Metabolic impact of a successful lifestyle intervention in patients with new onset type 2 diabetes; a pilot study

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Abstract

Introduction: The aim of this pilot study was to determine the metabolic impact of intensive lifestyle intervention in patients with recent onset type 2 diabetes.

Methods: 22 patients with a recent diagnosis of type 2 diabetes mellitus were enrolled in a group lifestyle intervention programme comprising an 8-month weight reduction phase followed by an 8-month maintenance phase. Clinical and metabolic measurements were made in follow-up assessments at baseline and at 4, 8 and 16 months.

Results: Average weight loss (mean [95% confidence limits]) compared to baseline was -7.7 [6.6 - 9.7] kg, p<0.001 at 8 months representing an 8.1 (range 4.2 – 17.3) % reduction. After the 8-month maintenance phase, weight loss was -5.7 [4.5 – 6.9] kg, p<0.001, a 5.9 (range 0 – 11.8) % reduction compared to baseline. There were favourable improvements in fasting glucose, insulin and HbA1c but no significant changes in adiponectin, leptin or in post-glucose Glucagon-like Peptide-1 (GLP-1) levels. A 75g oral glucose tolerance test performed at the end of the programme showed only 4 of 18 participants tested could be categorized as diabetes by WHO criteria.

Conclusions: The study demonstrates the benefit of a motivational, intensive lifestyle intervention programme, delivered in a cost effective manner, achieving significant and sustained weight loss in patients with new onset type 2 diabetes.

Keywords: Lifestyle intervention, type 2 diabetes

Introduction

The current recommendations from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) for patients with new onset type 2 diabetes are that at diagnosis highly motivated individuals with an HbA1c near target (<7.5%) could be given the opportunity to engage in lifestyle change for 3 to 6 months. Those with moderate hyperglycaemia or in whom lifestyle changes are anticipated to be unsuccessful should be promptly started on an antihyperglycaemic agent such as Metformin [1].

The ADA and EASD also recommend that individualised medical nutrition therapy should be provided; preferably by a registered dietitian with a weight loss goal for all overweight or obese individuals with diabetes. In a systematic review of 80 weight loss studies of more than 1 years duration, moderate weight loss can be achieved with a mean weight loss of 5 to 8.5 kg (5% to 9%) during the first 6 months from interventions involving a reduced energy diet and/or weight loss medications but with weight plateauing after 6 months [2].

However in practice in the UK community based programmes for patients with newly diagnosed type 2 diabetes invariably fail to achieve sustained benefits from lifestyle interventions alone in terms of weight loss and biochemical outcomes [3]. To our knowledge the cost effective lifestyle programme that would achieve long-term improvement in new onset type 2 diabetes patients in the UK is still lacking. The resource burden is usually the primary reason and therefore cost effective interventions with an optimum level of intensity and long-term follow-up for maintenance are still to be developed [4].

Locally we reviewed the clinical and biochemical outcomes of more than 6700 patients entering our established community based programme for new onset type 2 diabetes and found that within the first 3 months almost 50% of patients were already commenced on oral agents [5].

The primary aim of the study was to determine the clinical and metabolic impact of a motivational intensive group lifestyle intervention programme in patients with new onset type 2 diabetes and that if successful could be offered in the community setting.

Patients and Methods

Subject recruitment

Patients with recent onset type 2 diabetes were recruited from an established local community group diabetes education program where they are seen usually within two weeks of diagnosis [6]. Patients who were unable to give consent or attend at least 75% of the programme sessions for medical or other reasons, those prescribed oral hypoglycaemic, anti-obesity or any other prescription medications that may interfere with the study results or whose BMI was <25, were excluded. The study was...
approved by the Dorset Ethics Committee.

The intervention
The intensive group lifestyle programme was developed by a research dietitian, lifestyle coach, exercise physiologist, psychologist, diabetes nurse and physicians working in collaboration.

The core 8-month program was made up of 13 informal structured group sessions. The content is described in Appendix 1. Following on from the core programme, participants entered an 8-month maintenance phase consisting of 5 group sessions. Patients were also offered two individual appointments to address individual concerns. The group size was 6-8 patients. Each group session started with a confidential “weigh in” followed by a 1.5-hour education session. Each session covered a topic related to nutrition, physical activity and behavioural change. Three of the sessions included a topics related to diabetes management.

