A Retrospective Study on the Safety and Efficacy of a Ketogenic Feeding Tube Diet in the Treatment of Obesity

Abstract

Background: According to the US Department of Health and Human Services, 35.7% of adults and 17% of children in the USA are currently obese. With no American state having an obesity prevalence of <20% and thirteen states having a prevalence rate ≥ 30%, surgical interventions such as gastric restrictive or diversion bariatric operations are becoming increasingly necessary. Non-surgical therapies like very low calorie diets (VLCD) and low calorie diets (LCD) are limited in potency of nutritional ketosis because carbohydrate-free formulas are not palatable to the patient. The current study therefore sought to evaluate a physician-supervised, outpatient, 10-day ketogenic feeding tube diet as an option for overweight or obese patients using a carbohydrate-free mixture of protein, fats and micronutrients.

Methods: This is a retrospective clinic chart review (n=218) of patients who underwent a medically supervised weight loss program using a feeding tube to induce and maintain a state of nutritional ketosis. After medical evaluation, a pediatric feeding tube was inserted through the nose under local anesthesia and a carbohydrate-free ketogenic mixture delivering approximately 600 to 800 kcal/day was administered continuously. Over a 24-month period, 218 patients were treated, and 177 were identified as having verifiable initial and final weights, serial blood chemistry, urinary ketone levels, and fat free mass (FFM) as measured by DEXA.

Results: The mean age of patients was 44.7 years (range 20-70 years), 83.1% were female, 65% were Caucasian. The mean BMI was 31.8 kg/m² (SD=5.0); the mean duration of treatment was 8.7 days (range 2-13 days). There was a significant increase in urinary ketones (p<0.001). There was a significant reduction in total body weight of 4.9 kg (SD=2.0, p<0.001) and BMI of 1.95 kg/m² (SD=0.68, p<0.001). The procedure was tolerated well with little or no discomfort by 72.9%; 15.8% removed the feeding tube early due to discomfort or personal reasons; 3.4% did not tolerate the treatment and 6.8% had their feeding tube reinserted during the treatment. There were no serious complications.

Conclusion: The ketogenic feeding tube diet induced nutritional ketosis and led to a clinically significant weight loss in the 10-day program. This approach may play a role in the treatment of obesity to initiate weight loss in lifestyle or medication programs, to break through weight loss plateaus, or for preoperative weight loss prior to bariatric surgery. It may also be a useful medical strategy for patients who do not qualify for or refuse bariatric surgery, but are significantly overweight and in need of medical intervention after failing lifestyle modifications. [No Trial Registration required]

Keywords

Obesity; Bariatric surgery; Ketogenic diet; Weight loss; Feeding tube diet; KE Diet®; Nasogastric tube diet; KEN; NEC

Abbreviations

KEN: Ketogenic Enteral Nutrition; NEC: Nutrizione Enteral Ketogena; LCK: Low Carbohydrate Ketogenic diet; MCT: Medium-Chain Triglycerides; LCT: Long-Chain Triglycerides; FFM: Fat Free Mass; FM: Fat Mass; BMI: Body Mass Index; DEXA: Dual Energy X-ray Absorptiometry; pH: power of Hydronium ion; VLCD: Very Low Calorie Diets; LCD: Low Calorie Diets

Background

With the current obesity epidemic increasing worldwide, new innovative medical strategies are required to provide safe and effective weight loss to prevent or treat the metabolic disruptions caused by this disease. According to the US Department of Health and Human Services, 35.7% of adults and 17% of children in the USA are currently obese [1]. With no American state having an obesity prevalence of <20% and thirteen states having a prevalence rate ≥ 30%, medical interventions such as gastric restrictive or diversion bariatric operations are becoming increasingly necessary [2]. The introduction and development of bariatric surgical techniques have greatly assisted in achieving...
sustained weight loss, however not all patients are candidates or are not willing to accept weight loss surgery. Furthermore, many bariatric surgeons request a 5-10 kg weight reduction prior to weight loss surgery to reduce hepatomegaly and facilitate surgery [3].

