



A self-controlled trial with Lifestyle-Intervention of Daily-two-only-Meals-and-Exercise (2-OMEX) for achieving remission in Type 2 Diabetes, measured by HbA1C Levels in Sangli, India

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Abstract

Introduction: Type-2 diabetes mellitus (T2DM) has attained the status of a global pandemic, spreading from affluent industrialized nations to the emerging economies. Knowledge of the modifiable risk factors of T2D is important, as it forms the basis for designing cost-effective preventive and therapeutic strategies to slow the epidemic in populations at increased risk

Objectives: The *Primary objective* of this study was to determine if 2-OMEX lifestyle causes significant decline of HbA1C levels. The *Secondary objective* was to determine if 2-OMEX lifestyle causes reduction in weight, waist size, and requirement of anti-diabetic molecules/doses in four months.

Methodology: This was a self-controlled trial, conducted in view of providing an accessible, affordable, and feasible lifestyle intervention for remission of T2DM and prevention of its progression. 45 patients diagnosed with T2DM were given 2-OMEX lifestyle intervention and followed for a period of 3 months.

Results: The results of intervention were, statistically significant ($p < 0.05$) reduction of HbA1C, weight, waist size and Body Mass Index (BMI). Anti-diabetic medications were stopped in 6.9% patients due to constant normoglycemic state and HbA1c reduction to non-diabetic levels.

Conclusion: If the diabetes epidemic is to be slowed or halted, lifestyle intervention trials need to be implemented with appropriate cultural adaptations.

Keywords: Type-2 Diabetes mellitus, Obesity, Lifestyle modification, Modifiable risk factors

Introduction

Diabetes is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.

The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves,

heart, and blood vessels. ^[1,2] The prevalence of diabetes in India and world is on rise in last few decades. There is significant global variation in susceptibility to T2D, although genetic factors do play an important role. The rapidity with which diabetes prevalence is on rise, reflects the far-ranging and rapid socioeconomic. Traditionally, obesity and its correlate, insulin resistance, have been considered the major mediators of T2D risk; however, recent evidence shows that early loss of β -cell function plays an important role in the pathogenesis of T2D, especially in nonobese individuals such as South Asians. ^[3] About 10% adults in India have T2D and 10% are pre-diabetic. ^[4] This disease is assumed to be a lifelong chronic disease requiring medication. The most recent position statement issued by the ADA regarding standards of medical care in diabetes and a consensus statement by the American College of Endocrinology (ACE) and the American Association of Clinical Endocrinologists (AACE) recommend lifestyle intervention as the preferred treatment option for prediabetes and newly diagnosed diabetes up to 3 months, as it has been shown to be safe and highly effective, reducing the progression to type 2 diabetes by more than 40%. ^[5,6]

There have been attempts to find out ways by which the possibility of diabetes mellitus can be delayed or prevented by lifestyle modifications or by medicines. But we have to understand that this is a lifestyle disease. There have been reports about clinical remission of diabetes by reduction of food intake, and/or use of medication. Food restriction may be done with bariatric surgery, or by restricting food intake by health education and scheduling smaller meals, intermittent fasting etc. ^[7-9] Now there is some empirical evidence on 2-meal a day regime with 45 min exercise in the form of walking at least 4.5 km (2-OMEX), as a part of 'World free of obesity and diabetes' campaign. ^[10-13]

This study was conducted with the rationale of addressing T2DM remission, and whether it is achievable by limiting to two-meals-a-day coupled with some mandatory exercise which is a part of diabetes management in any standard treatment guidelines. If this is feasible, a very cost-effective and sustainable solution will be available to counter the advancing wave of T2DM in India. The *Primary objective* of this study was to determine if 2-OMEX lifestyle causes significant decline of HbA1C levels.

