Case Discussion: The Use of Very Low Calorie Diets in the Management of Type 2 Diabetes Mellitus

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Introduction

It was believed that Type 2 diabetes (DM2) was a progressive condition, with gradual decrease in beta-cell function. Data from the United Kingdom Prospective Study indicate that approximately only 50% beta-cell function remains at the time of diagnosis which decreases to 30% within 6 years.[1] This reduction in beta-cell function is associated with treatment intensification including additional oral hypoglycaemic agents and ultimately insulin.[1] Due to the decrease in beta-cell function, the first phase insulin response (insulin secretion within the first 10 minutes after eating) is believed to be permanently lost in people with Type 2 diabetes.[2,3] Lim et al. (2011) challenged this view when the first phase insulin secretion normalised following a very low calorie diet (VLCD) (less than (<) 600 kcal) for 8 weeks.[4] Subsequently, glycaemic control normalised and DM2 was in remission. It is not surprising that this study led researchers to question if DM2 could be reversed[3] and sparked mass interest in these diets from people living with DM2.[5]

Weight Loss Approach

Traditionally medical nutritional therapy (MNT) for DM2 has focused on weight loss as an integral part of the overall management of DM2. Weight loss guidelines advocate for moderate calorie restriction of 500-1000 kcal from maintenance requirements to achieve approximately 0.45-0.9 kg weight loss per week.[6] This widely practised guideline is not surprising, as a raised body mass index (BMI) is documented to be one of the primary causes of DM2.[7] However, more recent evidence indicates that waist circumference is a greater predictor of obesity related conditions, including insulin resistance and DM2.[8,9] The reason for this is that waist circumference is a surrogate marker of visceral or central adiposity.[10] Visceral adiposity produces various adipokines involved in the development of DM2. Thus, the focus was to reduce BMI and waist circumference.

Despite the focus on weight loss, it is interesting to note that weight loss does not always improve glycaemic control.[12] Furthermore, glycaemic control can improve without weight loss.[13] Arguably, the most pronounced effects of weight loss on glycaemic control are seen following bariatric surgery. Early research showed that the rates of diabetes remission were nearly 90% 10 years after bariatric surgery.[14] Research at the time associated diabetes remission with 15-20% weight loss.[15] However, the effects of weight loss via conventional MNT appear to be less effective. Data from the LOOK AHEAD trial revealed that those participants who ≥ 15% weight loss only reduced fasting blood glucose levels by 1.6 mmol/l and haemoglobin A1c (HbA1C) by 0.9%, far from remission levels.[16] These findings posed the question: are there factors at work beyond weight loss?

The Ectopic Approach

With bariatric surgery there is rapid weight loss via VLCD (<800 kcal) pre and post-surgery.[17] The use of VLCD prior to surgery reduces the overall size of the liver (through a decrease in hepatic fat content), thus making the procedure easier to perform.[17,18] This is especially interesting in the light of recent evidence that suggests that ectopic fat in the liver and pancreas may be better predictors of DM2 than either waist circumference or BMI.[3,19] The Fat Spillover Theory (Figure 1) proposed that, due to genetic, ethnicity and age, fat 'spills over' from the subcutaneous tissue into the ectopic fat with the attendant metabolic abnormalities, including diabetes.[19] The understanding of ectopic fat and how it is reduced through VLCD explains why diabetes remission occurs within days after the surgery, before substantial weight loss has occurred.[20] The approach to the management of DM2 then would seem to be to reduce ectopic fat.

Although, excess calories are the cause of obesity and ultimately ectopic fat in DM2, there are various other mechanisms that drive ectopic fat accumulation. The Twin Cycle (Figure 2) explains this

process in detail.[3] During long term excess intake of calories, any excess carbohydrate intake undergoes de novo lipogenesis (conversion of excess carbohydrate to fatty acids), which promotes fat accumulation in the liver. De novo lipogenesis is stimulated by insulin, which is particularly relevant in patients with DM2 who present with initial hyperinsulinaemia due to insulin resistance. The increased de novo lipogenesis promotes further fat accumulation in the liver, which further increases insulin resistance and hepatic glucose production. Over time, this increases fasting blood glucose levels, which results in hyperinsulinaemia. The excess fat in the liver leads to an increase in very-low-density lipoprotein (VLDL) triglycerides, which increases fat delivery to all tissues, including the pancreatic islet cells. The excess fat in the islet cells impairs the acute insulin secretion in response to food, which results in postprandial hyperglycaemia and ultimately the onset of clinical diabetes. The Twin Cycle is switched off by severe calorie restriction, which may suggest that the reason moderate calorie restriction does not achieve diabetes remission is that the calorie content is too high to prevent hyperinsulinaemia and down-regulate de novo lipogenesis.

