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Lifestyle interventions and Metformin 1000 mg daily significantly reduce incidence of type two diabetes mellitus among Egyptians with impaired glucose tolerance

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ABSTRACT

The dramatic increase in newly diagnosed cases of type 2 diabetes is a major public health concern within Egyptians in recent years and it is estimated that by the year 2030, Egypt will have at least 8.6 million adults with diabetes. Several studies worldwide were done and concluded that type 2 DM is preventable by specific interventions. Rural Egyptians are thought to be less risky for developing type 2 diabetes because of the less sedentary lifestyle and less obesity compared to urban population, but the problem is that in rural areas the diagnosis of the disease is underestimated because of the less available medical care and primary screening programs. This work applies certain interventions among risky individuals in rural Egypt to determine the rate of type 2 diabetes progression in Asyut university hospital to prove whether they are effective in preventing it among them or not. Randomized 80 subjects with IGT were classified into two groups, group A was given Metformin 500 mg twice daily plus given instructions regarding lifestyle modifications, and group B which was the control group and it was given nothing. Follow up was done for one year and incidence of new cases of diabetes in both groups plus comparable effects on body weight and BMI were recorded. Four cases were newly diagnosed as diabetic patients among group (A) while 12 patients were diagnosed among group (B) by the end of the year and this signifies that new case diabetes was significantly reduced among group (A) than group (B) in favor of group (A). In conclusion, the study ascertained that lifestyle interventions and Metformin 1000 mg daily significantly reduce incidence of type two diabetes mellitus among Egyptians with impaired glucose tolerance (IGT).

Keywords: Diabetes prevention, diabetes in Egypt, Metformin, lifestyle modification.

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Abbreviations: BG: Blood glucose; BMI: body mass index; DPP: diabetes prevention program; DPS: Diabetes prevention study; IDPP: Indian diabetes prevention program; IFG: impaired fasting glucosem, IGT: impaired glucose tolerance; 2hrPP: 2 hour post-prandial.

INTRODUCTION

Diabetes mellitus (DM) is one of the most common chronic diseases in nearly all countries, and continues to increase in numbers and significance as changing lifestyles lead to reduced physical activity, and increased obesity and the global prevalence of DM in the year 2010 among adults has been estimated to be 6.4% (Shaw et al., 2010).

In Egypt, it is estimated that by the year 2030, Egypt will have at least 8.6 million adults suffering the disease (Shaw et al., 2010), it is the eleventh most important cause of premature mortality in Egypt, and it represents the sixth most important cause of disability burden

(NICHP, 2004).

Prospective randomized controlled studies such as the Diabetes Prevention Program (DPP) in the USA (The Diabetes Prevention Program Research Group, 2002), the Finnish Diabetes Prevention Study (DPS) (Tuomilehto et al., 2001), the Da Qing IGT and Diabetes Study in China (Pan et al., 1997) have shown that lifestyle modification involving diet and enhanced physical activity helps to delay or prevent the progression of IGT to diabetes. Pharmacological agents such as metformin have also been found to be effective.

Developing nations, especially Egypt, face an enormous burden from a high prevalence of diabetes; therefore, primary prevention is desirable in these countries (Shaw et al., 2010).

We therefore conducted this study in Egyptian subjects with IGT with the aim of determining whether the incidence of type 2 diabetes could be modified by interventions in rural Egyptians and whether the rate of progression to DM among risky individuals is similar to that found in international large studies.

PATIENTS AND METHODS

Population

This study was conducted on random sample of 80 subjects with risk factors for type 2 DM as (positive family history, obesity, sedentary lifestyle and hypertension) (Majgi et al., 2012), and with impaired glucose tolerance and impaired fasting blood glucose levels (based on a fasting BG and 2hr PPG levels after 75 g glucose test), who were attending the outpatient clinic of diabetes prevention and internal medicine clinic in Asyut University Hospital since November 2009 till November 2010. All patients are among the rural subjects, as we wanted to identify the risk of diabetes progression among this category of people. Rural Egyptians are thought to be less risky to developing type 2 diabetes because of the less sedentary lifestyle and less obesity compared to urban population, but the problem is that in rural areas the diagnosis of the disease is underestimated because of the less available medical care and primary screening programs (Herman et al., 1995).