The *Secondary objective* was to determine if 2-OMEX lifestyle causes reduction in weight, waist size, and requirement of anti-diabetic molecules/doses in four months. The hypothesis of insulin resistance causing T2DM is plausible. Meal frequency limitation will likely limit the insulin spikes and thus reduce the cause for insulin resistance and ultimately reduction of the resulting incidence of obesity. ^[14,15] Diabetes mellitus is a lifestyle disease, this study was done with an attempt to commemorate a solution for a lifestyle disease in the form of lifestyle modification.

Methodology

This was a Self-controlled Clinical trial. Approval was acquired from Bhartiya Vidyapeeth (Deemed-to-be university) Ethics committee, Sangli before starting the study. A pool of diagnosed type 2 diabetes patients ^[16,17] with HbA1C >6.5% and/ or taking anti-diabetic medications enrolled under Diabetes Reversal Center (DRC), Sangli. Assuming a 20% remission rate with no lifestyle intervention, while that with the 2-OMEX intervention to be 70% and a dropout rate of 10%, an adjusted sample size was 46. 51 patients enrolled for the study voluntarily, of which 6 patients dropped out in between the trial and were thus excluded from the study. Those diagnosed with T2DM at least 1 month before the initiation of our study, belonging to the age group of 30-70 years, without any complications, HbA1C >6.5%, with or without any anti-diabetic medications/ insulin treatment and candidates who could self-report/report their daily findings with assistance of family member in 2-OMEX diary were included in the study. Patients with cardiovascular disease, nephropathy, retinopathy, neuropathy diabetic foot, and also T2DM in pregnancy, those who did not give consent, those staying outside Sangli, and those who were not able to do physical activity/exercise for any reason of physical or feasibility issues were excluded from the study. The participants who discontinued 2-OMEX intervention at any point during the study and the participants who develop adverse events or complications during the study period were

The eligible participants were asked to provide previous records of investigations and treatment taken for diabetes. Appropriate tests were done for assessment of complications if any. Clinical

assessment for neurological and cardiovascular function were conducted by the physician at DRC. They continued the ongoing treatment by their treating diabetologist along with the lifestyle intervention given in the study. Those who had not started anti-diabetic medications were given choice of choosing only lifestyle intervention prescribed in the campaign, for the remission of their diabetes. The participants were monitored regularly by the physician and co-author of this study at the DRC. The selected patients were detailed about 2-OMEX lifestyle. All participants were monitored for reduction of anti-diabetic molecules as the HbA1C levels decreased. Counselling was done regularly to make sure that all the participants sustained the lifestyle intervention by keeping 2-OMEX. They were advised to do exercise in the form of walking for at least 4.5 km in 45 minutes. Daily diary or digital records were used for monitoring this reported activity. HbA1C was measured each month by HPLC method in a standard allotted National Accreditation Board for Testing and Calibration Laboratories (NABL) accredited laboratory. Other covariates like weight, waist size, blood pressure was measured as per standard methods. Fasting insulin was measured before and after trial period of 3 months. Any patient showing clinical or lab signs of deterioration was discontinued and referred to standard treatment.

2-OMEX Lifestyle intervention: Two meals a day regime popularly known as 'Dixit diet' was advised to the patient as lifestyle intervention. In this plan, patient has to have fixed time for meals; with each meal in the order of: 6-8 dry fruits (no raisins, dates,

apricot), then 1 bowl salad (excluding beetroot, carrots), followed by 1 bowl of sprouted beans/pulses or 2 boiled eggs, and then all food items cooked at home. Patient can only have fluids like water, black tea without any sugar/ jaggery/ honey/ sugar substitute/ milk; diluted homemade buttermilk can be consumed in between these two meals. Patient also has to strictly walk for minimum 4.5 km in 45 min every day. ^[10-13]

The participants were monitored regularly and advised to have a glucometer at home by the physician and co-author of this study at the DRC. They were advised to continue the consultation with their treating diabetologist. Since this is a lifestyle intervention in the form of diet and exercise, the adverse event that may occur is hypoglycemic episode, in which case all the patients were advised to have glucometer to monitor any symptom of hypoglycemia. Patients were educated regarding the symptoms of hypoglycemia and their management, by the physician at DRC. After treating the acute episode of hypoglycemia, the patient can get advice for their further management from their treating diabetologist or the physician available at DRC. IBM SPSS v26 and Open Epi was used for statistical analysis. Paired t-test and Fischer Exact test were the tests of significance used.