Studies have suggested that low-carbohydrate ketogenic diets (LCK diets) result in significant weight loss [4-6] and appear to significantly reduce hunger [7-9]. However, major limitations of pre-operative LCK diets are compliance and the time (at least six months) to achieve the required weight loss. However, a recent Italian study consisting of a retrospective analysis of over 19,000 patients suggested that ketogenic eternal nutrition cycles with a protein-only solution (KEN or NEC) administered via a nasogastric tube was safe and resulted in a rapid fat mass reduction in obese patients [10].

A ketogenic diet is defined as a high-fat, adequate-protein, low-carbohydrate diet that induces a ketogenic state in the body called nutritional ketosis, which is controlled and very different from the uncontrolled and severe ketosis seen in diabetic ketoacidosis, which is due to lack of insulin [11]. When glycogen stores are reduced, a process known as lipolysis is induced, causing the cleavage of triacylglycerols. This process produces three fatty acid chains and one glycerol molecule. The extrapolated fatty acids are then used as an alternative energy source through a beta-oxidation process that produces acetyl-CoA, which is subsequently used in the citric acid cycle [12].

If the body continues to derive energy in this manner, due to prolonged fasting or starvation, the liver produces three water soluble compounds (β-hydroxybutyrate, acetoacetate and acetone). These compounds collectively are known as ketone bodies and can be measured through urine analysis or in the blood. Patients with elevated urine ketone levels are said to be in a state of nutritional ketosis [12].

However, not all triglycerides induce the same level of ketosis. Long-chain triglycerides (LCTs) differ from medium-chain triglycerides (MCTs) in that the MCT’s carbon chains are shorter than those of LCTs. Consequently, MCTs produce ketones that are more readily absorbed by the body and produce a higher yield of ketones per unit of energy than LCTs. Furthermore, MCTs are transported to the liver via the hepatic portal system very quickly rather than the slower lymphatic system resulting in faster metabolism and therefore are more rapid and efficient in inducing nutritional ketosis [13,14]. It is for these reasons that MCTs are considered more ketogenic than LCTs.

While prolonged exposure to liquid protein diets, such as MCT oil diets, can produce complications, such as reduced vitamin absorption, studies suggest that if the duration of the diet is ten days or less no significant complications arise [15,16]. Consuming high quantities of MCT oil has been shown to cause abdominal cramps, diarrhea, and vomiting in some patients. A general standard of a 45% MCT oil ratio has been generally regarded as a balance between achieving adequate nutritional ketosis and minimizing gastrointestinal complaints [17].

While it is always preferable to use the oral feeding route rather than the enteral feeding route, experience has shown that a carbohydrate-free solution of protein, fats and micronutrients is highly non palatable to nearly all patients, and the daily volume required (approx. 2,000 ml) makes the oral route impossible as an option in this type of ketogenic diet.

The current retrospective study was performed to evaluate a physician-supervised, outpatient 10 day ketogenic feeding tube diet that utilizes a continuous infusion of a carbohydrate-free mixture of medium chain triglycerides, whey protein isolate and micronutrients as a treatment option for obese patients.

Methods

Patient selection

This study reviewed weight loss clinic charts over a 24-month period at The KE Diet® Center in Miami, Florida, USA. All patients were self-referred from media and internet sources and most travelled from out of town. All patients were screened over the telephone for BMI > 27 kg/m², failed lifestyle modification and serious medical conditions. Those that qualified were accepted to travel to Miami for a history and physical examination by a physician, blood and urine tests and a DEXA scan. Further exclusion criteria included significant renal, cardiac, pulmonary, or psychiatric disease, pregnancy, breast-feeding or a BMI of less than 27 kg/m². Total Body Tissue Quantification on day 0 and 10 was measured by DEXA (GE Lunar Prodigy Primo™ v.107).