The Glucotoxic and Lipotoxic Approach

Chronic hyperglycaemia temporarily suppresses insulin secretion and promotes insulin resistance. This has been termed glucotoxicity.[21] The clinical significance of such is clearly seen in patients treated with short-term insulin therapy at the time of diagnosis to correct the glucotoxicity. Results from the meta-analysis by Kramer, Kaercher and Retnakara concluded that patients treated with insulin for 2-3 weeks at the time of diagnosis improved insulin secretion and reduced insulin resistance.[22] After 2 years of such treatment, 42.1% of patients were in remission (off all oral hypoglycaemic agents). Excess calorie consumption and adiposity (especially ectopic fat) can result in chronic elevation of free fatty acid. The increase in free fatty acids temporarily suppresses insulin secretion and promotes insulin resistance. This has been termed lipotoxicity.[21] The treatment of lipotoxicitiy is to reduce excess adiposity and improve glycaemic control, which in turn reduces free fatty acids.[21]

Therefore, the better approach would appear to be aggressive rapid resolution of both the gluco- and lipo-toxicity. As previously mentioned, insulin therapy is the most studied approach. The question therefore is: could MNT therapy be used as an effective alternative? Although there is no data to specifically address this question, we propose that conventional MNT will be ineffective. The reason being that the conventional MNT does not rapidly improve glycaemic control or reduce body weight but rather takes several months.[23] However, VLCDs have been reported to rapidly improve glycaemic control and body weight within one week.[4] VLCDs have shown to produce more rapid improvements in weight loss and glycaemic control compared to moderate calorie restriction at 3 months.[23] Therefore, if gluco- and lipo-toxicity were treated via MNT, it is reasonable to suggest that a VLCD would be the best approach.

Results on the use of very low calorie diets

The effects of VLCD are not new. In 1985, it was shown that 87% of the reduction in fasting blood glucose over 40 days on a VLCD (330 kcal) occurred within the first 10 days in DM2, before substantial weight loss occurred.[24] Fasting blood glucose rapidly reduced from 16.5 to 8.8 mmol/l within 10 days. Thus, severe calorie restriction is a vital aspect of improving glycaemic control and VLCDs can rapidly improve fasting blood glucose levels. It is not surprising that calories influenced glycaemic control but what is interesting is the effect on the fasting blood glucose levels, which are largely determined by hepatic glucose output, insulin resistance and insulin secretion rather than dietary intake.[3]

The safety of VLCD came under the spotlight around 1970.[25] VLCDs became popular during this time due to the book *The Last Chance Diet Book*. There were 60 reported deaths from avid followers of this diet. The cause of death was due to ventricular arrhythmias. On closer evaluation it was noted that these diets were made up exclusively of poor quality protein with no micronutrient supplementation. The opinion at the time was that the deaths were due to electrolyte disturbances which would be a more likely cause of arrhythmias.[25] Thus it was believed these people died due to protein and or micronutrient malnutrition. However, VLCDs currently contain high quality protein, carbohydrates, fat and micronutrients and have shown to be safe in a review by Henry.[25]

A second possible explanation as to why such diets did not receive much interest could be due to the following common belief systems: "Small sustained changes in energy intake or expenditure will produce large, long-term weight changes" and "Large, rapid weight loss is associated with poorer long-term weight-loss outcomes, as compared with slow, gradual weight loss".[26] These two belief systems have been deeply entrenched in obesity management but have been labelled to be nothing more than a myth.[26] Thus, small modest changes in weight do not produce large amounts of weight loss and rapid weight loss does not produce greater weight gain.[26]

Despite the negative connotations surrounding VLCDs, the results from the study by Lim in 2011 got the world's attention.[4] In this study, 11 people with DM2 (DM duration = 2.5 years) were taken off all oral hypoglycaemic agents and placed on a VLCD (600 kcal) for 8 weeks. Within 1 week, fasting blood glucose normalised and diabetes went into remission. Hepatic glucose production normalised, first phase insulin response returned and both hepatic and pancreatic fat reduced to levels similar in those without diabetes. Three months following the VLCD, there was a mean weight gain of 3.1 kg, however hepatic fat content did not increase and pancreatic fat continued to decrease. Despite the weight gain, 7 out of the 11 people were still in remission.

