Original Research Article

Evaluation of lifestyle change & metformin on cardiovascular risk in prediabetes

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Abstract

Aim: To determine the effect of lifestyle change & metformin on cardiovascular risk in prediabetes. **Methodology:** One hundred thirty five subjects were randomized to 3 groups. Group I were on standard care, group II were on intensive life style modification and group III were on intensive LSM+metformin 500 mg twice daily. Standard lifestyle modification measures through moderate intensity activity and dietary changes. BMI, WHR, FBS, haemoglobin A1c (HbA1c), lipid profile were measured at baseline and at 6 months. **Results:** Positive family history for hypertension was observed in 14 in group I, 15 in group II and 22 in group III. Group I had 2, group II had 4 and group III had 3 subjects which showed positive family CVD history. There was significant reduction in weight, BMI, FBS in all groups (P< 0.05). WHR in group I, HbA1c in group III, LDL- C level in group I and triglyceride level in group I showed significant difference (P< 0.05). **Conclusion:** All groups exhibited reduction in fasting blood glucose and weight over six months. Larger scale studies are required for better outcomes.

Keywords: fasting blood glucose, metformin, cardiovascular risk, lifestyle modification

Introduction

Elevated levels of cardiovascular disease(CVD) risk factors and increased prevalence of CVD are seen in individuals with prediabetes [1,2]. Impaired glucose tolerance (IGT) is defined as a fasting glucose level < 7.0 mmol/l and a 2-hours level postoral glucose challenge between 7.8 and 11.1 mmol/l, imparts a markedly increased risk of development of type 2 diabetes with a range from 3.58 to 8.73% per year[3]. The Indian Diabetes Prevention Programme study showed a relative risk reduction of nearly 30 per cent for the development of diabetes with lifestyle modification (LSM) and metformin[4]. Chronic subclinical inflammation is associated with the prediabetic state. A significant linear increase in the incidence of diabetes is seen with increasing quartiles of high-sensitivity C-reactive protein (hsCRP). hsCRP level decreases with interventions such as LSM and drugs such as statins and metformin[5].

The Diabetes Prevention Program (DPP) demonstrated the effectiveness of both intensive lifestyle intervention and metformin therapy in delaying or preventing the development of type 2 diabetes in an ethnically diverse population with IGT[6]. A study in the United States revealed that half of the decline in CVD death was due to improvements in risk factors; 79 per cent attributable to primary prevention and 21 per cent to secondary prevention[7].

Evidence regarding the effects of lifestyle intervention on CVD risk reduction has previously been systematically synthesized by examining 6 of the 7 CVD health indicators mentioned above, especially by examining the different stratum of BMI (e.g., moderate weight loss will reduce both diabetes and CVD risk among overweight or obese populations, as indicated by the 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk[8].

Considering this, the present study was undertaken with the aim to determine the effect of lifestyle modification & metformin on cardiovascular risk in prediabetes.

Methodology

This randomized controlled study was perused with the permission of ethical review committee. A total of one hundred thirty five subjects reported for heath check up were recruited for the study. Inclusion in the study was done with their written consent.

Test such as fasting blood sugar (FBS) or random blood sugar (RBS) was performed to know the prediabetes status. Prediabetes was assessed based on to the American Diabetes Association (ADA) 2011 guidelines. All subjects were assessed for blood pressure, body mass index (BMI) and the waist-hip ratio (WHR). Subjects were randomized to 3 groups. Group I were on standard care, group II were on intensive life style modification and group III were on intensive LSM+ metformin 500 mg twice daily. Standard lifestyle modification measures through moderate intensity activity and dietary changes. BMI was calculated as weight in kg divided by the square of height in meters (kg/m2). WC was obtained at the midpoint between the anterior superior iliac crest and the lowest rib. Hip circumference was measured at the level of the maximal gluteal protrusion. WHR was calculated as waist circumference (cm) divided by hip circumference (cm). FBS, haemoglobin A1c (HbA1c), lipid profile were measured at baseline and at 6 months. Monitoring of ILSM was done by a trained healthcare facilitator. Analysis of the results for statistical inference was carried using chi- square test, where level of significance was set below 0.05.

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Results

Table 1:Baseline characteristics

Parameters	Group I	Group II	Group III	P value
Number	45	50	40	>0.05
M:F	25:20	30:20	15:25	>0.05
Family diabetes history	15	18	16	>0.05
Family hypertension history	14	15	22	>0.05
Family CVD history	2	4	3	>0.05

Out of 45 subjects in group I, males were 25 and females were 20. Group II had 30 males and 20 females and there were 15 males and 25 females in group III. 15 subjects in group I, 18 in group II and 16 in group III had positive family diabetes history. Positive family history for hypertension was observed in 14 in group I, 15 in group II and 22 in group III. Group I had 2, group II had 4 and group III had 3 subjects which showed positive family CVD history. A non- significant difference was seen among all groups (P> 0.05) (Table 1).