Study design

After obtaining informed consent and ethical approval, and undergoing a full history and physical examination by a physician, patients were taught how to fill and use a portable rechargeable infusion pump (Kangaroo Joey™ – Covidien) and were given a container of carbohydrate-free whey-protein powder with a vitamin premix, and medium chain triglyceride oil (derived from coconut oil-MCT oil, Nestle Nutrition), which was infused continuously through the feeding tube and the rate adjusted to induce maximum urinary ketosis and hunger-suppression. Polyethylene glycol 3350 (Miralax™) was used to treat constipation, and a telephone number was supplied by which a medical doctor could be reached at any time during the 10-day treatment cycle. A 6 French pediatric feeding tube was inserted through the nose under local anesthesia (lidocaine hydrochloride jelly 2%-Akorn) and attached to the cheek using clear adhesive tape (Polyakin™-Covidien). A predetermined infusion rate of the whey protein, vitamin and medium chain triglyceride mixture was then administered continuously via a battery powered feeding pump order to achieve the desired ketotic state and suppress hunger fully. The feeding tube infusion was continued 24 hours per day for the duration of the treatment. Patients were allowed to disconnect the feeding tube from the pump for 10 minutes per day to shower or bathe. All patients received an oral proton pump inhibitor (lansoprazole 15 mg daily) and were allowed to drink water as needed and black coffee, tea and/or beef bouillon twice daily. No food by mouth was permitted during the treatment. Patients were asked to keep

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a daily log of their weight, urine ketone levels, hunger levels, bowel movements and any abdominal bloating or diarrhea.

The medium chain triglyceride range was 30 to 60 ml/day and the range of whey protein/vitamin powder was 100 to 120 g per day dissolved in 2000 ml of water and infused at 85 ml per hour. Medium chain triglyceride rates and whey-protein powder concentrations were adjusted throughout the cycle to maximize nutritional ketosis, control hunger and minimize abdominal bloating and/or diarrhea.

The following variables were assessed at baseline (day 0): age, sex, weight, body mass index, vital signs, complete blood count, total cholesterol, triglyceride, uric acid, sodium, potassium, chloride, urea nitrogen, creatinine, glucose, CO₂, urine ketone level, urine pregnancy test (if indicated), fat mass, and fat free mass. Patients were seen in the clinic for follow up on days 3, 5 and 10. Follow up tests included weight, vital signs, hunger level, abdominal bloating/pain, diarrhea/constipation, urine ketone levels with repeat blood tests done on day 5 (sodium, potassium, chloride, urea nitrogen, creatinine, glucose, CO₂, uric acid). Total Body Tissue Quantification was performed on days 0 and 10 by DEXA scan. Patients were also contacted by telephone every day by a nurse for follow up.

**Outcome measures**

The primary outcome was an increase in urine ketone levels from day 0 to day 3 and day 5. Urinary ketone levels were measured on a 5-point scale: 0, 15, 50, 150 mg/dL. Secondary outcomes included reductions in body weight, body mass index, hunger sensation, fat mass, fat free mass, stability of vital signs, fatigue, constipation, diarrhea, abdominal bloating or pain, nasal or throat irritation and retching and/or vomiting. Side effects were collected on a standardized form and rated on a 5-point ordinal scale: 0, 1, 2, 3 and 4.

**Statistical analysis**

Due to the ethical issue of starving patients for ten days no control group was used. Statistical analysis therefore included 2-tailed paired sample t-tests for the analysis of initial, final, and average values. Due to the quantity of paired-sample t-test arrangements a one-way analysis of the variables was used to decrease the probability of a type I error. Regression analysis along with correlation matrices were used to evaluate relationships between key variables, symptoms, and outcomes. Symptons and averages were evaluated as described in (Table 1). The nature of the study was multivariable and a test for homogeneity of the variances, partial correlation controlling for ketone levels, and post hoc tests were therefore preformed to control for type I errors. Post hoc analysis was done in the form of a Schiffe’s test, Tukey’s test, and Tukey’s-B test.