The programme was run by a research dietitian trained in motivational interviewing and behavioural change techniques. The dietitian used counselling skills to build rapport with the patients in order to maintain attendance levels and to retain them in the study, as well as motivating them to work towards their lifestyle change goals. Topics related to diabetes management were introduced by the diabetes nurse.

At recruitment patients were invited for an individual appointment with the research dietitian to assess the patient’s diet and collect all other necessary information such as social and medical history. During this assessment the patient’s motivation and confidence levels to make the necessary lifestyle changes were assessed. This data was used to design each patient’s Individual Diet Plan (IDP) and to help set their individual short and long term lifestyle and weight loss goals.

The key elements of the programme were:
1. Setting and reviewing progress of weight loss and other lifestyle change goals.
2. Group support and relapse management.
3. Individualised approach to achieve the goals (e.g. IDPs, flexible individual appointments to address individual needs).
4. Intensive on-going intervention with structured education sessions and weekly supervised exercise programme.
5. Advice on diabetes management.
6. A flexible maintenance programme following on from the 8-month intensive programme.

Weight loss goals
The aim was to achieve a 5% weight loss at 4 months with a continuation of up to 10% weight loss at 8 months. Patients were given the freedom to set higher goals as long as their BMI didn’t drop below 22kg/m² and lose the weight at a rate of no more than 0.5–1 kg a week.

Behavioural change component
The central aspect of the programme was to change lifestyle using goal based behavioural change techniques. The behavioural change interventions included such strategies as self-monitoring, stimulus control, goal setting, slowing rate of eating, ensuring social support, problem solving, relapse prevention, stress managements and cognitive restructuring (modifying thoughts aimed at positive thinking). These interventions were further reinforced with positive visualisation and relaxation techniques.

Patients were taught the importance of self-management using food and activity diaries and weighing themselves weekly.

Dietary intervention component
Sessions covered such dietary topics as healthy eating and portion control, energy balance, food labelling, nutritional claims, fat and cardiovascular health, salt and blood pressure and sugar and artificial sweeteners. The diet was based on a low GI diet principle with the emphasis on reducing starchy carbohydrate portions. Patients were advised on choosing only whole grains and vegetables as a starchy component of the diet and avoiding processed and highly refined carbohydrate rich foods. Patients were educated on the effect of carbohydrate on glycaemia.

During the second session each patient received their IDP. The IDP is a food portion plan with a 400-1000 kcal/day deficit, with a description of portion sizes for each food group and examples of different kcal value snacks. Daily recommended energy requirements were estimated based on the dietary history obtained during the initial consultation and Scofield’s equation with 400 – 1000 kcal/day deficit. The amount of energy restriction depends on the initial intake; therefore some patients were able to reduce their intake by 1000 kcal; whereas others were only able to cut out 400 kcal to remain on at least 1200kcal/day diet. The IDP was based on the “UK Balance of Good Health” guidelines with given number of portions from each food group. To make the concept of dietary advice easy to use each portion of starchy food, protein based food and dairy products is equal to approximately 100 kcal. Each portion of fat is approximately equal to 30kcal. Each portion of fruit is equal to approximately 40 kcal. Regarding vegetables patients were advised to eat as much as they like but not less than the advised amount.

Exercise programme component
The exercise component consisted of a weekly 1-hour circuit training class of ten exercise stations alternating between resistance, cardiovascular and respiratory exercises at a local gym. Each individual was personally advised on the most appropriate intensity for them relevant to their age and health status and any appropriate modifications to
take account of any mechanical limitations.

**Blood sampling and laboratory procedures**

During the intervention phase participants attended following an overnight fast at baseline, at 4, and 8 months, when weight, height, percent body fat, waistline circumference and blood pressure were recorded. Blood samples were collected for measurement of glucose, HbA1c, lipids, insulin, GLP-1, leptin and adiponectin. They were given a 75g glucose load in the form of a glucose polymer and a repeat blood sample for stimulated GLP-1 level taken after 30 minutes. During the maintenance phase, weight and other physical measurements were made at 12 and 16 months and at the final 16 months visit participants were offered a standard 75g oral glucose tolerance test.

