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ORIGINAL RESEARCH

ASSESSMENT OF EFFECT OF ATORVASTATIN ON GLYCAEMIC PARAMETERS IN NORMOGLYCAEMIC AND PREDIABETIC SUBJECTS

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ABSTRACT

Background: To assess effect of Atorvastatin on glycaemic parameters in normoglycaemic and prediabetic subjects.

Methods: Seventy- eight patients, aged 18 to 60 years of both genders receiving Atorvastatin (≤1 month) for dyslipidemia were divided into three groups of 26 each. Group I was normoglycaemic, group II was impaired fasting glucose (IFG) (baseline fasting blood glucose level 100-125 mg/dl with normal 2 hours GTT) and group III was impaired glucose tolerance (IGT) (baseline 2 hours post glucose blood sugar 140-199 mg/dl) group. Every subject took atorvastatin, and they were all followed up with after six, twelve, and eighteen months. Every follow-up evaluation included an assessment of glycaemic status. Parameters such as FBS (mg/dl), 2-hr PPBS (mg/dl) and HbA1c % were recorded.

Results: At T1, T2 and T3, FBG (mg/dl) in group I found to be 89.4, 92.3 and 96.4, in group II was 111.3, 113.2 and 117.5 and in group III was 108.2, 109.1 and 108.4 respectively. 2 hours PPBG (mg/dl) in group I was 116.5, 120.4 and 123.9, in group II was 126.7, 128.9 and 131.4 and in group III was 154.3, 160.7 and 166.5 respectively. HbA1c % in group I was 5.3, 5.6 and 5.8, in group II was 5.6, 6.2 and 6.4 and in group III was 6.1, 6.3 and 6.5 respectively.

Conclusion: Longer durations of atorvastatin therapy have been shown to induce glucose intolerance in people who are normoglycemic and to accelerate the development of diabetes in people who are prediabetic.

Keywords: Atorvastatin, diabetes mellitus, dyslipidemia

INTRODUCTION

Globally, diabetes mellitus affects 387 million people and is predicted to affect 592 million by 2035, making it a public health concern. With over 62 million diabetics and predictions that the number could rise to 80 million by 2030, diabetes is on the verge of becoming a possible epidemic in India.[1] Obesity and dyslipidemia are often linked to type 2 diabetes, which is a combined risk factor for cardiovascular disease. Diabetes is a coronary heart disease (CHD) risk factor for setting therapeutic objectives for LDL cholesterol of less than 100 mg/dl, which would necessitate the use of cholesterol-lowering medications, especially statins, according to the National Cholesterol Education Program Adult Treatment Panel III (ATP III).[2,3]

Statin medication lowers cardiovascular risk, but there is disagreement over whether it also increases the risk of developing diabetes.[4] Atorvastatin is a commonly prescribed medication used to lower cholesterol levels, specifically low-density lipoprotein (LDL) cholesterol, and reduce the

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risk of cardiovascular events. While its primary role is in lipid management, there has been interest in understanding its effects on glucose metabolism, especially in individuals with normoglycemia (normal blood sugar levels) and prediabetes (higher than normal blood sugar levels, but not yet in the diabetic range).[5]

Atorvastatin has been associated with modest reductions in insulin sensitivity in some studies, which could contribute to slight increases in fasting glucose levels, particularly in individuals with prediabetes.[6] There is limited evidence suggesting that statins, including atorvastatin, may affect pancreatic beta-cell function, potentially influencing glucose metabolism. However, the exact mechanisms and clinical implications are still under investigation.[7] The present study was conducted to assess effect of Atorvastatin on glycaemic parameters in normoglycaemic and prediabetic subjects.

MATERIALS & METHOD

This prospective, observational study comprised of seventy- eight patients, aged 18 to 60 years of both genders receiving Atorvastatin (≤1 month) for dyslipidemia. Approval from the ethical review committee was obtained. The prediabetic stage was defined as FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) impaired fasting glucose (IFG), or 2 hours plasma glucose in the 75g oral glucose tolerance test (OGTT): 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT), or HbA1c: 5.7 -6.4%.