Study design and intervention

For each subject history of DM in first degree relatives, history and clinical examination of hypertension (defined as ≥140/≥90) and thorough history about lifestyle characteristics including diet, level of exercise and type of work were obtained. Also, assessment of BW and BMI was done. Sedentary lifestyle was determined according to subject's job, method of usual transportation and usual daily activities, then they were randomly classified into two groups: Group A (intervention group): in which 40 participant were instructed about lifestyle interventions: (wt loss, exercise, and healthy diet) plus metformin 500 mg twice daily, and Group B (control group): which was followed up with no specific instructions nor interventions.

For the intervention group (A), instructions were given on an individual basis to stress on lifestyle modifications including: decrease in total caloric intake, decrease carbohydrates and fat in diet, Increase fibers and vegetables, exercise regularly for 20 min a day by any available local means and Metformin 500 mg twice daily was also given.

A special preprinted diet plan instruction sheet was prepared in our diabetes prevention outpatient clinic and it was used to deliver these instructions.

Follow up was done for both groups regularly every month for one year to ensure that subjects follow the instructions and to revise their compliance, follow up was for: Body weight (kg), BMI (kg/m^2), fasting BG level (mmol/dl) and 2hrPPBG level (mmol/dl) all at baseline and at the end of the study (after one year).

Primary outcome

The primary outcome was defined as development of diabetes, indicated by either a fasting plasma glucose of ≥7.0 mmol/L (≥126 mg/dl) and/or a 2hrPP plasma glucose concentration of ≥11.1 mmol/L (≥200 mg/dl) as defined by WHO 1999 (Ramachandran et al., 2006) during an annual follow-up.

Motivation and adherence

The intervention procedure was explained individually at the time of randomization. Thereafter, monthly by outpatient visits and some by telephonic contacts.

Statistical analysis

Statistical analysis was performed using the (SPSS version 9.0) statistical software package, continuous variables were expressed as mean ± SD. Categorical variable were expressed as numbers and percentages. P-value was determined as:

a) $p > 0.05$ was considered statistically insignificant.
b) $p < 0.05$ was considered statistically significant
c) $p < 0.001$ was considered statistically highly significant

Informed verbal consents was taken from all subjects, this study was approved by ethical committee of our institute.

RESULTS

Among the 40 subjects of group (A): 21 of them (52.5%) were with positive family history for type 2 DM and 19 (47.5%) were with negative family history. Sedentary lifestyle was a feature among 29 of the group (72.5%) (known through thorough history). 22 patients of the group (A) were hypertensive (55%), and 18 were not (45%), The mean body weight for group (A) was 96.9 kg (± 7.1) and mean BMI was 30.7 kg/m^2 (± 2.4), the mean fasting glucose level for the participants in group (A) was 6.16 mmol/L (± 0.4) and the 2hrPPG level was 9.5 mmol/L (± 0.8). Among the 40 subjects of group (B): 24 had a positive family history (60%), while 16 were with negative family history (40%), 27 participants were with sedentary lifestyle, 25 were hypertensive (62.5%) and 15 were not (37.5%), the mean body weight was 94.9 kg (± 6.2) and mean BMI was 31.2 kg/m^2 (± 1.6), mean fasting BG was 5.9 mmol/L (± 0.4) and mean 2hrPPG level was 9.4 mmol/L (± 0.7), with no significant statistical difference in these characteristics between two groups:

Table 1. Descriptive statistics of the studied groups.

Parameter		Group A	Group B	P-value
Sex	Male Female	20 (50%) 20 (50%)	21 (52.5%) 19 (47.5%)	NS
Age (years)		55.6 ± 6.2 year	55.6 ± 6.6 year	NS
Family history for DM	Positive Negative	21 (52.5%) 19 (47.5%)	24 (60%) 16 (40%)	NS
Lifestyle	Sedentary Active	29 (72.5%) 11 (27.5%)	27 (67.5%) 13 (32.5%)	NS
Hypertension	Yes No	22 (55%) 18 (45%)	25 (62.5%) 15 (37.5%)	NS
Fasting glucose		6.16 ± 0.4 mmol/L	5.9 ± 0.4 mmol/L	NS
2 HR PPG		9.5 ± 0.8 mmol/L	9.4 ± 0.7 mmol/L	NS
Weight		96.9 ± 7.1 kg	94.9 ± 6.2 kg	NS
BMI		30.7 ± 2.4 kg/m^2	31.2 ± 1.6 kg/m^2	NS