Blood for GLP-1 was taken directly into cooled EDTA tubes containing DPP-IV inhibitor at a final concentration of 100 μmol/L (Linco Research, Millipore, MO, USA). Samples for insulin, GLP-1, leptin and adiponectin were stored at -40°C until analysis.

Glucose and lipids were measured using an Olympus automated clinical chemistry analyser (Olympus Diagnostics Ltd, Watford, UK). HbA1c was measured using a Menarini HA-8140 HPLC analyser (Menarini Diagnostics, Wokingham, UK). Insulin was measured by a solid phase, two site, chemiluminescent immunometric assay using an Immulite 2500 analyser (Siemens Diagnostics, Llanberis UK). HOMA IR was calculated using the HOMA calculator downloaded from the Oxford diabetes clinical trials unit website (http://www.dtu.ox.ac.uk/index.php?maindoc=/homa/download.php). Intact GLP-1 (7-37 and 7-36 amide), leptin and adiponectin were measured in plasma by specific ELISA methods (Linco Research, Millipore, MO, USA).

**Statistical analysis**

The study was a non-randomised, single arm, pilot intervention study with repeated measurements over four visits. Anthropometric data were normally distributed and expressed as mean ± sd. Pre and post intervention data were compared with paired t-tests using a 5% significance level. Biochemical data were not normally distributed and are expressed as median (interquartile range). Pre and post data were compared using the Wilcoxon test or Friedman test with 5% significance level.

**Results**

22 patients (14 male; age [mean ± sd] 60 ± 9.6 years) with new onset type 2 diabetes provided written consent for participation in the study. One participant (male) withdrew before the fourth month; a further participant (male) withdrew between 4 and 8 months and a third (male) between 8 and 16 months. Data from baseline, 4-month and 8-month assessments for the 20 participants completing the intervention phase are shown in Table 1.

**0-8 months**

All participants lost weight during the first four months of the study; mean loss [95% CI] was 5.9 [4.8–7.2] kg, p<0.001 (Figure 1). Between 4 and 8 months 18 out of 20 participants either maintained weight (defined as change of ± 0.5 kg) or lost further weight (loss for the period was 1.8 [0.7-3.0] kg, p<0.001 and from baseline was 7.7 [6.3-9.3] kg, p <0.001) representing a mean reduction in body weight of 8.1 (range 0.7 -17.3)%. In the two participants who gained weight (1.9, 3 kg) during the second 4-month period overall reductions of 0.6 and 10.3 kg from baseline were still observed. There were similarly significant decreases in BMI, waist circumference and % body fat (Table 1).

Glycaemic control, as measured by changes in fasting glucose, HbA1c, fasting insulin and HOMA-IR, calculated as an index of insulin resistance, was significantly improved over the eight months (Table 1). There were also significant reductions in systolic and diastolic blood pressure over the eight months period. Of 15 patients on antihypertensive medication at recruitment, two had a dose increase and one a dose reduction during the study period. No changes in total cholesterol or triglycerides were noted influenced by the majority of patients being on lipid lowering medication but HDL cholesterol (median [IQ range]) was significantly increased at 8 months compared to baseline (1.25 [0.47] vs 1.13 [0.45] mmol/L, p<0.01).

Leptin levels were significantly decreased at 8 months though no changes in Adiponectin were noted. Similarly there were no changes in either fasting or stimulated GLP-1 levels over the 8-month period (Table 1).