Results

A total of 45 patients were included in the analysis. Mean \pm S.D. of the patients was 51.7 ± 3.2 . Majority of the patients (42.2%) belonged to age group 51-60 years. Females were more than males among the study population. (Table 1).

Table 1: Demographic details

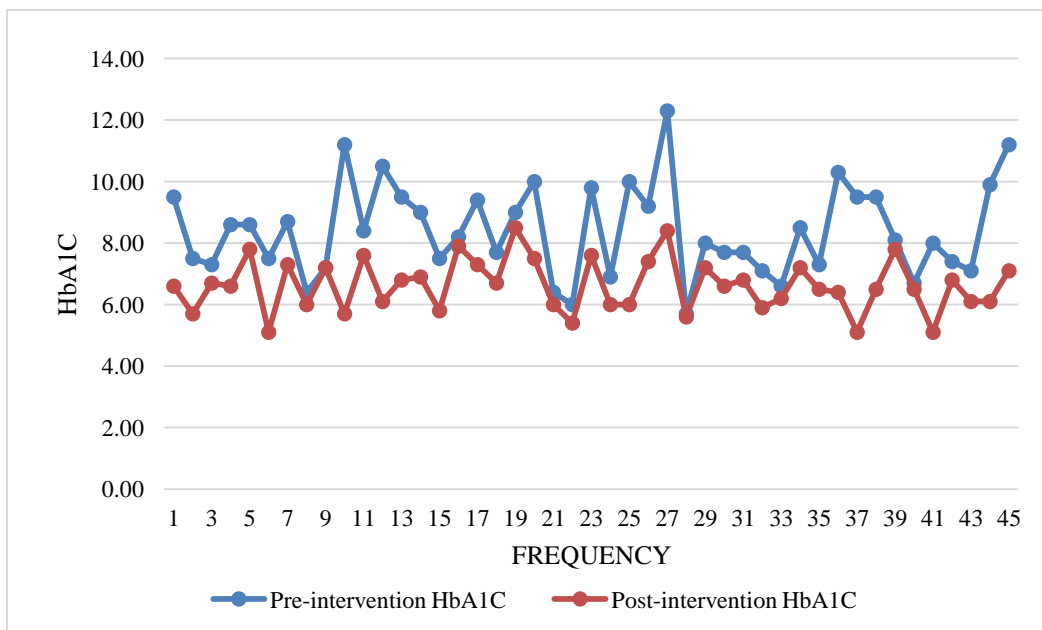
Demographic Parameters	N	%
Age group (in years)		
31-40	6	13.33
41-50	14	31.11
51-60	19	42.22
>60	6	13.33
Gender		
Male	19	42.22
Female	26	57.78

29 (64.5%) patients were taking medications before participating and of these, antidiabetic molecules were reduced in 27 (93.1%) patients and completely stopped in 2 (6.9%) patients after 2-OMEX lifestyle intervention. 16 (35.5%) were recently diagnosed with T2DM and voluntarily decided to comply to the study intervention only. Paired t-test was applied, and there was significant difference ($p < 0.05$) between the pre- and post- 2-OMEX lifestyle intervention parameters like BMI (kg/m^2), weight, waist size, and HbA1C. (Table 2, Figure 1) The mean post-interventional HbA1C was 6.6 ± 0.8 . Pearson’s correlation test was applied, there was no significant correlation between reduction in weight and reduction of HbA1C. (Pearson’s correlation coefficient = -0.051 ; $p = 0.739$)