Data such as name, age, etc. was recorded. Patients were divided into three groups of 26 each. Group I was normoglycaemic, group II was impaired fasting glucose (IFG) (baseline fasting blood glucose level 100-125 mg/dl with normal 2 hours GTT) and group III was impaired glucose tolerance (IGT) (baseline 2 hours post glucose blood sugar 140-199 mg/dl) group. Every subject took atorvastatin, and they were all followed up with after six, twelve, and eighteen months. Every follow-up evaluation included an assessment of glycaemic status. Parameters such as FBS (mg/dl), 2-hr PPBS (mg/dl) and HbA1c % were recorded. The results were compiled and subjected to statistical analysis using the Mann- Whitney U test. P value less than 0.05 was regarded as significant.

RESULTS

Table I Baseline characteristics

Parameters	Group I	Group II	Group III	P value
BMI (Kg/m2)	23.6	24.1	24.3	0.94
SBP (mm of Hg)	125.6	124.4	126.8	0.81
DBP (mm of Hg)	70.2	68.6	74.2	0.63
FBG (mm of Hg)	86.4	117.2	106.2	0.04
2 hours PPBG (mm of Hg)	112.4	128.4	154.2	0.02
HbA1c %	5.7	5.9	6.3	0.05
TC (mg/dl)	214.6	187.4	190.6	0.92
TG (mg/dl)	206.4	156.8	168.4	0.15
HDL-C (mg/dl)	42.8	41.6	41.2	0.64
LDL-C (mg/dl)	135.2	112.6	118.4	0.75

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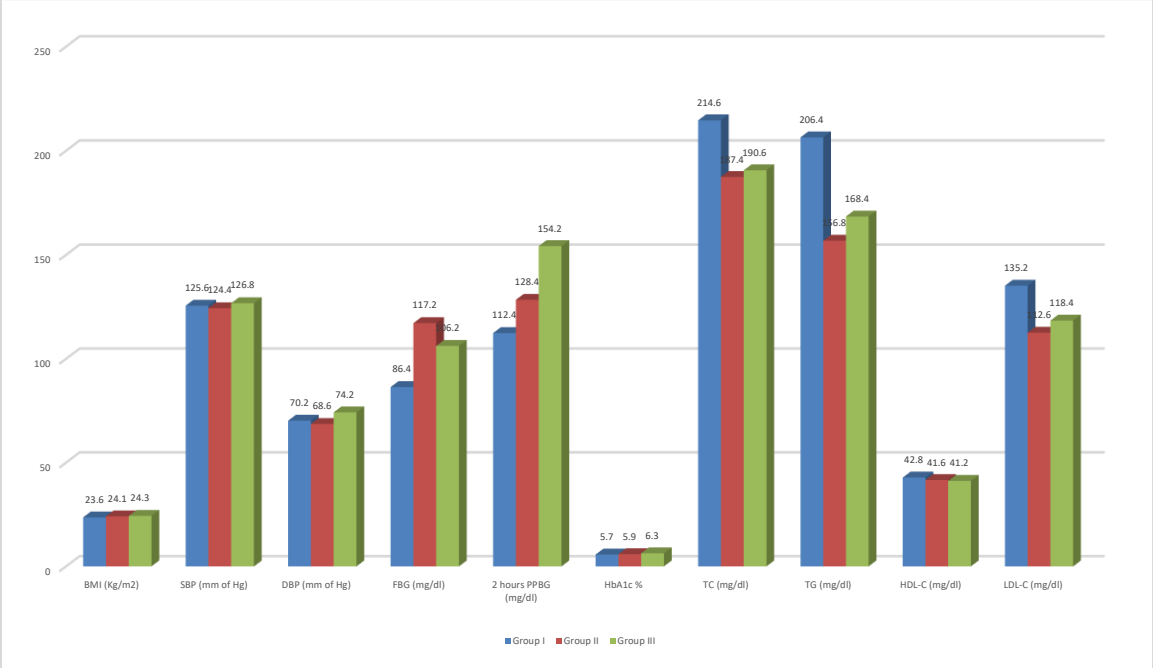
In group I, group II and group III, the mean BMI (Kg/m2) was 23.6, 24.1 and 24.3 respectively. SBP (mm of Hg) was 125.6, 124.4 and 126.8, DBP (mm of Hg) was 70.2, 68.6 and 74.2, FBG (mm of Hg) was 86.4, 117.2 and 106.2, 2 hours PPBG (mm of Hg) was 112.4, 128.4 and 154.2 HbA1c % was 5.7, 5.9 and 6.3, TC (mg/dl) was 214.6, 187.4 and 190.6, TG (mg/dl) was 206.4, 156.8 and 168.4, HDL-C (mg/dl) was 42.8, 41.6 and 41.2 and LDL-C (mg/dl) was 135.2, 112.6 and 118.4 respectively. The difference was non- significant (P> 0.05) (Table I).

