Original Article

Tube feeding with a diabetes-specific feed for 12 weeks improves glycaemic control in type 2 diabetes patients

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SUMMARY

Background and aims: Assess longer-term (12 weeks) effects of a diabetes-specific feed on postprandial glucose response, glycaemic control (HbA1c), lipid profile, (pre-)albumin, clinical course and tolerance in diabetic patients.

Methods: In this randomized, controlled, double-blind, parallel group study 25 type 2 diabetic patients on tube feeding were included. Patients received a soy-protein based, multi-fibre diabetes-specific feed or isocaloric, fibre-containing standard feed for 12 weeks, while continuing on their anti-diabetic medication. At the beginning, after 6 and 12 weeks, several (glycaemic) parameters were assessed.

Results: The postprandial glucose response (iAUC) to the diabetes-specific feed was lower at the 1st assessment compared with the standard feed (p = 0.008) and this difference did not change over time. HbA1c decreased over time in the diabetes-specific and not in the standard feed group (treatment*time:p = 0.034): 6.9 ± 0.3% (mean ± SEM) at baseline vs. 6.2 ± 0.4% at 12 weeks in the diabetes-specific group compared to 7.9 ± 0.3% to 8.7 ± 0.4% in the standard feed group. No significant treatment*time effect was found for fasting glucose, insulin, (pre-)albumin or lipid profile, except for increase of HDL in the diabetes-specific group.

Conclusions: The diabetes-specific feed studied significantly improved longer-term glycaemic control in diabetic patients. This was achieved in addition to on-going anti-diabetic medication and may affect clinical outcome.

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1. Introduction

A major goal of diabetes management is to achieve glycaemic control. A growing body of evidence suggests that in addition to fasting glucose concentrations postprandial glucose concentrations should also be targeted to improve glycaemic control. Due to its effect on (postprandial) blood glucose excursions and lipid levels, nutrition plays an important role in achieving metabolic control in diabetes patients. The short-term consequences of hyperglycaemia include: polyuria, increased thirst, dehydration, weight loss and fatigue. Furthermore, hyperglycaemia is associated with an increased infection risk and impaired wound healing. Long term complications are the microvascular and macrovascular complications.

Some diabetic patients with functioning gastrointestinal tract who cannot maintain sufficient oral intake need tube feeding as the treatment of choice. Diabetes-specific formulas are developed to control blood glucose concentrations. A recent systematic review showed that use of diabetes-specific formulas is associated with...
improved glycaemic control compared with standard formulas\textsuperscript{11} and should therefore be considered in hyperglycaemic hospitalized diabetes patients.

Only a few studies have investigated the effect of longer-term feeding with a diabetes-specific tube feed on glycaemic control of diabetes patients.\textsuperscript{12–14} The trial duration in these studies ranged from 13 days (median)\textsuperscript{13} to 12 weeks.\textsuperscript{12,14} None of these studies investigated the effect of bolus supplementation on postprandial glucose levels after longer-term feeding with a diabetes-specific formula. It had been shown that a soy-protein based, high MUFA, multi-fibre diabetes-specific tube feed lowered the postprandial glucose response compared to a standard formula after a single bolus\textsuperscript{15} and during continuous feeding lasting 6 h.\textsuperscript{16} In the present study effects of 12 weeks supplementation of this diabetes-specific tube feed on glycaemic control (including postprandial glucose responses and HbA1c) and lipid parameters were assessed. Study duration was 12 weeks to be able to also study effects on HbA1c.

2. Subjects and methods

2.1. Subjects

Patients diagnosed with type 2 diabetes according to the WHO criteria were included. Inclusion criteria were: disease duration for more than 6 months, age > 18 years, 6.0% < HbA1c < 9.5%, in need of nutritional support by tube feeding for at least 12 weeks by either percutaneous endoscopic gastrostomy or nasogastric tube and a functioning gastrointestinal tract. Exclusion criteria were: concomitant therapy with systemic glucocorticoids or acarbose, acute severe heart failure (NYHA class 4), end stage liver failure, renal failure requiring dialysis, any acute gastrointestinal disease within 2 weeks prior to study entry, jejunal feeding, drug or alcohol abuse, (planned) pregnancy or lactation and participation in any other studies concomitantly or within four weeks prior to entry into the study. Investigator’s uncertainty about willingness or ability of patients to comply with the protocol requirements was another exclusion criterion.

