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Original Article

A pilot intervention study to evaluate compliance to a peptide-based oral nutritional supplement in an adult population with impaired gastrointestinal function

Jeffrey L. Nelson

Research and Development, Abbott Nutrition, Columbus, OH, USA

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SUMMARY

Background: Patients with gastrointestinal dysfunction have a reduced ability to digest and absorb nutrients and are often unable to tolerate oral nutritional supplements (ONS) containing whole protein. Peptide-based formulas have been shown to be more efficacious and better tolerated compared with whole protein formulas in malnourished patients. Compliance to ONS is essential to maximizing outcomes. We evaluated compliance to twice-daily use of a peptide-based ONS (220 mL Vital® 1.5, Abbott Nutrition, Columbus, Ohio, USA) in adult patients with chronic malabsorption or maldigestion, over a 16-day treatment period.

Results: 25 evaluable participants (of 35 participants enrolled) were compliant to the study product for 97% of the 16-day treatment period, with the number of days compliant being 15.52, and the average daily percentage of the prescribed product consumed being 98.31%. A significant increase in mean body weight gain, mean body mass index and serum prealbumin of 0.90 Kg ($p = 0.0035$), 0.32 ($p = 0.005$) and 1.87 mg/dL respectively, was also observed. There were no significant changes in the total energy, protein, carbohydrate and fat intake from food alone before and during the study product intake. No safety concerns were observed.

Conclusion: Oral supplementation with the peptide-based ONS (Vital® 1.5, Abbott Nutrition, Columbus, Ohio, USA) in adults with chronic malabsorption or maldigestion is safe and effective in improving nutritional status.

E-mail address: jeffrey.l.nelson@abbott.com.

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1. Introduction

Food assimilation is the most important function of the gastrointestinal (GI) tract. Nearly all nutrients must be digested or broken down because they cannot be absorbed in their natural form. The GI tract must, therefore, be able to convert various forms of food into simple molecules which can then be transported across cell membranes. Digestive enzymes and an adequate absorptive surface area, as well as the presence of other substances which alter the physical properties of food, are all required for proper digestion. These allow food to be mechanically or enzymatically broken down and solubilized to digestive end-products for the absorption process across the intestinal mucosa (epithelial cells that line the GI tract). The absorbed nutrients must be transported into the blood and lymph to be stored or used by peripheral tissues. Any disease that interrupts this delicate sequence of reactions important in digestion and absorption may lead to maldigestion or malabsorption resulting in an inability to utilize the nutrients provided to the GI tract. Thus, malabsorption of food can lead to poor nutritional status or malnutrition [1–3].

GI dysfunction and feeding intolerance can occur in adults with conditions such as celiac disease, chronic diarrhea, cystic fibrosis, early enteral feeding, inflammatory bowel disease (e.g., Crohn's Disease and ulcerative colitis), malnutrition, pancreatic disorders (e.g., pancreatitis), pre/post-operative feeding, and short-bowel syndrome (e.g., surgical removal of a portion of the GI tract). Patients with impaired GI function have a reduced ability to digest and absorb nutrients and need appropriate nutritional support. Given the GI dysfunction, these patients are often unable to tolerate oral nutritional supplements (ONS) containing whole protein or long chain triglycerides [4] and require a formula containing hydrolyzed protein and medium chain triglycerides; these formula minimize the need for hydrolysis of protein by the brush border peptidases in the intestinal lumen [5,6] and are more easily absorbed [4,7].

Peptide-based formulas contain protein that is hydrolyzed or pre-digested into peptides of varying lengths including di- and tri-peptides and amino acids [4]. Hydrolyzed or peptide-based protein systems help improve absorption and tolerance compared to protein systems composed entirely of free amino acids or intact protein [6,8–10].

While ONS have been shown to be clinically effective in the management of disease-related malnutrition, it is essential to achieve good compliance to the ONS to maximize outcomes [9]. The aim of our study was to evaluate the use of and compliance to twice-daily use of a peptide-based ONS in adult patients with chronic malabsorption or maldigestion who required supplemental nutrition as assessed by a clinician.