The study by Lim left several questions unanswered, including whether this intervention will work in those who have had diabetes for a longer time. The answer to that question was provided by Steven and Taylor in 2015.[27] They placed 29 people with DM2 on a VLCD (624-700 kcal). They were grouped according to duration

of Diabetes with short duration of diabetes (mean = 2.3 years) and long term diabetes (mean = 12.7 years). All hypoglycaemic agents (including insulin) were stopped. After 8 weeks the mean fasting blood glucose had decreased from 9.6 to 5.8 mmol/l in the short duration group and from 13.4 to 8.4 mmol/l in the long duration group. Eighty seven percent of those in the short duration group and 50% of those in the long duration group were in remission after 8 weeks. Further evaluation revealed that the fasting blood glucose was 5.8 mmol/l, 6.2 and 10.6 mmol/l at 8 weeks for those with diabetes for <4 years, 8-12 years and >12 years respectively. Thus, remission was less likely to occur in those with a longer diabetes duration. However, it should be noted that even though remission occurred in only 50% of those with long term diabetes, there was substantial improvement in glycaemic control despite no hypoglycaemic agents.

A further question Lim left unanswered was what are the effects beyond 3 months? Steven and Taylor's team published their work in March 2016 on the 6 month follow up of their previous study.[28] A weight maintenance diet was used to reintroduce solid food. One shake (Product C, Table 1) was exchanged for 1 solid meal every 3 days. Once patients were entirely on the weight maintenance diet 40% of the overall sample remained in remission. Interestingly, after 6 months this increased to 43%. Weight increased by only 900 g after 6 months of being on the VLCD. Remission at 6 months occurred in 60% and 21% of the short and long duration groups respectively.

Naturally, the final question is what about the long term consequences? Unfortunately there is limited data. The studies available often provided minimal follow up education beyond the VLCD phase.

Wing et al. assessed the effects of a VLCD (400 kcal) vs. a low (1000-1500 kcal) calorie diet in 36 individuals (16 VLCD, 17 low calorie) at 1 year.[29] HbA1c was 10.4% at baseline in both diets and decreased more so in the VLCD at 1 year (9.2 vs 11.8%). Fasting blood glucose also decreased more so in the VLCD (14.2 to 10.4 mmol/l vs. 12.8 mmol/l to 14.5 mmol/l). The improvements in glycaemic control were despite similar weight loss at 1 year. Thus, suggesting an effect beyond weight loss.

Snetl et al. sought to determine the effects of a 16 week VLCD (450 kcal) in DM2 (DM duration = 9 years) patients treated with insulin (mean dose of 86 units) with or without oral agents.[30] The study provided only basic dietary advice following the VLCD, with no follow up education. So possibly, due to the lack of education and follow up there was 13 kg weight gain, months after the completion of the VLCD. Despite the massive weight gain, body weight, hepatic, visceral, subcutaneous and pericardial fat were lower than they were at baseline. HbA1c decreased from 8.4% to 7% at 3 months during the VLCD and increased to 7.7% 18 months from baseline. Although the reduction of 0.7% from baseline was not statistically significant, we would argue that the results are clinically significant, especially since fewer patients were on insulin (100% on insulin vs. 28% on insulin at 18 months). The lesson learnt from this study is that 16 weeks of a VLCD despite inadequate follow up produces long term benefits.

Diabetes UK started a study to afford clarity on the use of VLCD (800 kcal) for people with DM2. This interest gave rise to The DIRECT (DIabetes REmission Clinical Trial) study which received funding to the tune of £2 489 198.[31] The study will be completed in October 2018.