Table 2:Change of clinical and laboratory parameters over time in all groups

Parameters	Group I	Group II	Group III
Weight (Kg)			
Baseline	71.5	71.6	69.4
6 months	69.2	70.1	67.2
P value	<0.05	<0.05	<0.05
BMI (kg/m2)			
Baseline	28.5	29.2	28.5
6 months	28.0	28.4	27.4
P value	<0.05	<0.05	<0.05
SBP (mmHg)			
Baseline	124.4	123.6	124.2
6 months	125.4	122.6	122.1
P value	>0.05	>0.05	>0.05
FBS (mg/dl)			
Baseline	109.7	10.9.6	108.2
6 months	98.0	96.9	07.1
P value	<0.05	<0.05	<0.05
WHR			
Baseline	0.87	0.88	0.86
6 months	0.86	0.87	0.85
P value	<0.05	>0.05	>0.05
HbA1c (%)			
Baseline	6.15	6.02	6.11
6 months	6.00	5.98	5.02
P value	>0.05	>0.05	<0.05
Total cholesterol (mg/dl)			
Baseline	192.1	178.8	174.2
6 months	194.3	171.2	184.4
P value	>0.05	>0.05	>0.05
HDL-C (mg/dl)			
Baseline	38.2	36.6	38.2
6 months	39.0	37.2	39.0
P value	>0.05	>0.05	>0.05
LDL-C (mg/dl)			
Baseline	121.4	118.4	105.2
6 months	130.2	110.4	113.2
P value	<0.05	>0.05	>0.05
Triglycerides (mg/dl)			
Baseline	172.2	108.4	156.2
6 months	136.4	124.2	146.3
P value	<0.05	>0.05	>0.05

There was significant reduction in weight, BMI, FBS in all groups (P< 0.05). WHR in group I, HbA1c in group III, LDL- C level in group I and triglyceride level in group I showed significant difference (P< 0.05) (Table 2, graph 1).