2. Methods

2.1. Study design and participants

This was a prospective, single-arm, single-treatment study, conducted at a single hospital outpatient clinic site in Canada. All enrolled participants or participants' legally acceptable representative provided a written informed consent and applicable privacy authorization, and the study protocol and all relevant documentation were approved by an Institutional Review Board/Independent Ethics Committee (University of Manitoba Biomedical Research Ethics Board).

Male and female participants $\geq$18 years of age; presenting with chronic malabsorption or maldigestion and requiring supplemental nutrition as assessed by a clinician, who agreed to consume two servings of the study product a day for 16 consecutive days during the treatment period, were eligible to participate in the study. Potential participants were excluded if they presented with antibiotic associated gastrointestinal intolerance; had current active malignant disease or was treated within the last 6 months for cancer, except basal or squamous cell skin carcinoma prior to enrollment; had diabetes mellitus as evidenced by taking anti-hyperglycemic medications; had immunodeficiency disorder; had a history of allergy to any of the ingredients in the study product; had a known aversion to flavor of product being tested; had known dementia, brain metastases, eating disorders, history of significant neurological or psychiatric disorder, or any other psychological condition that may interfere

with study product consumption; had an obstruction of the gastrointestinal tract precluding ingestion or absorption of the study product; or were taking part in a non-Abbott approved clinical trial.

2.2. Study procedures

The ONS investigated in this study is Vital® 1.5 (Abbott Nutrition, Columbus, Ohio, USA), a nutritionally complete, well-tolerated, easily absorbed, ready-to-feed, peptide-based formula for adult patients experiencing GI dysfunction and/or feeding intolerance in acute care, long-term care, or home care environments. The protein system in the ONS is peptide-based, containing 70% hydrolyzed whey protein and 30% hydrolyzed casein. The fat blend contains 70% medium chain triglycerides (MCT), an easily digested and well-absorbed fat source, and canola oil.

The schedule of assessments is presented in Table 1.

During the Screening visit, participants tasted a sample of the product to ensure that they did not have an aversion to the product flavor. Height and weight for use in calculation of body mass index (BMI) was recorded and blood for serum prealbumin was also drawn (prior to product intake). On days 1–3 and 20–22, participants collected daily dietary intake via a diary record.

After the **Screening visit**, participants entered an **Adaptation period** (days 4–6) where they continued with their standard of care and normal feeding routine while beginning the intake of the study product (Vital® 1.5, Abbott Nutrition, Columbus, Ohio, USA). They were encouraged to ramp up this intake in increments of half serving (220 mL per serving) to achieve an intake of two servings/day by day 7. During the **Adaptation period**, adverse events (AEs) were captured via a daily diary record.

Following the **Adaptation period**, participants entered a **Treatment period** (days 7–22) where they consumed two servings of the study product per day, in addition to their normal daily dietary

Table 1
Schedule of assessments.

Assessment	Screening visit	3-day dietary intake[d]	Phone	Adaptation period	Phone	Treatment period	Phone	Exit (+72 h)	Safety phone call
	day 0	day 1–3	day 3	day 4–6	day 6	day 7–22 3-day dietary[d] (day 20–22)	day 19	day 23	5–7 days post day 23
Informed consent	X								
Eligibility criteria	X								
Product taste test	X								
Urine pregnancy test[a]	X								
Medical history/physical exam	X								
Blood draw[b]	X							X	
Demographics	X								
Anthropometrics (weight/height/BMI)[c]	X							X	
3-day dietary intake		X				X			
Product intake				X		X			
Remind participant to start product			X		X				
Remind participant to start diet diary							X		
Medications	X	X	X	X	X	X	X	X	
Adverse events	X	X	X	X	X	X	X	X	
Safety phone call									X

[a] In applicable female participants.
[b] Participants had their blood taken for the measure of prealbumin; at the Screening visit, the blood draw was performed after the product sample taste test.
[c] Height for use in BMI calculation was measured at screening, body weight was measured at the Screening visit and Study exit.
[d] During study days 1–3 and 20–22 participants collected daily dietary intake via a diary record.

intake. The product provided an additional 660 kcals/day and additional protein (30 g/day), fat (24 g/day) and carbohydrate (80 g/day). All appropriate measurements including product intake, medications and AEs were collected daily. Prior to starting intake of the study product and before **Study exit** (day 23), participants collected daily dietary intake via a diary record, on days 1–3 and days 20–22 respectively.