Table II Assessment of parameters

Parameters	Group I	Group II	Group III	P value
BMI (Kg/m2)	23.6	24.1	24.3	0.94
SBP (mm of Hg)	125.6	124.4	126.8	0.81
DBP (mm of Hg)	70.2	68.6	74.2	0.63
FBG (mg/dl)	86.4	117.2	106.2	0.04
2 hours PPBG (mg/dl)	112.4	128.4	154.2	0.02
HbA1c %	5.7	5.9	6.3	0.05
TC (mg/dl)	214.6	187.4	190.6	0.92
TG (mg/dl)	206.4	156.8	168.4	0.15
HDL-C (mg/dl)	42.8	41.6	41.2	0.64
LDL-C (mg/dl)	135.2	112.6	118.4	0.75

The mean BMI (Kg/m2) was 23.6, 24.1 and 24.3, SBP (mm of Hg) was 125.6, 124.4 and 126.8, DBP (mm of Hg) was 70.2, 68.6 and 74.2, FBG (mm of Hg) was 86.4, 117.2 and 106.2, 2 hours PPBG (mm of Hg) was 112.4, 128.4 and 154.2, HbA1c % was 5.7, 5.9 and 6.3, TC (mg/dl) was 214.6, 187.4 and 190.6, TG (mg/dl) was 206.4, 156.8 and 168.4, HDL-C (mg/dl) was 42.8, 41.6 and 41.2 and LDL-C (mg/dl) was 135.2, 112.6 and 118.4 in group I, II and III respectively. The difference was significant (P< 0.05) (Table II, graph I).



Graph I Assessment of parameters

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Table III Comparison of FBG, 2 hours PPBG and HbA1c at regular interval

Parameters	Period	T1	T2	T3	P value
FBG (mg/dl)	Group I	89.4	92.3	96.4	0.98
	Group II	111.3	113.2	117.5	0.56
	Group III	108.2	109.1	108.4	0.72
2 hours PPBG (mg/dl)	Group I	116.5	120.4	123.9	0.05
	Group II	126.7	128.9	131.4	0.97
	Group III	154.3	160.7	166.5	0.34
HbA1c %	Group I	5.3	5.6	5.8	0.64
	Group II	5.6	6.2	6.4	0.81
	Group III	6.1	6.3	6.5	0.93

At T1, T2 and T3, FBG (mg/dl) in group I found to be 89.4, 92.3 and 96.4, in group II was 111.3, 113.2 and 117.5 and in group III was 108.2, 109.1 and 108.4 respectively. 2 hours PPBG (mg/dl) in group I was 116.5, 120.4 and 123.9, in group II was 126.7, 128.9 and 131.4 and in group III was 154.3, 160.7 and 166.5 respectively. HbA1c % in group I was 5.3, 5.6 and 5.8, in group II was 5.6, 6.2 and 6.4 and in group III was 6.1, 6.3 and 6.5 respectively.

Graph II Comparison of FBG, 2 hours PPBG and HbA1c at regular interval

DISCUSSION

For normoglycemic individuals, atorvastatin is generally considered safe in terms of glycemic control. In prediabetic individuals, monitoring of fasting blood glucose and HbA1c levels is recommended during atorvastatin therapy, although routine adjustments in therapy based solely on mild changes may not be necessary.[8] Lifestyle modifications (e.g., diet, exercise) remain crucial in managing lipid levels and glucose metabolism in both normoglycemic and prediabetic individuals.[9] The present study was conducted to assess effect of Atorvastatin on glycaemic parameters in normoglycaemic and prediabetic subjects.