The local ethical committees approved the study protocol. For Brazil, approval from the Brazilian National Committee of Ethics in Research (CONEP) and the Brazilian National Agency of Health Surveillance (ANVISA) was also obtained. In Israel, approval was obtained from the Ministry of Health. All participants or their legal guardians gave written informed consent prior to study screening. The study was performed in accordance with the principles of the Declaration of Helsinki.

2.2. Sample size calculation

Sample size was determined based on the assumptions alpha = 0.05, power = 80% and a two-sided test. Calculation was performed for the parameter postprandial glucose response, as assessed with positive incremental area under the curve (iAUC). In a comparable, prior performed study with this diabetes-specific tube feed\textsuperscript{15} a standard deviation of 92.7 for iAUC, was observed. To a comparable, prior performed study with this diabetes-specific assessed with positive incremental area under the curve (iAUC). In performed for the parameter postprandial glucose response, as lasting 6 h.\textsuperscript{16} In the present study effects of 12 weeks supplementation of this diabetes-specific tube feed on glycaemic control (including postprandial glucose responses and HbA1c) and lipid parameters were assessed. Study duration was 12 weeks to be able to also study effects on HbA1c.

2.3. Study design

This 12-week multi-centre study had a randomized, controlled, double-blind, parallel group design. Patients were recruited from 5 centres: Tel Aviv Sourasky Medical Centre (Tel Aviv, Israel), Leicester Royal Infirmary (Leicester, UK), Queens Medical Centre (Nottingham, UK), Hospital de Real Beneficiencia Portuguesa e Sao Paulo (São Paulo, Brazil) and Saint Louis University Medical Centre (St Louis, USA). Patients were randomly assigned to the diabetes-specific or standard tube feed in blocks of four, using four different randomization codes. Study centers each received their own randomization list.

Subjects in the diabetes-specific tube feed group received a soy-protein based formula with high monounsaturated fatty acids (MUFA), containing a fibre mixture (Nutrison Advanced Dason, Nutricia, the Netherlands) with 45 En% carbohydrates, 38 En% fat (26 En% MUFA), 17 En% protein and 1.5 g/100 kcal fibre. The control group received a commercially available isocaloric, fibre-containing standard tube feed (55 En% carbohydrates, 30 En% fat (14 En% MUFA), 15 En% protein, 2 g/100 kcal fibres). Table 1 shows the composition of both formulas. Patients had to receive at least 75% kcal of total daily energy requirements by tube feed for a period of 12 weeks. Total daily energy requirements were based on standard calculations for energy requirements of the individuals. During the 12-week study period, the tube feed could be given as a bolus, intermittent or continuous feeding.

Patients were assessed after an overnight fast (from 10.00 PM) at the beginning of the study (1st assessment, week 0, visit 1) after 6 (visit 2) and 12 (visit 3) weeks. Patients had to refrain from diabetes medication before and during blood collection on these days. Venous blood was collected using a venous cannula. Fasting blood sample was obtained for determination of plasma glucose levels, HbA1c, insulin, plasma lipids, high-sensitivity C-reactive protein (hs-CRP), albumin, pre-albumin and safety parameters (alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), blood urea nitrogen (BUN) and creatinine). After 15 min patients received 200 ml bolus of the formula within 30 min. Blood samples were taken at 0, 15, 30, 45, 60, 75, 90, 120, 150, 180, 210 and 240 min after starting tube feeding to determine postprandial plasma glucose levels. Body weight, blood pressure and heart rate were also monitored along each assessment.