Non-serious and serious AEs (SAEs) were collected from the time the informed consent form was signed until two days after **Study exit** (day 23) to assess potential safety issues related to the consumption of the study product. Non-serious and SAEs occurring from the **Screening visit** until **Study exit** were reported on an Adverse Event Report form. Any SAE that was ongoing and product-related two days after **Study exit** (day 23) was followed until the event was resolved or there was a satisfactory explanation. Within 5–7 days after Study Exit (day 23), a safety telephone call was made to participants to assess any AEs that may have occurred within the two days post **Study Exit** visit.

2.3. Study variables

The primary variable in the study was compliance to the study product during the treatment period. Compliance was assessed by the proportion of days compliant during the treatment period, and by analyzing the average daily percent of prescribed study product consumed during the treatment period. Secondary variables included AEs, anthropometrics and medication use. Exploratory variables included prealbumin level and dietary intake.

2.4. Sample size estimation

A study sample size estimate of 25 evaluable subjects was determined as follows. When the sample size is 25, a two-sided 95% confidence interval for the mean percent of days compliant during the treatment period will extend 2.21% from the observed mean, assuming the standard deviation is known to be 5.64%, based on a previous study. In addition, when the sample size is 25, a two-sided 95% confidence interval for the mean daily percent of the prescribed study product consumed during the treatment period will extend 13.5% from the observed mean, assuming the standard deviation is known to be 34.5% based on the cumulative caloric deficits in [11]. Enrollment of 35 subjects to obtain 25 evaluable subjects was planned assuming a 28% attrition rate.

2.5. Statistical analysis

All continuous variables were summarized using mean, median, standard deviation, standard error, 25th percentile, 75th percentile, minimum, maximum, and 95% confidence interval. Proportions and 95% confidence interval for proportions were presented for all categorical variables. All change variables were analyzed using one-sample paired t-test and normality of the data was assessed using stem-and-leaf plot, normality plot, and Shapiro–Wilk test. A p-value of <0.05 was considered significant.

Table 2
Primary diagnosis of study participants.

Primary diagnosis	N
Crohn's disease	22
Celiac disease	3
Ulcerative colitis	3
Irritable bowel syndrome	2
Short bowel syndrome	1
Chronic pancreatitis	1
Retractile mesenteritis	1
Primary biliary cirrhosis	1
Perforated appendix	1

3. Results

A total of 35 participants were enrolled in the study, of which 25 participants were found to be evaluable. Ten participants failed *a priori* protocol-specified evaluability criteria – two participants failed one or more eligibility criteria, and ten failed to have at least 14 days with a minimum of 75% study product consumption. Participants may have failed one or both criteria. The primary diagnosis of the participants is outlined in Table 2.

The baseline characteristics of the study participants are outlined in Table 3.

3.1. Compliance

The proportion of days that the participants were compliant to study product during the 16-day treatment period was 97 ± 1.49% with a minimum of 69% and a maximum of 100%. The number of days compliant during the treatment period was 15.52 ± 0.24 days with a minimum of 11 and a maximum of 16 days. The average daily percentage of the prescribed study product consumed during the treatment period was 98.31 ± 0.81% with a minimum of 85.16% and a maximum of 100%.

