

Utilising a milk-based meal replacement programme in a bariatric patient with poorly controlled type 2 diabetes mellitus

Michelle Maher¹, Mohammed Faraz Rafey^{1,2}, Helena Griffin¹, Katie Cunningham¹ and Francis M Finucane^{1,2}

¹Bariatric Medicine Service, Centre for Diabetes, Endocrinology and Metabolism, Galway University Hospitals, Galway, Ireland and ²HRB Clinical Research Facility, National University of Ireland Galway, Galway, Ireland

Correspondence
should be addressed
to F M Finucane
Email
francis.finucane@hse.ie

Summary

A 45-year-old man with poorly controlled type 2 diabetes (T2DM) (HbA1c 87 mmol/mol) despite 100 units of insulin per day and severe obesity (BMI 40.2 kg/m²) was referred for bariatric intervention. He declined bariatric surgery or GLP1 agonist therapy. Initially, his glycaemic control improved with dietary modification and better adherence to insulin therapy, but he gained weight. We started a low-energy liquid diet, with 2.2 L of semi-skimmed milk (equivalent to 1012 kcal) per day for 8 weeks (along with micronutrient, salt and fibre supplementation) followed by 16 weeks of phased reintroduction of a normal diet. His insulin was stopped within a week of starting this programme, and over 6 months, he lost 20.6 kg and his HbA1c normalised. However, 1 year later, despite further weight loss, his HbA1c deteriorated dramatically, requiring introduction of linagliptin and canagliflozin, with good response. Five years after initial presentation, his BMI remains elevated but improved at 35.5 kg/m² and his glycaemic control is excellent with a HbA1c of 50 mmol/mol and he is off insulin therapy. Whether semi-skimmed milk is a safe, effective substrate for carefully selected patients with severe obesity complicated by T2DM remains to be determined. Such patients would need frequent monitoring by an experienced multidisciplinary team.

Learning points:

- Meal replacement programmes are an emerging therapeutic strategy to allow severely obese type 2 diabetes patients to achieve clinically impactful weight loss.
- Using semi-skimmed milk as a meal replacement substrate might be less costly than commercially available programmes, but is likely to require intensive multidisciplinary bariatric clinical follow-up.
- For severely obese adults with poor diabetes control who decline bariatric surgery or GLP1 agonist therapy, a milk-based meal replacement programme may be an option.
- Milk-based meal replacement in patients with insulin requiring type 2 diabetes causes rapid and profound reductions in insulin requirements, so rigorous monitoring of glucose levels by patients and their clinicians is necessary.
- In carefully selected and adequately monitored patients, the response to oral antidiabetic medications may help to differentiate between absolute and relative insulin deficiency.



Background

Treatment of poorly controlled type 2 diabetes (T2DM) in patients with severe obesity is challenging. Not all affected individuals choose bariatric surgery or drug therapy (1). Only a small proportion of patients with severe obesity achieve meaningful weight loss with conservative lifestyle interventions in primary care (2). In general, health gains through lifestyle modification in patients who are overweight with T2DM require a weight reduction of 10% or more (3). Commercial meal replacement programmes have recently shown promise in managing T2DM (4), but side effects including constipation, dizziness, alopecia, nausea, headache, diarrhoea, abdominal pain and cholelithiasis are common (5), and these interventions may not be cost effective (6). The use of semi-skimmed milk (with micronutrient, salt and fibre supplementation) in a low-energy liquid diet (LELD) as an alternative to commercial meal replacement has not previously been described but may have therapeutic potential.

Case presentation

A 45-year-old white male carpenter was referred by his GP to our bariatric clinic for assessment and management of severe obesity, complicated by poorly controlled T2DM of 10-year duration. He had well-controlled hypertension and dyslipidaemia and stable non-alcoholic steatohepatitis. He was taking a basal bolus insulin regime of insulin aspart 20, 18 and 22 units with meals and insulin glargine 40 units nocte, a total dose of 100 insulin units per day. He was also taking metformin 500mg three times daily, ramipril 2.5mg once daily, simvastatin 30mg once daily and aspirin 75mg once daily. He did not drink alcohol and had stopped smoking 6 months previously with a 26 pack year history. His mother and sister had T2DM. He was single and lived with two siblings. On systems review he had noted persistently elevated glucometer readings for several months, with thirst, polydipsia, polyuria and nocturia, consistent with poor glycaemic control. On examination, he weighed 113.8kg, height 168.2cm with a BMI of 40.2kg/m². His waist was 117cm, hip 120cm with a waist-to-hip ratio of 0.98. His BP was 105/62mmHg. He had no evidence of retinopathy, neuropathy or cutaneous markers of insulin resistance.