Comparison between the incidence of new case diabetes: in both groups after one year showed 4 newly diagnosed cases of DM among group (A) with a percentage of (10%) **,** and 12 newly diagnosed cases of DM among group (B) with a percentage of (30%). difference between the two groups in the incidence of new case DM was statistically significant.

The change in body weight and BMI in the two groups after one year: The comparison between wt loss in both groups was highly significant in favor of group (A). Also there was a significant reduction in BMI between the two groups in favor of group (A).

Effect on blood glucose levels in both groups: The comparison of effects on 2hr PP glucose was highly significant in favor of group (A) (Table 1).

DISCUSSION

The most important observation in this study is a reduction in the incidence of new case diabetes mellitus in the intervention group (A) more than group (B) after one year by using lifestyle interventions plus metformin 500 mg twice daily. Also these interventions are capable of reducing body weight and BMI in intervention group after the end of the study which is a result that match those with major trials in diabetes prevention as DPP (The Diabetes Prevention Program Research Group, 2002).

The dose of metformin used in this study (1000 mg/day) is higher than that of the dose used in the IDPP study (500 mg/day) (Ramachandran et al., 2006), and less than that of the dose in the DPP (1700 mg/day) (The Diabetes Prevention Program Research Group, 2002), yet, it is effective in reduction of progression rate to diabetes among risky upper Egyptians. The dose used in this study is higher than that used in the IDPP and that may be related to the relative higher values among Egyptians over those found in Indians (Ramachandran et al., 2006).

The progression rate of IGT to diabetes is very high in upper Egyptian subjects, as shown by incidence of 30% per year in the control group, and this is significantly higher than that of Indians (18.3% per year) in the IDPP (Ramachandran et al., 2006), Chinese (11.3% per year) in DA QING study (Pan et al., 1997), Americans (11 per 100 person-years) in DPP [3] and in the FENNISH study subjects (6% per year) (Tuomilehto et al., 2001).

The reduction in body weight and BMI is highly significant among risky individuals who followed the lifestyle instructions plus metformin in group (A) in our study, and these results are consistent with the results of the FENNISH (Tuomilehto et al., 2001) and DPP (The Diabetes Prevention Program Research Group, 2002) studies (Table 2).

CONCLUSION

To conclude, our study showed that the rate of progression of type 2 diabetes among rural Egyptians is higher than that in all previous international studies in the field of diabetes prevention in spite of the lower rate of sedentary life style and the less incidence of obesity. It

Table 2. Comparison between clinical and metabolic parameters after one year in both study groups.

Parameter	Group 1	Group 2	P value
Mean wt reduction	-2.48 kg	+0.83 kg	<0.001
Mean reduction in BMI	-0.86 kg/m^2	+1.08 kg/m^2	<0.001
Mean FG reduction	-0.45 mmol/L	+1.65 mmol/L	<0.001
Mean 2hrPP reduction	-1.39 mmol/L	+1.45 mmol/L	<0.001
No of new case DM	4 (10%)	12 (30%)	<0.001

also proved that reduction of both body weight and BMI plus metformin with a dose of 1000 mg/day which is slightly lesser than that of DPP (The Diabetes Prevention Program Research Group, 2002) and higher than that of the IDPP (Ramachandran et al., 2006) causes a significant decrease in fasting and postprandial blood glucose levels, and consequently decreases the number of new cases of type 2 DM significantly among upper Egyptians.

LIMITATIONS

Our study has the limitations of the small number of subjects (80), and the shorter duration of follow up compared to the large number of subjects and longer duration found in the large trials as DPP (The Diabetes Prevention Program Research Group, 2002). We need to enlarge the number of subjects and prolong the duration of follow up in the future work. Also a wider spectrum of better assessment of other metabolic risk factors that are not included in this study (as lipid profile and HBA1C) might be done in the future research.

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