**Results**

**Efficacy**

A total of 218 self-referred patients from July 2011 to August 2013 were evaluated at the Miami clinic with BMIs ranging from 21.9 to 54.4 kg/m² (mean = 31.8, SD = 5.01). Of the 218 patients evaluated, 11 were evaluated but never returned for the treatment, 30 patients did not have verifiable office data, of which 21 had undergone multiple treatments beyond the first treatment and had only telephone data available and were therefore excluded; 177 were first time patients accepted for the feeding tube diet after having verifiable data such as initial and final weights, serial blood chemistries, urinary ketone levels, fat free mass (FFM) and fat mass as measured by DEXA.

Baseline characteristics are shown in (Table 1). The mean patient age was 44.7 years (range 20-70 years) with an 83.1% female and 65% Caucasian ratio. The mean duration of treatment was 8.7 days (range 2-13 days) and 72.9% (n=129) tolerated the procedure well with little or no discomfort; 15.8% (n=28) removed the feeding tube early due to discomfort or personal reasons; 3.4% (n=6) did not tolerate the treatment and 6.8% (n=12) had their feeding tube exchanged or reinserted during the treatment due to blockage or inadvertent removal.

The mean total body weight decreased from 88.1 kg at baseline to 83.2 kg at day 10 (p=0.001). Paired sample t-tests indicated that there was significant total weight loss (mean = -4.97kg, SD = 2.00kg) ([t(175)]=32.885, p < 0.001), BMI reduction (mean= -1.95kg/m², SD=0.68, p=0.001) ([t(175)]=35.088, p < 0.001), percent fat reduction (mean=1.38, SD=4.41) ([t(109)]= -3.281, p<0.001), lean mass increase (mean=7.56, SD=4.45) ([t(110)]=17.901, p < 0.001), total FFM reduction (mean = -3.5kg, SD=1.93, p<0.001) ([t(109)]= 18.816, p<0.001), and total fat mass reduction (mean = -1.5 kg, SD=1.28,) ([t] =, p <0.001).

Paired sample t-tests indicated that no significant changes were seen in specific gravity, pH, leucocyte count, nitrates, protein, or glucose as measured by automated (Urisys™ 1100, Roche) urine analysis dipstick (Chemstrip™ 10 MD, Roche). There was also indication of a significant reduction in patient’s pulse (mean=-3.47, SD=12.92) ([t (151)]= -3.309, p = 0.001), systolic (mean= 114.12, SD=14.67) ([t(148)]=94.985, p< 0.001) and diastolic (mean=1.950, SD=9.013) ([t(160)]=2.746, p = 0.007) blood pressures.

Partial correlation analysis indicated that there were significant correlations between total weight lost and average
hunger \( r (171) = -1.69, p = 0.027 \) and average discomfort \( r (171) = -0.213, p = 0.005 \) when controlling for average ketone levels. No correlation was seen between total weight loss and diarrhea or between total BMI loss and diarrhea when controlling for average ketone levels. Multiple regression analyses suggested a quadratic relationship between total number of days on the diet and total weight lost \( F(1, 145) = 5.43, p = 0.02 \). A summary of the analysis can be seen in (Figures 1 and 2) respectively.

### Safety

Side effects included minor abdominal bloating, constipation and/or diarrhea and halitosis. The most common complaint was mild diarrhea but only 17.5% \((n=31)\) reported any noticeable distress. Slight cramping and hunger was also seen but both were readily controlled by altering the MCT oil rate with a significant inverse correlations between day 5 MCT oil rate and day 5 hunger \( r = -0.471, n=101, p = 0.01 \). A summary of the reported symptoms can be seen in (Table 3).

No serious complications were reported but in one patient the feeding tube could not be inserted and the procedure was cancelled. There was one reported complication due to the feeding tube’s adhesive tape causing a minor skin rash on the cheek. There were no other reported complications due to feeding tube’s insertion or use.