Case studies

Initial Approach

Our first experience with VLCD (800 kcal) came from our work with Mr X. He lived with Type 2 diabetes for 5 years and weighed 259 kg at the initial consultation. He was treated with 30 units of Actraphane BD and Metformin 1 g BD**.** His mean fasting blood glucose was 10 mmol/l and pre-dinner was 16 mmol/l. Over the course of 4 months through moderate (2100 kcal) calorie restriction his weight reduced to 209 kg. His mean fasting blood glucose was 7 mmol/l and pre-dinner readings were 12 mmol/l. He was adamant that he wanted to stop using insulin. However, despite the 50 kg weight loss this seemed unlikely. He was placed on VLCD consisting of Product A (Table 1) 230 ml, three times a day (675 kcal) with non-starchy vegetables, such as leafy vegetables ad lib in attempt to discontinue insulin. Although Product C (Table 1) was used in most of the international studies, it is not available in South Africa and thus Product A was used instead (Table 1). The approach was to place him on the VLCD for 2 weeks, as by that stage 80% of the liver size and subsequently liver fat would have decreased based on the experience of a similar VLCD (456-680 kcal) study.[32] His insulin was stopped the day before he started on the diet but the Metformin remained.

Within the first week he had lost 8 kg, and his mean fasting blood glucose was 6.5 mmol/l and pre-dinner was 10 mmol/l despite no insulin. He reported that he was not hungry and agreed to continue into the second week. Due to logistical reasons, we were unfortunately not able to weigh him the following week. Despite this limitation, his mean fasting blood glucose levels were 5 mmol/l and pre-dinner 7 mmol/l. He was then placed on a moderate calorie diet (1700 kcal). Over the Christmas period he gained 3 kg, but as seen in the study by Lim there was no change in glycaemic control, with fasting readings of 5.5 mmol/l and pre-dinner 7 mmol/l. It has now been 5 months since the VLCD. He presently weighs 193 kg and his mean fasting blood glucose levels are 6 mmol/l and pre-dinner 8 mmol/l, despite no insulin.

Revised Approach

Since our initial experience, we have revised our approach and place our patients on VLCD (800 kcal) for 2 weeks consisting of only 3 shakes of Product A and non-starchy vegetables ad lib (<800 kcal). This is then followed by two weeks of 2 shakes a day and one solid meal, usually a dinner of lean protein and vegetables, without a specific calorie restriction. Despite the latter, some patients prefer to continue on 3 shakes a day as they find it easier to adhere to. Following the VLCD, patients were requested to follow a moderate calorie diet with one shake per day. The use of a meal replacement

once a day following a VLCD produces 3.9 kg greater weight loss than dietary education alone.[33]

Results

It is important to note that all the patients discussed under the "revised approach" section, going forward, have seen dietitians for a number of years with various dietary approaches being used. From our experience, none of these approaches have resulted in the level of enthusiasm and motivation that we have witnessed with the use of the VLCD. Furthermore, we have also not seen this level of success in such a short space of time.

Our patient sample (Table 2) had diabetes for 9.9 years, were obese and had very poor glycaemic control and poor overall metabolic markers status. The reason for this was that the programme was offered to patients with suboptimal metabolic control. Anthropometric measurements were taken at the start of the diet and glycaemic control was determined based on the self-monitoring of blood glucose levels in the preceding month.

Patients each started the programme at various times, thus the overall length of being on the programme varied considerably (mean 3.8 weeks). This influenced which stage of the programme the patient was on. Thus, this does limit the ability to assess the overall effectiveness of the programme. However, despite these limitations the data was compiled.

The mean changes (Table 3) were in weight – 4.39 kg, in waist circumference – 4.32 cm and in BMI - 1.40 kg/m^2 over the 3.8 weeks duration of the study. Fasting blood glucose, pre-lunch and pre-dinner readings decreased by -3.07, -3.65 and -2.9 mmol/l, respectively (based on the mean of the readings over 3 days).

The improvements in glycaemic control were noted despite a trend towards a reduction of hypoglycaemic agents including insulin (Table 3). Gliclazide was most often stopped as patients experienced hypoglycaemia. Patient 11 decided to stop all her treatment and was thus in "remission".