Table 2: Reduction of Physical measurements and HbA1C

Parameters	Pre-intervention	Post-intervention	Total Reduction	p value
Weight (Mean + S.D.)	74.4 ± 13.5	70.4 ± 12.7	4.3 ± 2.3	<0.001
BMI (Mean + S.D.)	29.3 ± 6.1	27.7 ± 5.6	1.7 ± 0.9	<0.001
Waist (Mean + S.D.)	104.9 ± 10.3	99.6 ± 9.7	5.3 ± 2.7	<0.001
HbA1C (Mean + S.D.)	8.4 ± 1.4	6.6 ± 0.8	1.8 ± 1.4	<0.001
Fasting Insulin (Mean + S.D.)	12.5 ± 5.5	10.7 ± 5.9	1.7 ± 6.8	0.09

Figure 1: Reduction in HbA1C



Discussion

Diabetes is a group of metabolic diseases characterized by hyperglycaemia caused by defects in

insulin secretion and/or action, or both. Sustained hyperglycaemia due to diabetes can lead to long-term damage, dysfunction, and failure of various organs. [1,2] The world faces the rising prevalence and poor

outcomes of type 2 diabetes (T2DM). A rising trend has been observed in the prevalence of diabetes in India and the World. India has a high burden of T2DM (5.3% to 13.6%) and impaired glucose tolerance (8.3%–14.6%). [1] Indian diabetes risk score studies predict a high tide of T2DM in various Indian states. [2–5] The rapidity with which diabetes prevalence is on rise, reflects the far-ranging and rapid socioeconomic. Obesity and insulin resistance, which go hand in hand, have historically been attributed to for T2D risk; recent evidence shows that early loss of β -cell function contributes to the pathogenesis of T2D, especially in nonobese individuals like South Asians. [3] Among Indian adults, around 10% have T2D while 10% are pre-diabetic. [4] T2D is traditionally assumed to be a lifelong disease, which invariably requires medication. The latest position of the American Diabetes Association is that lifestyle intervention as the preferred treatment option for prediabetes and newly diagnosed diabetes up to three months. This is backed by a consensus between the American College of Endocrinology (ACE) and the American Association of Clinical Endocrinologists (AACE) as well. Lifestyle intervention is shown to be safe and highly effective, reducing the progression from pre-diabetic to T2D by more than 40%. [5,6]

Although several modalities of delaying and even preventing T2D using lifestyle modifications or by medicines have been studied ad nauseum, the fact remains that T2D is essentially a lifestyle disease. There have been reports about clinical remission of diabetes by reduction of food intake, and/or use of medication. Food restriction may be done with bariatric surgery, or by restricting food intake by health education and scheduling smaller meals, intermittent fasting etc. [7-9] Now there is some empirical evidence on 2-meal a day regime with 45 min exercise in the form of walking at least 4.5 km (2-OMEX), as a part of ‘World free of obesity and diabetes’ campaign. [10-13]

This study was conducted with the rationale of addressing T2DM remission, and whether it is achievable by limiting to two-meals-a-day coupled with some mandatory exercise which is a part of diabetes management in any standard treatment guidelines. If this is feasible, a very cost-effective and sustainable solution will be available to counter the advancing wave of T2DM in India. The Primary

objective of this study was to determine if 2-OMEX lifestyle causes significant decline of HbA1C levels. The Secondary objective was to determine if 2-OMEX lifestyle causes reduction in weight, waist size, and requirement of anti-diabetic molecules/doses in four months. The hypothesis of insulin resistance causing T2DM is plausible. Meal frequency limitation will likely limit the insulin spikes and thus reduce the cause for insulin resistance and ultimately reduction of the resulting incidence of obesity. [14,15] This hypothesis is also supported by a quasi-experimental study conducted in Nashik, Maharashtra. It reported that the 2-OMEX intervention showing some association with HbA1c and OHA reduction could be working through either or both (a) modest calorie intake reduction and (b) fewer insulin secretion spikes due to fewer meals and hence less insulin resistance. [20] Diabetes mellitus is a lifestyle disease; this study was done with an attempt to challenge the current lifestyle and modify it to a feasible and healthy one.

Conflict Of Interest:

Dr J. V. Dixit, co-author of this study conducts the ‘World free of Obesity and Diabetes’ campaign. However, the findings of the study presented are not affected by this.

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