Investigation

At initial assessment his HbA1c was 72mmol/mol (8.7%), confirming poor glycaemic control. His lipid profile was

excellent with a total cholesterol of 3.3, LDL 0.8, HDL 1.0 and triglycerides of 1.9mmol/L. Liver profile and iron studies, as well as renal and thyroid function tests were all normal. His ECG was normal except for right bundle branch block.

Treatment

Various bariatric treatment options were discussed with the patient. He declined laparoscopic sleeve gastrectomy or GLP1 agonist therapy. There was no evidence of an underlying psychiatric or psychological disorder that required specialist input. He was assessed by the bariatric dietician and provided with advice on healthy eating. He was noted to have a large intake of sugary snacks as well as starchy carbohydrates (bread, potatoes) in his diet. Given his severe obesity and poor diabetes control despite insulin therapy and in the absence of other treatment options, the patient agreed to a trial of a milk-based 'LELD'. This consisted of three continuous 8-week phases, each with fortnightly clinical assessments. The patient's basal metabolic rate was estimated at 1983kcal using the 'Mifflin St. Jeor' formula (7). During the first (weight loss) phase lasting 8 weeks, he consumed an exclusively milk-based liquid diet, consisting of 2.2L of semi-skimmed milk (equivalent to 1012kcal, 75g of protein, 36g of fat and 113g carbohydrate) divided in seven equal portions per day. The volume of milk prescribed was determined by the patient's protein requirements, in order to reduce muscle loss. To minimise the risk of micronutrient deficiencies, he took a combined multivitamin and mineral supplement as well as fibre (ispaghula husk 3.5g twice daily) in order to mitigate the high risk of constipation and a stock cube for sodium replacement. He was seen by the consultant endocrinologist, bariatric nurse and dietitian and had bloods drawn every 2 weeks. During the second phase (weight stabilisation) from weeks 9 to 16 inclusive, there was a gradual reintroduction of low-calorie meals from a set menu, under the supervision of the bariatric dietitian with fortnightly visits continuing. During the third phase (weight maintenance) from weeks 17 to 24 inclusive, the milk-based component of the diet was stopped completely and a balanced diet was resumed, under dietetic supervision, with a similar calorific value to the exclusively milk-based liquid diet of approximately 1000kcal daily.

Outcome and follow-up

Five months after his initial assessment, his diet and glycaemic control had improved, although he gained

1.6kg (which we attributed to better endogenous insulinisation), as shown in Fig. 1. We started the LELED and he responded well, with his weight coming down from 115.2kg (BMI: 40.7 kg/m²) to 101.2kg (BMI: 35.8kg/m²) after 8 weeks and 94.6kg (BMI: 33.4kg/m²) after 24 weeks, a reduction of 20.6kg (7.3kg/m²). His insulin was cautiously but rapidly titrated downwards from 100 units per day to zero within a week of commencing the LELED. Glucometer readings and HbA1c (Fig. 1) rapidly normalised. Fifteen months after commencing the LELED (21 months after initial assessment), he had regained 2.2kg and had a normal HbA1c of 48mmol/mol, off insulin therapy. However 6 months later, although his weight had come down further to 92.6kg (BMI: 32.7kg/m²), his glycaemic control had deteriorated markedly, with a HbA1c of 104mmol/mol, without any apparent change in dietary behaviour (Fig. 1). While cognisant of the potential need to reintroduce insulin, we initially sought to intensify oral therapy and increased his metformin to 1g twice daily, added linagliptin 5mg once daily and canagliflozin 100mg once daily, all of which were well tolerated. This led to a gradual and sustained improvement in HbA1c over the following months, such that 55 months after initial assessment, his HbA1c was 50mmol/mol, his weight was 100.4kg (BMI: 35.5kg/m²) and he felt well.

Discussion

Although there is no evidence base for the use of a milk-based LELED in managing severe obesity and T2DM, we felt it was the best option for this patient because other treatments were declined and the patient expressed a

preference for this approach. Clearly, this intervention would not be suitable for all similar patients but may be useful in a small subgroup. Attrition from such an intensive dietary regimen is likely to be high. Although milk may be less expensive than commercial dietary supplements, 14 visits over 6 months to the bariatric clinic, with physician, nurse and dietetic assessment and phlebotomy at each visit consume substantial resources and may offset any economic gains from reduced medication usage.

