7±4.9
WBC	4.0-11.0x10^3/uL	8.4±2.4	8.1±2.4	8.4±2.1
RBC	4.2-6.1x10^6/uL	4.2±0.6	4.3±0.5	4.3±0.7
Hb	12-18 g/dL	12.2±1.8	12.5±1.5	12.7±1.8
Ht	37-52%	36.8±5.3	37.8±4.6	38.2±5.4
MCV	80-99fL	88.2±4.6	88.2±5.1	88.0±5.2
MCH	26-34pg	29.3±1.9	29.1±2.1	29.2±2.0
MCHC	33-37 g/dL	33.2±0.9	33.0±1.0	33.2±0.8
PLT	130-400x10^3/uL	287.1±66.2	265.0±57.1	273.8±83.0
MPV	7.2-11.1fL	9.7±0.9	10.1±1.0†	9.7±0.9
NEUT	40-74%	63.6±11.4	62.9±9.4	63.4±8.1
LYM	19-48%	25.2±9.4	25.0±8.3	24.6±6.5
MONO	2.0-10.0%	6.5±1.7	6.8±1.5	6.5±1.6
EOS	0-7%	4.3±3.4	4.9±4.0	5.0±3.3
BASO	0-1.5%	0.5±0.3	0.4±0.2	0.5±0.3

Data are expressed as Mean±SD.

Abbreviations: TRF: Transferrin, PA: Prealbumin, WBC: White blood cell count, RBC: Red blood cell count, Hb: Hemoglobin, Ht: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean cell hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, PLT: Platelet, MPV: Mean platelet volume.

†Paired t-test showed the comparison between month 1 and month 0 ($p<0.05$)

Blood cell count: All results for blood cell count were normal (Table 4). There was an increase in MPV (Mean platelet volume) ($p<0.05$).

DISCUSSION

Patients on nasogastric feeding usually had signs of malnutrition including weight less and low serum albumin levels. This research formula aimed to achieve dietary reference intakes (DRIs) recommended by Ministry of Health and Welfare, Taiwan, in order to improve nutritional status of such patients.

Participants maintained same energy intake during the intervention period. During the intervention period, participants displayed no intestinal symptoms, such as diarrhea and bloating and a slight increase in the defecation frequency (0.5 to 0.6 per day), indicating a good enteral tolerance to UNECE U-168.

After one month of supplementation, serum albumin levels and total protein levels were maintained at the similar levels to the baseline. Weight and BMI also did not change. This indicates that UNECE U-168 supplementation can sustain the nutritional status of the patients on a nasogastric diet.

Triglyceride levels (TG) was reduced from 119.8±43.1 mg/dL at the baseline to 97.4±38.1 mg/dL ($p<0.05$) (Month 1). LDL-C levels were also decreased from 92.8±22.0 mg/dL to 83.3±18.7 mg/dL ($p<0.05$). Total cholesterol (TC) levels were also reduced after one month of supplementation, however no significant difference was reached. This may be attributed to soybean protein and patented dietary fiber in UNECE U-168, which have been clinically proven to reduce cholesterol levels in patients with hyperlipidemia and hypercholesterolemia (Erdman and Committee, 2000; Reynolds *et al*., 2006).

It is important that any nutritional supplementation should not impose any adverse effects to the renal and hepatic function. AST and ALT were normal and also slightly decreased, however the difference was not significant. BUN and Cr values were all within the normal range. Other biochemical test results were all normal. Hence, both renal and hepatic functions were not affected by UNECE U-168 supplementation.

Conclusion: After one month of intervention, UNECE U-168 could maintain the nutritional status and blood glucose levels in diabetic participants with no adverse effects to renal and hepatic function.

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