For those treated with insulin, the mean fasting, pre-lunch and pre-dinner readings at baseline were 10.75, 12.55 and 10.30 mmol/l, respectively. The fasting, pre-lunch and pre-dinner readings decreased to 7.50, 7.30 and 6.98 mmol/l, respectively, over a mean of 4 weeks. Importantly, these improvements occurred despite having diabetes for 15 years, on average, and a reduction in insulin use. The total daily insulin dose was reduced from 121 to 69 units, a 43% reduction. The effect of improved glycaemic control, despite large reductions in total daily insulin, was arguably most noticeable in patient 1, despite only being on the diet for 2 weeks.

Most patients reported feeling satiated on Product A. A few patients changed to Product B for a number of reasons. Some patients experienced taste fatigue (n=3) as the product is only available in vanilla flavour. Some patients (n=5) experienced gastrointestinal side effects such as bloating, cramping and flatulence which may have been related to the polyols that are used to sweeten the product.

Many patients have reported feeling better, and more energetic despite the lower calorie intake. This could be attributed to an improvement in overall blood glucose control. There were two patients with fibromyalgia who reported feeling less fatigued and having less pain.

Challenges

There have been requests for more free vegetable recipes as it became tiresome having the same vegetable dishes to fill up on in some instances.

On initiation of the VLCD, it is important that medications be altered, especially the oral hypoglycaemic agents and insulin. We analysed home blood glucose readings closely and medical adjustments were given where necessary. For some patients few or even no reductions or increases in dosages were made.

Side effects that we observed in our patients were cold intolerance; the gastrointestinal symptoms that have been addressed above (n=5); hypoglycaemia (n=2) which can be corrected by decreasing the hypoglycaemic agents; as well as weakness which was reported by one man who was a power/weightlifter. Two patients reported that they were also constipated which could be improved by ensuring that adequate vegetable fibre was consumed.

Conclusion

The overall experience based on 11 patients, is that this is an effective approach to rapidly reduce blood glucose levels, reduce medication, and motivate patients. Based on the available literature we would deduce that this is the result from treating the cause of DM2 - ectopic fat- rather than its expression in the symptoms of metabolic derangements.

The obvious limitation of our work is that this is not a randomised controlled trial, but rather a case series which limits the ability to ensure that this approach is superior to conventional nutritional therapy. The short duration – mean 3.82 weeks – provides only short-term outcomes, thus, we propose that further long-term studies be conducted. Our current sample will be monitored and thus reported on further in due course.

The available guidelines surrounding the use of VLCDs are somewhat conflicting. The Canadian Diabetes Association does not suggest the routine use of very low calorie (<900 kcal) diets unless a patient is under medical supervision.[34] The latest guidelines from the American Diabetes Association suggest that VLCDs (≤800 kcal) can be used for 3 months provided that the treating clinician is adequately skilled and that the patient is monitored regularly. The National Institute of Health and Clinical Excellence does not discuss VLCDs for Type 2 diabetes, but a VLCD diet is mentioned in their obesity guidelines.[35] The guidelines suggest that VLCDs <1000 kcal can be used for a maximum of 3 months or 2-4 days a week, long term. However, VLCDs <600 kcal should only be used if clinical supervision is available. The Society of Endocrinology Metabolism and Diabetes of South Africa guidelines, which are due to released later this year,

mention that a VLCD (<800 kcal) diet can be used in Type 2 diabetes.

Based on the available literature, patients recently diagnosed with Type 2 diabetes would appear to be more likely to go into remission.[28] However, the efficacy of the diet in patients who are on large doses of insulin is less clear. Despite the former, our results suggest that such an approach can drastically reduce total daily insulin use. Arguably, the most important question is who is likely to adhere to this diet? At present, we do not know, but patient 11 provided the following piece of information. "You do not have diabetes (name of clinician), therefore you do not understand what I am willing to do to improve my health. Do not make the judgement of whether I will or will not be able to follow this diet." The lesson learnt is not to prejudge your patients but rather provide them with information regarding a VLCD as an alternative solution.