**8-16 months**

Data for the 19 (11 male) patients completing the 16-month programme is presented in Table 2. During the maintenance phase, between 8 and 16 months, despite 15 participants gaining small amounts of weight (2.38 ± 3.6 Kg), at 16 months overall weight loss still represented a 5.9% (range 0.27–11.8) reduction compared to baseline. Despite this sustained weight reduction, metabolic parameters other
Baseline 4 months 8 months p 0mv4m p 0mv8m p 4mv8m

Mean±sd

Weight, kg 95.9±17.5 90.0±17.1 88.2±16.4 <0.001 <0.001 0.006
BMI, kg/m² 33.1±5.3 31.5±5.3 30.5±5.2 <0.001 <0.001 0.004
Waist Circumference, cm 112.6±13.4 103.6±14.1 99.6±14.5 <0.001 <0.001 <0.001
% Body Fat, % 38.5±8.8 34.7±8.1 33.8±8.2 <0.001 0.008 ns
Systolic BP, mm Hg 144.6±22.0 130.4±21.0 126.3±13.3 0.002 <0.001 ns
Diastolic BP, mm Hg 83.3±11.1 73.0±10.5 71.6±7.9 <0.001 <0.001 ns

Mean±sd

Median [IQ Range]

HbA1c, mmol/mol 48.1 [11.18] 44.3 [6.55] 43.2 [10.12] 0.01 0.007 0.05
HbA1c, % 6.6 [1.15] 6.2 [0.6] 6.1 [0.6] ns ns ns
Fasting Glucose, mmol/L 6.5 [1.1] 5.95 [0.8] 6.0 [1.0] <0.001 <0.001 ns
Fasting Insulin, mIU/L 11.9 [7.8] 8.0 [9.0] 7.7 [5.0] 0.027 0.004 ns
HOMA – IR 3.8 [2.2] 2.1 [2.0] 1.9 [1.1] 0.02 0.002 ns
Cholesterol, mmol/L 4.5 [1.5] 4.1 [1.4] 4.1 [1.6] ns ns ns
Triglycerides, mmol/L 1.9 [1.2] 1.3 [0.7] 1.3 [1.0] <0.001 0.04 0.02
HDL-C, mmol/L 1.06 [0.45] 1.10 [0.43] 1.15 [0.47] ns 0.01 <0.001
GLP-1 Basal, pmol/L 2.15 [1.39] 1.88 [1.90] 2.51 [1.56] ns ns 0.03
GLP-1 30', pmol/L 6.45 [7.62] 8.70 [9.9] 6.78 [6.1] ns ns ns
Leptin, μg/ml 37.4 [36.0] 17.0 [30.1] 17.3 [18.9] 0.03 0.004 ns
Adiponectin, μg/L 6.8 [3.35] 7.5 [5.17] 6.2 [6.6] ns ns ns

Table 1. Summary of measurements at baseline, 4 and 8 months for 20 participants completing the first 8-month phase. Clinical measurements are expressed as mean ± sd; biochemical measurements as median [interquartile range].
Discussion

For individuals with new onset of type 2 diabetes current guidelines recommend weight loss and exercise as a first line treatment for all overweight and obese people with type 2 diabetes [1]. Many centres in the UK have adopted a community based DESMOND programme for people with new onset type 2 diabetes [7]. This is six hours long, is delivered in either one full day or two half day equivalents and facilitated by two educators. Unfortunately recently published data on the DESMOND programme demonstrate no significant impact on weight loss, biochemical or lifestyle outcomes at 3-year follow-up [3].

Here we have shown that a motivational based group intensive lifestyle programme can achieve sustained lifestyle improvement and weight loss in patients with new onset of type 2 diabetes without the need for oral antihyperglycaemic therapies. The 8-month group programme resulted in weight loss of 8.1% from baseline and abstinence from diabetes medications for all patients. The programme was well received, with only two of the 22 original participants failing to complete the 8-month study period and a further one missing the maintenance period follow-up. All participants achieved weight loss during the initial 8-month intervention, and despite a small amount of weight gain in some participants between 8 and 16 months maintenance period, overall weight reduction was achieved by 18 and maintained in one over the 16-month study period. Corresponding reductions in percentage body fat and waist circumference were observed, which together with improvements in lipid levels and blood pressure are associated with reductions in cardiovascular risk in obese individuals [8]. At the end of the 16 months, median HbA1c dropped from 6.6% to 6.3%, but the change was not significant. As reported elsewhere these patients had an optimal mean HbA1c already at baseline and it may be more difficult for it to be reduced further [9].