During the supplementation period the amount of product received was recorded daily. Occurrence of vomiting, incidence of infections and insulin use or (oral anti-diabetic) medication use

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Unit</th>
<th>Diabetes-specific tube feed*</th>
<th>Standard tube feed*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>kcal</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Protein</td>
<td>g/En %</td>
<td>4.3/17</td>
<td>3.8/15</td>
</tr>
<tr>
<td>• Casein</td>
<td>g</td>
<td>–</td>
<td>v</td>
</tr>
<tr>
<td>• Soy</td>
<td>g</td>
<td>4.3</td>
<td>v</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>g/En%</td>
<td>11.3/45</td>
<td>13.8/55</td>
</tr>
<tr>
<td>• Sugars</td>
<td>g</td>
<td>2.4</td>
<td>1.0</td>
</tr>
<tr>
<td>– fructose</td>
<td>g</td>
<td>2.3</td>
<td>v</td>
</tr>
<tr>
<td>• Polysaccharides</td>
<td>g</td>
<td>8.8</td>
<td>v</td>
</tr>
<tr>
<td>• Other</td>
<td>g</td>
<td>0.1</td>
<td>v</td>
</tr>
<tr>
<td>Fat</td>
<td>g/En %</td>
<td>4.2/38</td>
<td>3.4/30</td>
</tr>
<tr>
<td>• Saturated</td>
<td>g</td>
<td>0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>• MUFA</td>
<td>g</td>
<td>2.9</td>
<td>2.1</td>
</tr>
<tr>
<td>• PUFA</td>
<td>g</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Fibre</td>
<td>g</td>
<td>1.5</td>
<td>2.0</td>
</tr>
<tr>
<td>• Soluble</td>
<td>g</td>
<td>1.2</td>
<td>v</td>
</tr>
<tr>
<td>• Unsoluble</td>
<td>g</td>
<td>0.3</td>
<td>v</td>
</tr>
</tbody>
</table>

* Minerals and vitamins are present in both feeds in line with the regulations for Food for Specific Medical Purposes (FSMP (1999/21/EC)).
was recorded weekly. Stool consistency and frequency were recorded daily in week 1, 5 and 11. Adverse events and serious adverse events were recorded during the study.

2.4. Laboratory methods

Body weight was measured to the nearest 0.1 kg using a weighing scale or weighing chair without wearing shoes or heavy clothing. Blood pressure and heart rate were measured using standard equipment of the hospital. Analyses of blood samples were performed with commercially available equipment. Plasma glucose was measured by a colorimetric hexokinase assay (Roche, Indianapolis, USA). Serum insulin concentrations were determined with a chemoluminescent immunoassay (Immulite 2000 DPC, Wales, UK). HbA1c was measured with by affinity chromatography (Wako, Osaka, Japan). Serum total cholesterol and triglyceride levels were measured by cholesterol oxidase and enzymatic colorimetric assays, respectively (Roche, Indianapolis, USA). Homogenous assays were used to determine HDL cholesterol (Roche, Indianapolis, USA) and LDL cholesterol levels (Roche, Mannheim, Germany). VLDL was calculated with the formula: VLDL (mmol/l) = cholesterol (mmol/l)-HDL (mmol/l)-LDL (mmol/l). Serum albumin levels were measured with a colorimetric assay (Bromocresol Green, Roche, Indianapolis, USA). Serum pre-albumin and hs-CRP concentrations were determined with immunoturbidimetry (Roche, Mannheim, Germany). Safety parameters concentrations were determined at the different sites according to their standard procedures. Incremental areas under the curve (iAUC) were calculated for plasma glucose, according to the trimodal method.17

2.5. Statistical analyses

All descriptive and statistical analyses were performed on the All Subjects Randomized population (n = 25). Due to early terminations, data of seventeen patients were available for the second visit and of fourteen patients for the last visit.

Continuous outcome parameters were statistically analyzed with multilevel mixed effects models using linear regression methods. The models included treatment (diabetes-specific vs. standard tube feed), time (days since baseline visit), treatment*time interaction, duration of diabetes and duration of diabetes*time interaction as fixed factors and centre as random factor. If duration of diabetes was missing (for 6 cases), it was imputed based on height, weight, age, fasting glucose and gender. Omitting the 6 patients with missing values on duration in the statistical analyses did result in similar significances on iAUC and HbA1c values.

In the models of postprandial parameters (iAUC, (delta) peak plasma glucose) intervention effect was tested by evaluating the significance of the treatment parameter (at 1st assessment) and by evaluating the significance of the treatment by time interaction. Peak glucose was defined as the highest postprandial glucose concentration and delta peak glucose was defined as the highest postprandial glucose concentration minus the fasting glucose concentration. In the other models the intervention effect was tested by evaluating the significance of the treatment by time interaction parameter. Results are presented as estimated marginal means ± standard error of the mean (SEM).