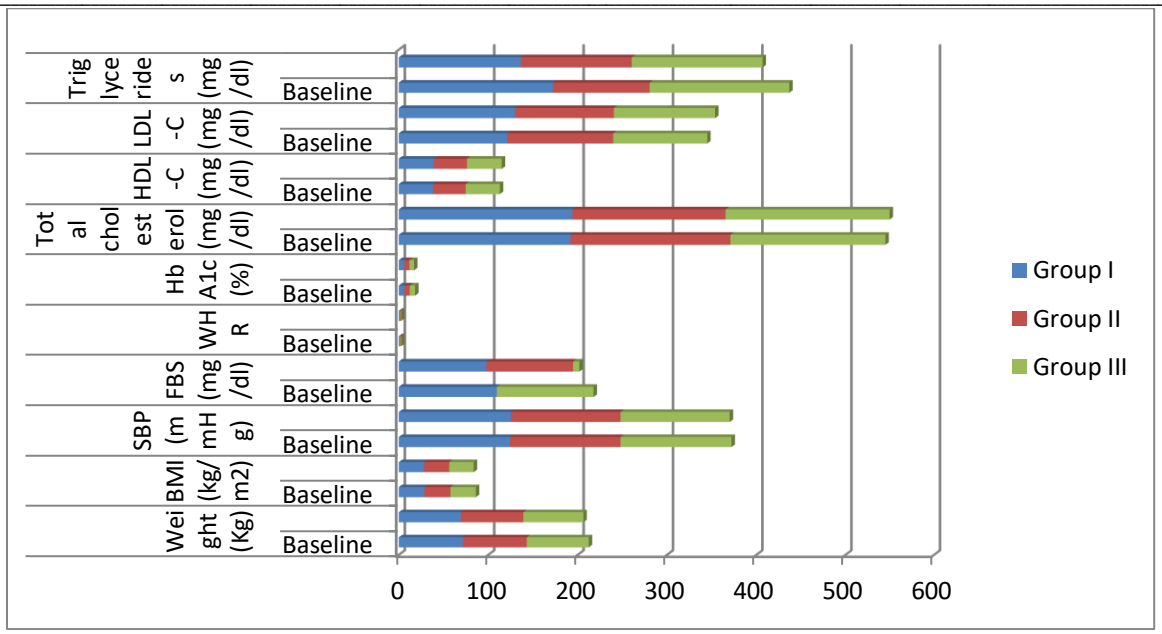

Fig 1: Clinical and laboratory parameters

Discussion

International Diabetes Federation (IDF) (2017) stated that 352 million adults between the ages of 20 and 79 (7.3% of that population) could be classified as having prediabetes[9]. To date no general agreement on laboratory thresholds for prediabetes exists[10]. The American Diabetes Association (ADA) defines prediabetes as impaired fasting glucose (IFG) of 5.6–6.9mmol/L and/or 2h post-challenge glucose of 7.8–11.0mmol/L with a 75 g oral glucose tolerance test (impaired glucose tolerance [IGT]) or based on a HbA1c value of 5.7–6.4%[11]. The World Health Organization (WHO) sets the threshold for prediabetes at an IFG of 6.1–6.9mmol/L. The ADA's lower threshold for IFG is based on the rationale that an IFG near the level of 6.1mmol/L is associated with a higher risk of micro- and macrovascular complications[12].Our study included 135 subjects which were randomized into 3 groups. Group I were on standard care, group II were on intensive life style modification and group III were on intensive LSM+metformin 500 mg twice daily. Kulkarni et al[13] assessed effects of exercise and metformin were evaluated on highsensitivity C-reactive protein (hsCRP) and carotid intima-media thickness (CIMT), surrogate markers of atherosclerosis and CVD compared with standard care. A total of 103 participants were randomized into three arms and followed up for six months. At six months, there was a reduction from baseline in weight and fasting blood sugar (FBS) in all three arms and a reduction in haemoglobin A1c (P=0.03) only in the ILSM+Met arm. The differences in hsCRP over six months within the STD, ILSM and ILSM+Met arms were −0.12 (95% confidence interval, −1.81, 2.08), −0.58 (−2.64, 0.43) and −0.11 (−1.84, 1.56), respectively. There was no difference in hsCRP, CIMT (right) or CIMT (left) between the three arms at six months. Our results demonstrated that group I, males were 25 and females were 20. Group II had 30 males and 20 females and there were 15 males and 25 females in group III. 15 subjects in group I, 18 in group II and 16 in group III had positive family diabetes history. Positive family history for hypertension was observed in 14 in group I, 15 in group II and 22 in group III. Group I had 2, group II had 4 and group III had 3 subjects which showed positive family CVD history. A study comprised of 3,234 individuals with IGT randomly assigned to receive intensive lifestyle intervention, metformin, or placebo. Annual assessment of blood pressure, lipids, electrocardiogram, and CVD events was undertaken. Hypertension was present in 30% of participants at study entry and then increased in the placebo and metformin groups, although it significantly decreased with intensive lifestyle intervention. Triglyceride levels fell in all treatment groups, but fell significantly more with intensive lifestyle intervention. Total cholesterol and LDL cholesterol levels were similar among treatment groups. Intensive lifestyle intervention significantly increased the HDL cholesterol level and reduced the cumulative incidence of the proatherogenic LDL phenotype B. At 3 years of follow-up, the use for pharmacologic therapy to achieve established goals in the intensive lifestyle group was 27–28% less for hypertension and 25% less for hyperlipidemia compared with placebo and metformin groups. Over an average of 3 years, 89 CVD events from 64 participants were positively adjudicated studywide, with no differences among treatment groups[14].It was seen that there was significant reduction in weight, BMI, FBS in all groups (P< 0.05). WHR in group I, HbA1c in group III, LDL- C level in group I and triglyceride level in group I showed significant difference. Zhang et al[14] assessed the effectiveness of lifestyle interventions on CVD risk among adults without IGT or diabetes. Compared to usual care (UC), lifestyle interventions achieved significant improvements in SBP (-2.16mm Hg[95%CI, -2.93, -1.39]), DBP (-1.83mmHg[-2.34, -1.31]), TC (-0.10mmol/L[-0.15, -0.05]), LDL-C (-0.09mmol/L[-0.13, -0.04]), HDL-C (0.03mmol/L[0.01, 0.04]), and TG (-0.08mmol/L[-0.14, -0.03]). Similar effects were observed among both low-and high-range study groups except for TC and TG. Similar effects also appeared in SBP and DBP categories regardless of follow-up duration. PA+D interventions had larger improvement effects on CVD risk factors than PA alone interventions. In adults without IGT or diabetes, lifestyle interventions resulted in significant improvements in SBP, DBP, TC, LDL-C, HDL-C, and TG, and might further reduce CVD risk.

Conclusion

All groups exhibited reduction in fasting blood glucose and weight over six months. Larger scale studies are required for better outcomes.

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