Weight loss achieved, patient retention rate and dietitian's and nurse's time spent (average 4.1 hours per patient over 16-month period) to deliver the programme in our study compare favourably with lifestyle interventions elsewhere. For example, one 6-month intensive behavioural intervention programme of 20 weekly group sessions with an additional 6-month follow-up reported a 6.3% weight loss from a median baseline of 100 kg after 6 months with a 2.8% reduction at programme end. It is noteworthy that only 27 of 50 individuals recruited completed the study [10]. In a multicentre study of 494 individuals with recent onset type 2 diabetes comparing 12-month intensive diet or intensive diet plus exercise, comprising an average of 6.5 hours direct nurse’s and dietitian’s time per patient, achieved mean weight loss of 2.0 and 3.0% at 6 months, which was sustained at 12 months [11]. Furthermore, improvements in glycaemic control in patients with type 2 diabetes can occur even without weight loss if carbohydrate consumption is restricted and the protein content of the diet is increased [12].

The discovery of gut-derived Glucagon-like peptide-1 (GLP-1) and its important physiological effects has resulted in an important therapeutic role for GLP-1 therapies in diabetes and obesity [13,14]. Despite this the precise role of GLP-1 in the pathogenesis of diabetes remains unclear. In addition, adipocyte derived factors leptin and adiponectin may also have a role in obesity and type 2 diabetes [15,16]. Here we found a significant reduction in leptin levels over 8 months in keeping with other observations showing reductions in circulating leptin with negative energy balance and falling body fat mass [17]. This, however, was not maintained during the maintenance phase. No increase in adiponectin was noted in contrast with previous observations in severely obese women showing a weight loss of 5 - 10% was sufficient to show an increase [18].

Intact GLP-1 levels, both fasting and stimulated at 30 mins after oral glucose, showed no change over 8 months. The GLP-1 response to nutrient intake has been reported as attenuated in type 2 diabetes [19] and there has been some debate as to whether this observed abnormality is a cause or consequence of type 2 diabetes. Studies in identical twins [20] and first degree relatives of patients [21] found reduced GLP-1 secretion only in those with diabetes, suggesting that abnormal GLP-1 release may be a consequence of diabetes. In this small study, despite significant and sustained weight loss and associated improvement in glycaemic control over 8 months; there was no increase in either fasting or stimulated GLP-1 levels.

There are some limitations to this study. The overall number in the study is small but group numbers were deliberately kept to 6-8 to facilitate participation and interaction. In so doing a high compliance rate was achieved with favourable and prolonged weight change and accompanying improvements in glycaemic control resulting in a delay in introduction of medication when compared with usual care.

A further limitation is a lack of control group. Given the recommendations for early lifestyle intervention in type 2 diabetes, it was not possible to simply withhold treatment and the usual care of newly diagnosed patients.

The specific assay used for intact GLP-1 only measures a small proportion of total GLP-1 secreted as intestinal GLP-1 is rapidly degraded by the enzyme dipeptidyl peptidase IV (DPP-IV) [22]. To avoid inactivation in vitro, blood was
taken directly into cooled sample tubes containing a DPP-IV inhibitor. While a single stimulated GLP-1 level is a less accurate measurement of GLP-1 production than serial measurements and AUC calculation, we adopted this approach for reasons of practicality and to allow blood sampling to be undertaken during group visits. The selection of a timed 30 minutes post glucose measurement was based on previous studies showing peak concentrations 30 minutes following glucose administration [23,24].

In conclusion, a group based lifestyle intervention programme resulted in significant and sustained weight loss in new onset type 2 diabetes patients with accompanying favourable changes in glycaemic control. Our findings further add to the current research to support improvement of diabetes services to enhance individually tailored lifestyle and dietary advice to individuals at an early stage of diagnosis. This intervention was designed to be delivered by dietitian and nurse and it could be easily adopted into community-based services at very little cost.

Additional files
Appendix 1

Competing interests
The Authors declare that they have no competing interests.

Authors' contributions
DK conceived the study and is guarantor. All authors contributed to the study design and helped with recruitment.
AB developed and ran the lifestyle program. JB, TS and SZ carried out the biochemical analyses and were involved in the statistical calculations. All authors helped to draft the manuscript and approved the final manuscript.

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