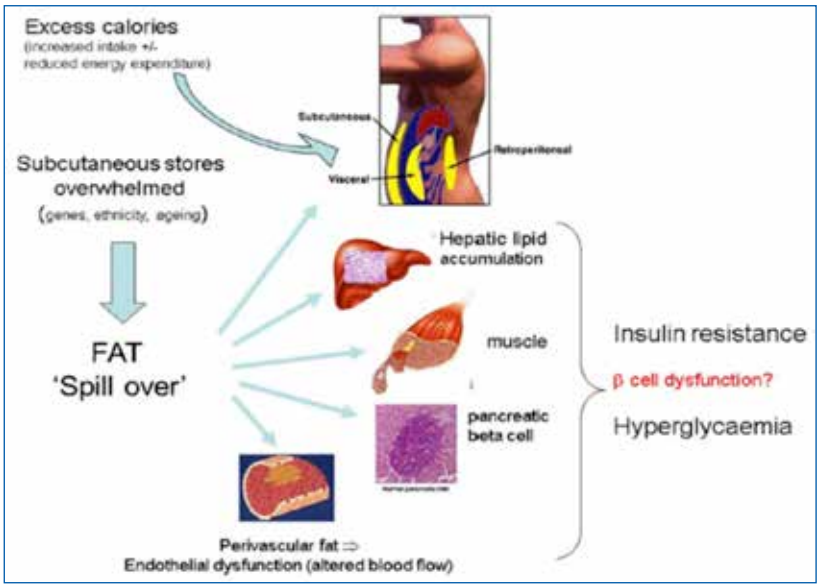

Figure 1: Ectopic fat concept and the development of insulin resistance and DM2: The illustration shows the development and location of ectopic fat when the ability to store subcutaneous fat is exceeded.[19]

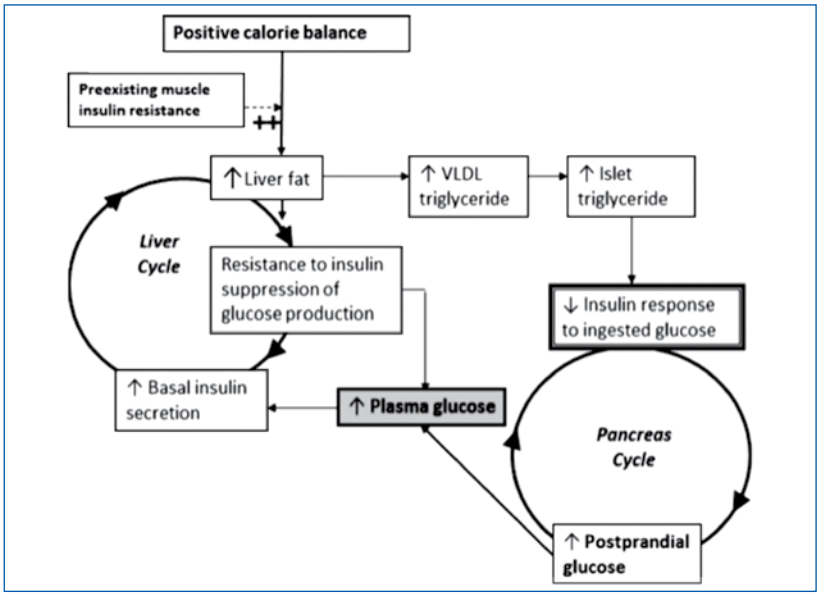

Figure 2: Twin cycle explains the aetiology of DM2 due to a positive calorie balance which leads to hepatic and pancreatic fat deposition.[3] This fat deposition causes insulin resistance and hyper-insulin secretion, which ultimately results in DM2.

Table 1: Nutritional Content of the Supplements

Per shake	Product A (237 ml)	Product B (230 ml)	Product C (237ml)
Energy (kcal / kJ)	225 / 947	230/ 967	207/870
Protein (g)	10.1	8.5	17.5
Fat (g)	8.2	7.5	4.5
Carbohydrate (g)	21.3	33.1	22.5
Fructooligosaccharides (g)	1.06	2.3	0
Polyols (g)	5.72	0	0
Fibre (g)	2.12	2.3	3.6