Of note, the patient's HbA1c had already improved substantially in the 5 months between initial assessment and starting the programme, which might indicate suboptimal adherence to insulin therapy at his initial presentation. As anticipated, the sustainability of the metabolic improvements seen during the intervention was an issue, with a requirement to 'rescue' the patient from poor glycaemic control with intensification of oral diabetes therapy 15 months after finishing the programme. While the accompanying weight loss at the time suggested the patient might need insulin reintroduced, with close monitoring, frequent clinic visits and the introduction of oral diabetes medications, we were able to avoid this. His poor glycaemic control along with weight loss suggested an 'absolute' insulin deficiency, and the reversibility of this without insulin treatment suggests the patient may have been prone to transient beta cell glucotoxicity which responded well to oral therapy. The fact that the patient gained weight at the same time that glycaemic control improved on oral agents that do not tend to cause weight gain suggests further that these drugs reversed relative beta cell dysfunction and enhanced endogenous insulinisation. Aside from reversal of glucotoxicity, these medications may have improved beta cell function through other mechanisms. For example, linagliptin, a dipeptidyl peptidase inhibitor, is known to increase beta cell mass and restore beta cell insulin secretion through alterations in levels of glucagon-like peptide-1. We did not measure insulin or islet cell auto-antibodies at any time, nor did we formally assess beta cell function as this was not felt to be necessary clinically, though had his clinical course proceeded less well, we would have, and future studies of the mechanistic basis for improvements in glycaemic control with this diet should consider this.

There has been much interest in the role of therapeutic ketosis in weight loss interventions (8). Ketosis has been shown to attenuate increases in ghrelin and appetite that occur with dietary restriction (9). However we did not measure ketones in this patient, so their contribution to our findings is uncertain. There may be unique characteristics of milk that account for some of the

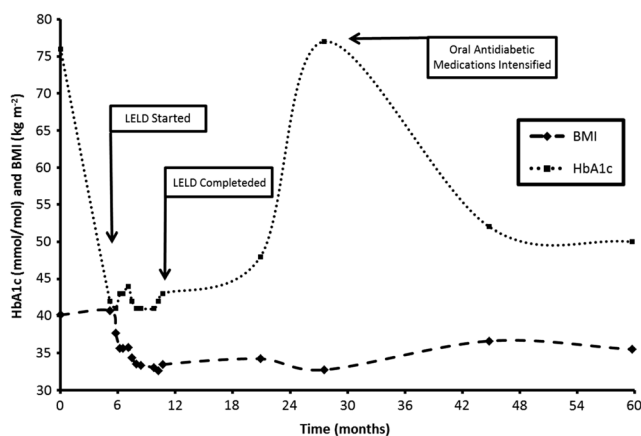


Figure 1
Changes in HbA1c and BMI during and after milk-based meal replacement programme.



improvements we observed. Milk whey protein attenuates muscle loss in adults with obesity during very-low-calorie diets (10). Milk enhances post-prandial glucose and lipid metabolism in men with obesity (11). Mechanistic studies in cohorts of patients undergoing milk-based meal replacement would help to determine the programme's influence on energy intake and expenditure, food preference, ketones and other 'proximal' outcomes aside from weight and glycaemic control. Ideally prospective studies and randomised controlled trials could help to determine the efficacy, safety and cost effectiveness of milk-based meal replacement.

Declaration of interest

F M F has in the past received honoraria, travel grants, unrestricted educational grants and served on advisory boards for Novo Nordisk, Eli Lilly, Pfizer Inc., Sanofi-Aventis, Astra Zeneca, Merck Sharp and Dohme, Boehringer Ingelheim, Janssen and Novartis. The other authors have nothing to disclose.

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Patient consent

Written informed consent for publication of their clinical details was obtained from the patient.

Author contribution statement

Michelle Maher led the description of the case, collation of data and drafting the manuscript. Mohammed Faraz Rafey helped in managing of case, collection of data and reviewing the manuscript. Helena Griffin and Katie Cunningham helped in managing the case and reviewing the manuscript. Francis M Finucane helped in collation of data, drafting the manuscript and supervised the project.

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