### Discussion

In studying this group of motivated individuals with obesity, we observed over a 10 day period, significant weight loss, reductions in BMI, reduction in fat free mass and fat mass, with water and muscle loss to a lesser degree. By day 5, we observed over a 10 day period, significant weight loss, with reductions in BMI, reduction in fat free mass and fat mass, which can be seen in (Table 3).

As expected, there was a significant increase in weight loss as the number of days on the diet increased. Although this data was not analyzed in this study, we also observed minor decreases in serum sodium and increase in uric acid levels by day 5 with no ill effects resulting. Reduction in hunger sensation is a striking feature of this type of ketogenic diet and was found to be statistically significant; nearly 85% of patients have no or little hunger of which 50% reported no hunger at all throughout the 10 day diet.

While one would expect any patient who does not eat for 10 days to lose approximately the same amount of weight, this would be almost certainly associated with significant hunger due to starvation. One limitation of our study is the lack of long-term follow up and limited maintenance weight loss program which will need to be evaluated in future studies. A small number of patients removed the feeding tube early for personal reasons and/or discomfort and/or failed to come into the office at the set interval times. While this did reduce the sample size, enough patients complied with the treatment to allow valid statistical analysis. Furthermore, while the sample consisted of mainly Caucasian females, ratios of gastric restrictive or diversion bariatric operations are dominated by this same population demographic.

The mean total weight reduction seen in our study during the first 10 days is similar to that seen in post-operative bariatric surgery patients and corresponds to the loss of 5-10% excess weight.

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### Table 2: Statistical results for main outcome measures.

|                      | Sum of Squares | DF | Mean Square | F      | Sig.  |
|----------------------|----------------|----|-------------|--------|-------|
| Avrg Hunger          | Between Groups | 1.642 | 9.678 | 11.320 | 1.149 | .60  |
|                      | Within Groups  |     |     |     | 2.499 | .006 |
|                      | Total          |     |     |     |       |     |
| Avrg Diarrhea        | Between Groups | .292 | 4.444 | 4.736 | 0.27  | .27  |
|                      | Within Groups  |     |     |     | 9.69  | .477 |
|                      | Total          |     |     |     |       |     |
| Avrg Cramps          | Between Groups | 13.416 | 87.031 | 100.447 | 1.220 | .537 |
|                      | Within Groups  |     |     |     | 2.270 | .13  |
|                      | Total          |     |     |     |       |     |
| Avrg Discomfort      | Between Groups | 1.174 | 3.643 | 4.817 | 1.07  | .022 |
|                      | Within Groups  |     |     |     | 4.746 | .000 |
|                      | Total          |     |     |     |       |     |
| Total BMI loss       | Between Groups | 727.435 | 40.160 | 767.595 | 60.620 | .245 |
|                      | Within Groups  |     |     |     | 247.548 | .000 |
|                      | Total          |     |     |     |       |     |
| Total Ket Level      | Between Groups | 4276.577 | 32928.862 | 37205.438 | 388.780 | 200.786 |
|                      | Within Groups  |     |     |     | 1.936 | .38  |
|                      | Total          |     |     |     |       |     |
| Total wt Loss Lb     | Between Groups | 21038.528 | 1882302 | 22920830 | 1753.211 | 11477 |
|                      | Within Groups  |     |     |     | 152.753 | .000 |
|                      | Total          |     |     |     |       |     |
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Table 3: Summary of reported symptoms.

|                  | Mean  | Std. Deviation | N   |
|------------------|-------|----------------|-----|
| Hunger Day 3     | 1.15  | 1.120          | 95  |
| Diarrhea Day 3   | .73   | .831           | 95  |
| Cramps Day 3     | .24   | .479           | 94  |
| Hunger Day 5     | 1.37  | 1.856          | 103 |
| Diarrhea Day 5   | .64   | .862           | 103 |
| Cramps Day 5     | .21   | .457           | 103 |
| Hunger Final     | .91   | 1.247          | 138 |
| Diarrhea Final   | .39   | .697           | 115 |
| Cramps Final     | .60   | 4.686          | 114 |
| Average Hunger   | 2.16  | 2.701          | 174 |
| Average Diarrhea | 1.03  | 1.38           | 174 |
| Average Cramps   | .65   | 3.83           | 174 |

Figure 1: BMI loss over time.