3.2. Body weight and body mass index

At baseline, the mean body weight was 63.81 ± 2.73 kg with a minimum value of 37 kg and a maximum of 98 kg. At the time of exit, the mean body weight was 64.71 ± 2.87 kg with a minimum of 38.30 kg and a maximum of 102.80 kg. There was a significant mean body weight gain of 0.90 ± 0.28 kg ($p = 0.0035$; Table 4).

At baseline, the mean body mass index (BMI) was 22.05 ± 0.95 with a minimum value of 15.22 and a maximum of 37.34. At the time of exit, the mean BMI was 22.36 ± 1.01 with a minimum of 15.76 and a maximum of 39.17. Results showed a significant mean BMI gain of 0.32 ± 0.10 ($p = 0.005$; Table 4).

3.3. Serum prealbumin

At baseline, the mean serum prealbumin level was 24.65 ± 1.08 mg/dL with a minimum value of 13 mg/dL and a maximum of 32 mg/dL. At the time of exit, the mean serum prealbumin level was

Table 3
Baseline characteristics.

Variable	
Total number of participants	25
Male, n (%)	12 (48)
Age, years, mean (SD)	53 (3)
Weight, kg, mean (SD)	63.81 (2.73)
Height, cm, mean (SD)	170.12 (1.81)
Body Mass Index, mean (SD)	22.05 (0.95)
Pre-albumin, mg/dl, mean (SD)	24.65 (1.08)

Table 4
Change in body weight, body mass index and prealbumin levels from study baseline to study exit.

	Baseline		Study Exit		Change, mean (SD) (p value)
	Mean (SD)	Min – Max	Mean (SD)	Min – Max	
Body Weight (kg)	63.81 (2.73)	37–98	64.71 (2.87)	38.30–102.80	0.90 (0.28) ($p = 0.0035$)
Body Mass Index	22.05 (0.95)	15.22–37.34	22.36 (1.01)	15.76–39.17	0.32 (0.10) ($p = 0.0050$)
Prealbumin level (mg/dL)	24.65 (1.08)	13–32	26.52 (0.88)	18–33	1.87 (0.75) ($p = 0.0211$)

Table 5
Three-day dietary assessments made before and during oral nutritional supplementation.

Intake	Study Days 1–3 (Study baseline)		Study Days 20–22 (Study exit)		Change from baseline to exit, mean (SD) (p value)
	Mean (SD)	Variation (Min – Max)	Mean (SD)	Variation (Min – Max)	
Total Energy, kCal	1721.20 (123.95)	275.70–2894.70	1687.93 (132.96)	446.70–2734.00	−33.26 (101.94) (p = 0.7470)
Protein, g	72.14 (6.26)	5.97–155.60	79.21 (7.65)	24.40–174.50	7.07 (4.72) (p = 0.1477)
Carbohydrate, g	218.39 (15.58)	59.60–365.07	204.18 (17.06)	38.63–328.70	−14.21 (13.78) (p = 0.3126)
Fat, g	62.58 (5.79)	1.60–126.23	62.24 (5.33)	16.80–108.93	−0.34 (4.75) (p = 0.9431)

26.52 ± 0.88 mg/dL with a minimum of 18 mg/dL and a maximum of 33 mg/dL. There was a significant increase in prealbumin of 1.87 ± 0.75 mg/dL (p = 0.0211; Table 4).

3.4. 3-Day Dietary Assessment – total fat, protein and carbohydrate intake

The 3-Day Dietary Assessment was based on food intake only and did not include values from the ONS. Non-significant changes were seen in the total energy, protein, carbohydrate and fat intake before (days 1–3) and during study product intake (days 20–22; Table 5).

3.5. Medications

No significant trends in medication use were noted as very few new medications were introduced during the trial. Participants continued the use of medications they were already on prior to study entry.

3.6. Safety results

The AEs reported were not unexpected for this patient population. The most common preferred term was abdominal discomfort (n = 10 subjects) which were all mild in severity. Overall, there were no safety concerns.

4. Discussion

The objective of this study was to evaluate the use of and compliance to twice-daily use of a peptide-based ONS in adult patients with chronic malabsorption or maldigestion who required supplemental nutrition as assessed by a clinician. A total of 35 participants were enrolled in the study to achieve 25 evaluable participants.