Outcome parameters with a discrete distribution were analyzed using Fisher’s exact test and results were presented as absolute number and percentages of subjects.

"Compliance" was defined as the total daily amount of tube feed received, relative to the amount received on the third day of the study (=reference amount corresponding with 100% compliance, taking a possible run-in period into account). Stool frequency and consistency were recorded daily in week 1, 5 and 11. Stool consistency was scored using the Bristol Stool Form Scale (7-point scale) for the first 5 bowel actions per day. Mean stool consistency and frequency and the change over time were compared between study groups using mixed models. The occurrence of vomiting, the occurrence of infections, number of early terminations, number of (serious) adverse events and proportion of subjects that experienced one or more adverse events was compared between both groups using Fisher’s exact test. p-Values were two-tailed and those <0.05 were considered statistically significant.

All analyses were performed by using SPSS (version 15.0.0 for Windows, Rel. 6 Sep 2006).

3. Results

In total, 181 patients were prescreened by the 5 centers, from September 2005 until May 2007. Main reasons that patients were not eligible for the study were: refusal (of the legal representative) to participate, (or for participation), HbA1c levels <6.0% or death during the screening period before randomization. Eventually, 25 subjects were randomized into the study, twelve in the diabetes-specific tube feed group and 13 in the standard tube feed group (Fig. 1). Twenty-one patients resided in hospitals and 4 patients were kept at home. Fourteen patients completed the 12-week study period. Ten patients dropped out of the study due to (serious) adverse events ((S)AE): 5 in the diabetes-specific group (2 AEs (vomiting or loose bowel action 6 times at night) and 3 SAEs (hospitalisation due to cellulitis of insertion site of PEG, death due to sepsis or cardiac arrest)) and 5 in the standard tube feed group (2 AEs (vomiting or fever) and 3 SAEs (death due to sepsis, respiratory insufficiency or chest infection)). One patient in the standard group was discharged from tube feeding.

3.1. Subject characteristics and demographics

No significant differences in subject characteristics and demographic data were observed (Table 2), except for duration of diabetes, which was significantly shorter in the diabetes-specific feed group compared with the standard feed group (5.0 ± 4.9 years versus 12.6 ± 8.4 years, respectively). In the diabetes-specific group, 2 patients received continuous feeding, 7 patients bolus feeding and 3 were on an intermittent feeding regime. In the standard tube feed group, the amounts of patients were 3, 10 and 0 respectively. Most study subjects had multiple pathologies and were immobile. The majority of patients had previous cerebral vascular accidents, resulting in dysphagia, hemiplegia and/or severe dementia.

3.2. Compliance to tube feeding

All subjects received more than 75% of the calculated total daily energy as tube feed per week. Compliance during the total study period was 97.9% in the diabetes-specific group and 98.5% in the standard feed group (p = 0.644). The mean daily intake was 1341.4 ml in the diabetes-specific group and 1432.3 in the standard feed group (p = 0.838) No significant differences in the amount received were found between the groups in the first week and this did not change over time. Most patients did not receive oral food in addition to the tube feeds.

3.3. Efficacy

Receiving a bolus of the diabetes-specific tube feed resulted in a lower postprandial glucose response (iAUC) compared with the standard feed at the first assessment (difference in intercept:...
p = 0.008) (Fig. 2a). This difference did not significantly change in time (treatment*time; \( p = 0.601 \)). Similar effects were observed for postprandial peak and delta peak glucose concentration: at the first assessment, a significantly lower peak (9.8 ± 1.0 versus 14.1 ± 1.1 mmol/L; \( p = 0.010 \)) and a lower delta peak (3.1 ± 1.1 versus 6.5 ± 1.1 mmol/L; \( p = 0.004 \)) of glucose concentration were observed in the diabetes-specific feed group. Again, these differences did not significantly change over time (\( p = 0.655 \) and \( p = 0.568 \), respectively). Tube feeding with the diabetes-specific feed resulted in a reduction in HbA1c over time compared with the standard feed (treatment*time: \( p = 0.034 \)) (Fig. 2b). Mean HbA1c (±SEM) decreased in the diabetes-specific feed group (6.9 ± 0.3% at baseline, 6.2 ± 0.4% at 12 weeks), whereas it increased in the standard feed group (7.9 ± 0.3% to 8.7 ± 0.4%).