Figure 2: Weight loss over time.

body weight (5-10 kg) suggested to reduce post-operative complications after bariatric surgery [3].

This type of ketogenic feeding tube diet also supports a non-surgical attempt at weight loss that can satisfy medical insurance requirements prior to authorizing bariatric surgery. While a small percentage of patients experienced discomfort and removed the tube the majority of patients tolerated the entire cycle with no complications and 13.6% (n=24) returned for multiple cycles [18].

One obvious question is why the need for nasogastric feeding and not simply provide liquid meal replacement boluses on an intermittent basis. We have found that our Carbohydrate-free mixture is totally non palatable to patients and that it would be physically impossible to drink 85 ml per hour of this mixture 24 hours per day for 10 days to produce the level of nutritional ketosis required to suppress hunger, burn fat and reduce weight at the level we observed. Only 1 patient out of 218 (0.46%) could not tolerate feeding tube insertion, over 73% of patients had little to no discomfort and only 3.4% of patients could not tolerate the diet. We observed no serious complications due to feeding tube insertion including no epistaxis, sinusitis, nasal septum perforation, laryngospasm or aspiration pneumonia. The published Italian data on over 19,000 patients using a similar diet also confirmed the safety and lack of complications relating to the use of a feeding tube [10].

Furthermore, generally accepted principles of surgical nutrition teach us that we should use a normal functioning digestive tract whenever possible. We believe we adhere to this teaching because we are indeed using the patient's own functioning digestive tract and are merely bypassing the oropharynx and delivering macro and micronutrients directly into the stomach. Aside from the obvious palatability and taste issues, it allows us to completely control and calculate precisely the nutrition our patients are receiving because clearly, they consume nothing else except water.

Our group has concluded that using this type of feeding tube diet allows the practitioner to produce such intense nutritional ketosis that hunger is virtually eliminated and 5-10% body weight is lost in 10 days. In the proper hands, this weight loss technique could be an extremely powerful weapon in the global war against obesity. We particularly believe it will be useful in pre-operative weight loss prior to bariatric or orthopedic surgery and in the failed bariatric surgery patient who regains weight after successful surgery.

We believe this weight loss method will prove very effective in the obese Type II Diabetes patient. We already have observed dramatic reductions in insulin and oral hypoglycemic agent requirements, as seen in other low carbohydrate ketogenic diet interventions [19]. More clinical studies will be required to evaluate this therapy for diabetes and weight loss.

Conclusion

The ketogenic feeding tube diet may play a role in the treatment of obesity to initiate weight loss in lifestyle or medication programs, to break through plateaus or for Pre-operative weight loss prior to bariatric surgery. It may also be a useful alternative medical strategy for patients who do not qualify for or refuse bariatric surgery but are significantly overweight and in need of medical intervention after failing lifestyle modifications.

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Conflict of Interest

i. Oliver R. Di Pietro is president, chief executive officer and majority shareholder of European Ketogenic Weight Loss Clinics, LLC d/b/a KE Diet® (USPTO Registered Trademark #4367202) which have applied for US and foreign patents (USPTO # 20130045915) on August 15, 2011.

ii. Marzia Lavinia Frezza is program director and minority shareholder in European Ketogenic Weight Loss Clinics, LLC and is the wife of Oliver R. Di Pietro.

iii. Eric C. Westman is the Chair of the Scientific Advisory Board of European Ketogenic Weight Loss Clinics, LLC and receives equity and compensation for his services.

iv. Ashley A. Nobili has no financial competing interests.

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