Table 2: Baseline Data: Anthropometric measurements and biochemical values

Patient	Age	Duration of diabetes (years)	Weight (kg)	Waist Circumference (cm)	BMI	Fasting (mmol/l)	Prelunch (mmol/l)	Predinner (mmol/l)	Mean BG (mmol/l)
1	64	17.00	94.60	117.00	36.00	11.70	19.80	15.50	14.20
2	51	20.00	86.00	106.00	31.50	10.00	12.20	7.20	10.20
3	65	15.00	95.90	116.00	36.00	12.60	14.90	13.20	14.00
4	44	10.00	113.00	125.00	44.70	12.10	10.10	11.00	10.00
5	44	0.58	98.00	108.00	35.60	11.30	5.90	11.60	9.60
6	58	13.00	121.00	130.00	36.40	9.20	8.10	7.20	8.10
7	54	5.50	139.50	133.00	42.00	10.60	7.70	8.40	9.00
8	44	4.00	93.00	102.00	32.00	10.10	8.70	8.40	8.70
9	51	9.00	93.50	107.50	35.10	9.70	9.30	9.20	9.20
10	68	5.00	87.80	116.00	33.00	7.30	8.10	9.20	8.40
11	43	0.50	74.50	98.00	32.20	7.80	7.30	7.50	7.80
Average:	53.2727	9.90	99.71	114.41	35.86	10.22	10.19	9.85	9.93

Post Intervention Data: Anthropometric measurements and biochemical values

Patient	Age	Duration of diabetes (years)	Weight (kg)	Waist Circumference (cm)	BMI	Fasting (mmol/l)	Prelunch (mmol/l)	Predinner (mmol/l)	Mean BG (mmol/l)	Duration on programme (weeks)
1***	64	17.00	91.50	115.50	34.80	7.60	8.60	5.80	7.40	2.00
2*	51	20.00	83.00	107.00	30.40	8.00	7.30	10.00	9.00	5.00
3**	65	15.00	91.00	108.00	34.20	8.80	5.00	11.60	8.80	6.00
4***	44	10.00	111.50	118.00	44.10	7.40	6.60	6.00	6.60	2.00
5***	44	0.58	96.00	108.00	34.80	5.20	6.80	7.30	7.00	2.00
6**	58	13.00	109.00	125.00	33.60	7.30	6.70	6.10	6.60	5.00
7**	54	5.50	133.00	130.00	40.10	7.30	6.40	5.80	6.50	3.00
8**	44	4.00	85.50	95.00	29.50	8.70	7.60	6.30	7.90	5.00
9***	51	9.00	90.90	106.50	34.10	7.10	6.80	6.40	6.70	1.00
10***	68	5.00	86.00	108.00	32.70	4.90	5.10	5.40	5.90	3.00
11*	43	0.50	71.10	90.00	30.70	6.30	5.10	5.70	5.70	8.00
Average:	53.2727	9.90	95.32	110.09	34.45	7.15	6.55	6.95	7.10	3.82
Change:			4.39	4.32	1.41	3.07	3.65	2.91	2.83	

Current stage of programme: *** = three shakes, ** = two shakes, *= one shake

Table 3: Baseline Data: Medication

Patient	Metformin (mg)	Gliclazide (mg)	Janumet (mg)	Victoza (mg)	Bolus Insulin (units)	Basal Insulin (units)	Total Insulin dose (units)
1	1000.00				105.00	100.00	205.00
2	2000.00				60.00	140.00	200.00
3		120.00				10.00	10.00
4	1700.00				30.00	28.00	58.00
5		120.00	50/500				
6					72.00	60.00	132.00
7	2000.00	60.00					
8	2000.00	120.00					
9							
10	2000.00	60.00					
11	500.00						
Average	1600.00	96.00	50/500		66.75	61.00	121.00

Post Intervention Data: Medication

Patient	Metformin (mg)	Gliclazide (mg)	Janumet (mg)	Victoza (mg)	Bolus Insulin (units)	Basal Insulin (units)	Total Insulin dose (units)	Duration on programme (weeks)
1***	1000.00				30.00	70.00	100.00	2.00
2*	2000.00				30.00	120.00	150.00	5.00
3**		120.00				10.00	10.00	6.00
4***	1700.00				24.00	20.00	44.00	2.00
5***			50/500					2.00
6**	1700.00				20.00	21.00	41.00	5.00
7**	2000.00	60.00						3.00
8**	2000.00			1.80				5.00
9***								1.00
10***	2000.00	60.00						3.00
11*								8.00
Average	1771.43	80.00	50/500	1.80	26.00	48.20	69.00	3.82
Change	-171.43	-240 †	0	-1.80	-40.75	-12.80	-52.00	

Current stage of programme: *** = three shakes, ** = two shakes, *= one shake, † reduction from those who used Gliclazide at basline

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