No significant treatment*time effect was found for fasting glucose, insulin or the lipid parameters, i.e: fasting triglycerides, total cholesterol, LDL and VLDL cholesterol. The treatment*time interaction was significantly different for HDL cholesterol (\( p = 0.010 \)), with an increase in the diabetes-specific feed group (1.04 ± 0.08 mmol/L at baseline to 1.23 ± 0.10 mmol/L after 12 weeks) and a decrease in the standard feed.

Table 2
Demographic data and subject characteristics at baseline for all randomized subjects.

<table>
<thead>
<tr>
<th></th>
<th>Total group (n = 25)</th>
<th>Diabetes-specific (n = 12)</th>
<th>Standard (n = 13)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Mean ± SD</td>
<td>76.2 ± 12.8</td>
<td>73.0 ± 14.7</td>
<td>79.2 ± 10.4</td>
<td>0.239*</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male n (%)</td>
<td>9 (36.0)</td>
<td>6 (50.0)</td>
<td>3 (23.1)</td>
<td>0.226*</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>16 (64.0)</td>
<td>6 (50.0)</td>
<td>10 (76.9)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)c</td>
<td>Mean ± SD</td>
<td>26.9 ± 4.1</td>
<td>28.4 ± 2.9</td>
<td>0.113*</td>
</tr>
<tr>
<td>Duration of diabetes (y)d</td>
<td>Mean ± SD</td>
<td>8.6 ± 7.6</td>
<td>5.0 ± 4.9</td>
<td>1.000*</td>
</tr>
<tr>
<td>Use of insulin:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes n (%)</td>
<td>11 (44.0)</td>
<td>5 (41.7)</td>
<td>6 (46.2)</td>
<td></td>
</tr>
<tr>
<td>No n (%)</td>
<td>14 (56.0)</td>
<td>7 (53.8)</td>
<td>7 (53.8)</td>
<td></td>
</tr>
<tr>
<td>Class of anti-diabetic medication:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No anti-diabetic medication (No) n (%)</td>
<td>2 (8.0)</td>
<td>1 (8.3)</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Only other anti-diabetic medication (O) n (%)</td>
<td>11 (44.0)</td>
<td>5 (41.7)</td>
<td>6 (46.2)</td>
<td></td>
</tr>
<tr>
<td>Metformin (M) n (%)</td>
<td>4 (16.0)</td>
<td>2 (16.7)</td>
<td>2 (15.4)</td>
<td></td>
</tr>
<tr>
<td>Sulphonylureas (S) n (%)</td>
<td>5 (20.0)</td>
<td>2 (16.7)</td>
<td>3 (23.1)</td>
<td></td>
</tr>
<tr>
<td>Combination of M, S n (%)</td>
<td>3 (12.0)</td>
<td>2 (16.7)</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%) – screening Mean ± SD</td>
<td>7.2 ± 0.7</td>
<td>7.0 ± 0.7</td>
<td>7.3 ± 0.8</td>
<td>0.301*</td>
</tr>
</tbody>
</table>

\( ^a \) Two-sample T-test was used for analysis of statistical difference between groups.

\( ^b \) Fisher’s Exact test was used for analysis of statistical difference between groups.

\( ^c \) Based on less cases due to missing values: BMI: n = 17; duration of diabetes: n = 19.

\( ^d \) Statistically significant, \( p < 0.05 \).
Albumin, pre-albumin, hs-CRP, BMI and diastolic blood pressure showed no significant treatment*time effect (data not shown), whereas for systolic blood pressure a borderline significance ($p = 0.054$) was found: it increased in the standard feed group (134.2 ± 5.4 mmHg at baseline to 140.3 ± 6.9 mmHg) and decreased in the diabetes-specific group (144.8 ± 5.4 mmHg at baseline to 123.8 ± 8.5 mmHg after 12 weeks). Based on adverse event reporting, 3 infections were reported in the diabetes-specific group and 6 in the standard group ($p = 0.411$). Data on the amount of insulin during the study was available for 8 out of 11 insulin using patients. Treatment*time was not significantly different for the mean use of insulin.