The primary variable in the study was compliance to the study product during the 16-day treatment period. Numerous studies have tried to identify factors affecting ONS compliance rates [12–15]. Age, product palatability, volume, energy density and macronutrient profile, and patient education and counseling are the key factors which influence compliance to supplements [12–14]. Compliance of patients receiving ONS, especially with peptide-based formulas, is low [16]. It has been reported that over 20% of randomized patients receiving ONS with peptide-based or whole protein formulas stop the treatment due to the unpalatability of the formula or intolerance [17]. However, results from our study demonstrated good participant compliance to taking the product (≥1.5 bottles per day; 220 mL per bottle); participants were compliant to taking at least 1.5 bottles per day of study product on 97% of the days during the treatment period with an average daily percent of the prescribed study product consumed during the treatment period being 98%. This would suggest that although participants had a condition of maldigestion/malabsorption, they successfully consumed the product throughout the study.

Peptide-based formulas, such as the study product (Vital® 1.5, Abbott Nutrition, Columbus, Ohio, USA), can be particularly useful in patients with GI dysfunction or feeding intolerance who cannot efficiently digest oral ONS containing whole protein or long chain triglycerides [4]. As mentioned previously, hydrolyzed peptide-based protein systems help improve absorption and tolerance, particularly when compared with protein systems composed entirely of free amino acids or intact protein [6,8–10]. Furthermore, studies have reported that peptide-based formulas are more efficacious and better tolerated compared with whole-protein formulas in malnourished patients [4,8]. We observed similar results in our study, where participants with malabsorption or maldigestion and requiring supplemental nutrition, showed significant gains in body weight and BMI, and improvement in serum-prealbumin, with no significant adverse events.

In our study participants, while body weight, BMI and prealbumin levels showed significant improvement during the study duration, assessment of dietary intake suggested that the participants' normal dietary consumption was not affected due to the intake of the study product - there were no changes in total energy intake, protein, carbohydrate, or fat intake. These data demonstrate that the oral nutritional supplement used in the study was truly supplementing the diet versus replacing meal intake. Disease and illness severity can sometimes reduce food intake; in patients with disease-related malnutrition with an inadequate dietary intake due to poor appetite, high protein ONS helps to increase protein intake [18]. A systematic review and meta-analysis in a range of patient groups and settings demonstrated the clinical and economic benefit of ONS, particularly high protein ONS [18]. The benefits include reduction in complications and readmissions and an improved intake of protein and energy without any impact on normal food intake [18]. It has been shown that ONS do not suppress food intake and usually enhance nutritional intake in most patient groups; this potentially contributes to the beneficial effects in malnourished patients with a poor appetite [19]. Furthermore, high protein ONS have very little effect on the amount of food consumed daily and, as with other ONS, does not tend to replace a meal but rather adds to the amount of nutrition consumed daily [18,20]. The effectiveness of high protein ONS in improving the daily macronutrient and micronutrient intake has also been reported in malnourished older adults with cardiopulmonary diseases after discharge. The results of this study are similar to those we observed in our study, and indicate that when consumed between meals, ONS does not impact the nutrient intake from food [21]. In routine clinical practice, nutrient intake from food is emphasized over ONS. However, it must be noted that nutritional deficits in malnourished adults with underlying illness, such as those in our study, can be met with a combination of ONS and normal food intake [21].

To conclude, the results of our study suggest that oral supplementation with the peptide-based ONS (Vital® 1.5, Abbott Nutrition, Columbus, Ohio, USA) in adults with chronic malabsorption or maldigestion was both safe and effective in improving nutritional status.

Statement of authorship

Jeffrey L. Nelson made substantial contributions to the design of the study, analysis and interpretation of data, and, drafting and revising the manuscript.

Conflicts of Interest

Jeffrey L. Nelson is an employee of Abbott Nutrition.

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