We found that in group I, group II and group III, the mean BMI (Kg/m2) was 23.6, 24.1 and 24.3 respectively. SBP (mm of Hg) was 125.6, 124.4 and 126.8, DBP (mm of Hg) was 70.2, 68.6 and 74.2, FBG (mm of Hg) was 86.4, 117.2 and 106.2, 2 hours PPBG (mm of Hg) was 112.4, 128.4

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and 154.2. Parida et al[10] evaluated the effect of Atorvastatin on glycaemic status of normoglycaemic and prediabetic individuals. Subjects were recruited depending on their glycaemic status into three groups: normoglycaemic, Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) group. All three groups as a whole, irrespective of dose of Atrovastatin therapy, showed a statistically significant ($p<0.0001$) increase in all glycaemic parameters. In normoglycaemic group with low dose Atorvastatin, there was no significant change in 2-hour Post Prandial Blood Sugar (PPBS) but change in HbA1c% ($p=0.0004$) and FBS ($p<0.0001$) was significant, whereas, with high dose, changes in 2-hr PPBS and HbA1c % were significant from 6 months onwards. In IFG group, both with low and high dose of Atorvastatin, there was significant change in all glycaemic parameters from 12 months onwards. In case of IGT, especially with high dose Atorvastatin, significant changes were evident from 6 months onwards. It was found that HbA1c % was 5.7, 5.9 and 6.3, TC (mg/dl) was 214.6, 187.4 and 190.6, TG (mg/dl) was 206.4, 156.8 and 168.4, HDL-C (mg/dl) was 42.8, 41.6 and 41.2 and LDL-C (mg/dl) was 135.2, 112.6 and 118.4 respectively. In our study, the mean BMI (Kg/m2) was 23.6, 24.1 and 24.3, SBP (mm of Hg) was 125.6, 124.4 and 126.8, DBP (mm of Hg) was 70.2, 68.6 and 74.2, FBG (mm of Hg) was 86.4, 117.2 and 106.2, 2 hours PPBG (mm of Hg) was 112.4, 128.4 and 154.2, HbA1c % was 5.7, 5.9 and 6.3, TC (mg/dl) was 214.6, 187.4 and 190.6, TG (mg/dl) was 206.4, 156.8 and 168.4, HDL-C (mg/dl) was 42.8, 41.6 and 41.2 and LDL-C (mg/dl) was 135.2, 112.6 and 118.4 in group I, II and III respectively. Collins et al[11] found that both among the participants who presented with diabetes and among those who did not, there were highly significant reductions of about a quarter in the first event rate for major coronary events, for strokes, and for revascularisations. For the first occurrence of any of these major vascular events among participants with diabetes, there was a definite 22% reduction in the event rate (601 [20.2%] simvastatin-allocated vs 748 [25.1%] placebo-allocated, $p<0.0001$), which was similar to that among the other high-risk individuals studied. There were also highly significant reductions of 33% (95% CI 17-46, $p=0.0003$) among the 2912 diabetic participants who did not have any diagnosed occlusive arterial disease at entry, and of 27% (95% CI 13-40, $p=0.0007$) among the 2426 diabetic participants whose pretreatment LDL cholesterol concentration was below 3.0 mmol/L (116 mg/dL). The proportional reduction in risk was also about a quarter among various other subcategories of diabetic patient studied, including: those with different duration, type, or control of diabetes; those aged over 65 years at entry or with hypertension; and those with total cholesterol below 5.0 mmol/L (193 mg/dL). In addition, among participants who had a first major vascular event following randomisation, allocation to simvastatin reduced the rate of subsequent events during the scheduled treatment period.

We observed that at T1, T2 and T3, FBG (mg/dl) in group I found to be 89.4, 92.3 and 96.4, in group II was 111.3, 113.2 and 117.5 and in group III was 108.2, 109.1 and 108.4 respectively. 2 hours PPBG (mg/dl) in group I was 116.5, 120.4 and 123.9, in group II was 126.7, 128.9 and 131.4 and in group III was 154.3, 160.7 and 166.5 respectively. HbA1c % in group I was 5.3, 5.6 and 5.8, in group II was 5.6, 6.2 and 6.4 and in group III was 6.1, 6.3 and 6.5 respectively. Lee et al[12] reported that statin discontinuation could be considered based on the pretreatment lipid profiles, especially for subjects with baseline LDL-C less than 123 mg/dL. However, considering that statin therapy is not for reducing LDL-C itself but for reducing CVD risk, their results should be interpreted carefully to make the decision whether statin should be continued or not.

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CONCLUSION

Longer durations of atorvastatin therapy have been shown to induce glucose intolerance in people who are normoglycemic and to accelerate the development of diabetes in people who are prediabetic.

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