3.4. Tolerance/safety

No significant differences in mean stool consistency were found during the first week and this did not change significantly in time either (treatment*time, $p = 0.99$). The stool frequency was significantly different during the first week ($p = 0.034$) with a frequency of 0.8 ± 0.3/day in the diabetes-specific feed group and 1.8 ± 0.3/day in the standard feed group and this did not significantly change in time. Occurrence of vomiting was not significantly different between groups.

Baseline BUN was increased above normal (mild toxicity) in almost half the subjects reflecting the diabetes population. In one subject in the standard feed group, the creatinine level was increased 3 times of the upper normal limit at week 12. This patient had multiple vascular pathologies and was also prescribed antibiotics during the study which could have influenced this renal biomarker. There were no clinically relevant abnormal liver (ALAT and ASAT) and renal function biomarkers (creatinine and BUN) that can be attributed to either study product.

Number of subjects with AE was not significantly different between groups (8 in the diabetes-specific group and 9 in the standard group), nor were the number of AEs per subject or the number of subjects that reported mild, moderate or severe AEs.

**Fig. 2.** Four hour postprandial glucose ($\text{iAUC}_{(0–4\text{h})}$) (panel A) or HbA1c (panel B) during 3 months of tube feeding (all subjects randomized population). The circles are raw data (open circles: standard product; filled circles: diabetes-specific product) and the lines are the predicted regression lines corrected for duration of diabetes (dotted line: standard feed, solid line: diabetes-specific feed). Difference in intercept: $p = 0.008$ (panel A), $p = 0.058$ (panel B), treatment*time: $p = 0.601$ (panel A), $p = 0.034$ (panel B).

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the diabetes-specific group, three SAEs occurred (death due to sepsis, death due to cardiac arrest, inpatient hospitalisation due to cellulitis at the insertion site of PEG). In the standard feed group five SAEs were recorded in four subjects. Three subjects died, due to a chest infection, respiratory insufficiency and sepsis, respectively. The fourth subject had an infection of unknown origin for which he needed hospitalisation and had another SAE (prolongation of existing hospitalisation for an amputation of his lower right limb). None of the SAEs was reported as related to use of the study product.

4. Discussion

Current study results indicate that a soy-protein based, high MUFAs, multi-fibre diabetes-specific tube feed can also lower postprandial glucose levels after 12 weeks use and further improves overall glycaemic control (HbA1c) in diabetes patients on regular anti-diabetic medical treatment.

Previous studies using a single administration of this diabetes-specific tube feed as continuous feeding during 6 h16 or as single bolus15 resulted in lower postprandial glucose responses compared to a standard formula. Present study extends these results regarding longer-term (12 weeks) feeding. Study results showed that this beneficial effect on postprandial glucose responses after 200 ml of the diabetes-specific tube feed did not change over time (12 weeks). Moreover, the cumulative effect of 12 weeks tube feeding with this formula resulted in lower HbA1c levels. These results add further evidence to the concept that longer-term use of a diabetes-specific tube feed improves overall glycaemic control compared with standard formulas. In other longer-term tube feeding trials (12 weeks and 13 days, respectively) with disease-specific, reduced carbohydrate, modified fat formulas a non-significant reduction12 or no reduction,13 respectively in HbA1c were found. On the other hand in another 12-week tube feeding trial with a high MUFAs diabetes-specific tube feed, a significant reduction of 0.8% in HbA1c was observed without improvement in the control group.14 Our findings are also in line with the conclusions of a recent systematic review on diabetes-specific formulas11 that the use of diabetes-specific formulas is associated with improved glycaemic control compared with standard formulas.

Postprandial glucose response is an important contributor to overall glycaemic control,9,10 and is, therefore, a major treatment target in diabetic patients.1 In their recent guidelines for management of postmeal glucose, the International Diabetes Federation addresses the importance of postmeal hyperglycaemia2 and summarizes present evidence of the harmful effects of postprandial hyperglycaemia. Short-term complications of hyperglycaemia including increased infection risk are very relevant in the vulnerable tube feeding target population. One longer-term tube feeding study determined the effect of diabetes-specific nutrition on clinical outcome. In this four weeks study, it was found that clinical outcome, when expressed on a numerical and percentage base, was better in the diabetes-specific group.23 Post-hoc analysis of these data demonstrated a tendency for a lower incidence of urinary tract infections, pneumonia and episodes of fever in the diabetes-specific versus standard group.11 In the present study, infection incidence, based on adverse event reporting, was studied. However, no conclusions could be drawn on this clinical outcome parameter since only a few infections occurred, and the incidence did not significantly differ between groups (3 in the diabetes-specific group and 6 in the standard group). No clinically relevant differences in tolerance and safety were observed between groups.

In this study elderly patients with mainly chronic neurological disease participated. These patients usually have an indication for tube feeding during a longer time period. Such a longer time period is necessary to determine possible effects of a diabetes-specific tube feed on overall glycaemic control, determined as HbA1c. These patients are usually vulnerable, relatively sick patients, which may explain the high drop-out rate in the present study. A much larger patient population in whom diabetes-specific formulas may be useful are the many diabetic patients who are admitted to hospital with an acute illness who require short-term feeding. A study to examine glycaemic control in this group would be difficult to plan due to the heterogeneity of clinical circumstances and the short-term indication for tube feeding, but this present trial, we believe, lends support to the rationale of diabetes-specific nutrition in this group as well.

The diabetes-specific tube feed tested in the present study is designed to enable a better glycaemic control through its specific nutritional composition. It contains a decreased amount of carbohydrates (45 En%) compared with the standard feed (55 En%). Furthermore, the type of carbohydrates is partly adapted. Besides polysaccharides, the diabetes-specific feed contains fructose (9.2 En%), which has a low glycaemic index of 19.20 Catalytic amounts of fructose, (7.5 g) were found to improve the glycaemic response to an oral glucose load of 75 g in type 2 diabetes patients21 and to decrease HbA1c.22 The main carbohydrates in the standard tube feed are also polysaccharides. The decreased amount of CHO's in the diabetes-specific tube feed is compensated by an increased amount of fat, mainly MUFA. A previous meta-analysis concluded that there is good scientific support for high MUFA diets as alternative to high CHO diets for medical nutrition therapy in diabetes.23 The diabetes-specific feed also contains soluble fibres. High soluble fibre-containing foods improve glycaemic control in part by delayed glucose absorption.24

The duration of diabetes was significantly different between both study groups. By correcting all our statistical analyses for duration of diabetes, we minimalized a possible confounding effect of diabetes duration on our outcome parameters. Since most patients did not receive oral foods in addition to tube feeds, confounding of the study results by the effects of other nutrition than the tube feeds is considered to be negligible. There was no intention to change the insulin/oral medication protocol during the study, and this was left to the responsible physicians. During the study, some changes in insulin were recorded. No significant time*treatment effects for insulin found, which indicated that there were no significant differences in (change of) insulin use during the course of our study. No changes in oral medication were recorded.

The diabetes-specific tube feed tested in the present study is developed to help improve glycaemic control. Since patients with an HbA1c < 6.0% are already in relatively good glucose control, we have excluded these patients from our study. Whether the results from the present study can be extrapolated to people with an HbA1c < 6.0% remains to be investigated.

In conclusion, our results indicate that also after 12 weeks use of the tested diabetes-specific tube feed, postprandial glucose responses continued to be lower compared with a standard feed. Furthermore overall glycaemic control (HbA1c) improved in the diabetes-specific group. Together, these results indicate beneficial implications of a high MUFA, soy-protein based, multi-fibre tube feed to the clinical course of diabetic patients requiring tube feed.

Conflict of interest

N. Vaisman: Consultant to Danone Research.
M. Lanzink, C. Rouws, K. van Laere; employee of Danone Research, Centre for Specialised Nutrition.
R. Segal: No conflict of interest.
E. Niv: No conflict of interest.
T. Bowling: No conflict of interest.
D. Waiztberg: Danone Research paid for flights and accommodation to attend research meetings to discuss the study. No other conflict of interest.


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NV was involved in study design and data interpretation, carried out the study and drafted the manuscript.

ML was involved in data interpretation and drafting of the manuscript.

CR and KvL participated in design of the study, data interpretation and critical revision of the manuscript.

RS and EN carried out the study.

TB and DW carried out the study and critically revised the manuscript.

JM collected data and critically revised the manuscript.

All authors read and approved the final manuscript.

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