



A STUDY ON EFFECT OF ATORVASTATIN ON INSULIN SENSITIVITY

General Medicine

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ABSTRACT

INTRODUCTION: The HMG CoA reductase inhibitors or statins have been a primary force in the management of hypercholesterolemia for many years and are important in the primary and secondary prevention of heart disease. However, increasingly it is being shown that the statins have clinical benefits that appear to be greater than those one would expect from improvement in the lipid profile alone. These pleiotropic actions include direct effects on vascular tissue, kidney, bone and glucose metabolism.

Clinical trials and animal studies have shown that statins reduce cardiovascular disease risks

These agents improve insulin sensitivity and reduce the likelihood of persons progressing from impaired glucose tolerance to type II diabetes.

Various studies have observed the effect of statins on insulin sensitivity in Type 2 Diabetic mellitus. Since statins are commonly used for the treatment of hypercholesterolemia in clinical practice, it is important to know their effect on insulin sensitivity.

AIMS AND OBJECTIVES: To evaluate the effects of Atorvastatin on insulin sensitivity.

MATERIALS AND METHODS: This study was done at Alluri Sitarama Raju Academy of Medical Sciences, Eluru From December 2020 to June 2021, Ninety patients are screened for the study from a random population of 110 hypertensive patients receiving atenolol as anti-hypertensive drug, by a random selection process, from which 68 patients are considered based on patient compliance

INCLUSION CRITERIA: Dyslipidaemia, Hypertension, Age 40 to 50 years, not receiving any drugs other than mentioned above, not suffering from any other diseases.

EXCLUSION CRITERIA: Those patients not satisfying the inclusion criteria are excluded.

RESULTS: In this study It is found that in the group receiving atenolol and atorvastatin, TC is reduced from initial values of 280 +/- 20 mg/dl to 202 +/- 12 mg/dl ($p=0.05$). HDLC is increased from 45 +/- 10 mg/dl to 52 +/- 12 mg/dl ($p=0.04$). LDLC reduced from 180 +/- 20 mg/dl to 148 +/- 12 mg/dl ($p=0.05$). VLDLC, Triglycerides values remain almost same, and changes are statistically insignificant. FBS values changed from initial 106 +/- 6 mg/dl to 88 +/- 4 mg/dl ($p=0.04$).

CONCLUSION: Statins improve insulin sensitivity even in normoglycemics and prevent the progression of IGT to type 2 diabetes and had a role in prevention of cardiac disease.

KEYWORDS

INTRODUCTION:

The 3-Hydroxyl-3 methyl glutaryl Coenzyme A (HMG CoA) reductase inhibitors or statins have been a primary force in the management of hypercholesterolemia for many years and are important in the primary and secondary prevention of heart disease.

However, increasingly it is being shown that the statins have clinical benefits that appear to be greater than those one would expect from improvement in the lipid profile alone. These pleiotropic actions include direct effects on vascular tissue, kidney, bone and glucose metabolism.

The hyperinsulinaemic / insulin resistant states is a metabolic condition linked to widespread and heterogeneous clinical syndrome like hypertension, obesity, type-2 diabetes, dyslipidaemia, atherosclerosis and coronary vascular disease. About 25% of the non-diabetic population shows abnormalities of insulin sensitivity and compensatory hyperinsulinaemia.

India is facing a diabetic explosion. It has the world's largest diabetic population about 25 million, and the number is predicted to rise to 35 million by 2010 and to 57 million by 2025. The exact nature of the increase in prevalence of type 2 diabetes is unknown, and both genetic and lifestyle factors are being blamed. The urbanization tendency of rural India puts the incidence of diabetes with all its complications and mortality on the rise. Insulin resistance is supposed to play a major role in the development of diabetes. Considering the magnitude and severity of hyperinsulinaemic / insulin resistant state, pharmaceutical measures are initiated early in an Indian.

Clinical trials and animal studies (in vivo and in vitro) have shown that statins reduce cardiovascular disease risks and events, progression of nephropathy, development of diabetes and fracture rates, these are benefits that go beyond lipid lowering alone. These agents improve insulin sensitivity and reduce the likelihood of persons progressing from impaired glucose tolerance to type II diabetes.

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This study was done at Alluri Sitarama Raju Academy of Medical Sciences, Eluru from December 2020 to June 2021, Ninety patients are screened for the study from a random population of 110 hypertensive patients receiving atenolol as anti-hypertensive drug, by a random selection process, from which 68 patients are considered based on patient compliance, intelligence to understand dietary prescriptions and directions and whether free from any other disease on initial medical testing. Written consent for the study as per protocol is obtained.

The patients were randomized into two groups, of 34 patients each, by a random selection process. The experimental group consisting of 34 dyslipidaemic and hypertensive patients receiving atorvastatin 10mg/day and atenolol 50 mg/day at the Hypertension OPD at Govt Stanley Medical College Hospital are chosen as volunteers and are

compared with another group of 34 hypertensive patients receiving atenolol 50 mg/day only. Uniform diet pattern is prescribed to all of them.

INCLUSION CRITERIA : Dyslipidaemia, Hypertension, Age 40 to 50 years, not receiving any drugs other than mentioned above, not suffering from any other diseases.

EXCLUSION CRITERIA: Those patients not satisfying the inclusion criteria are excluded.

RESULTS:

Table – 1 shows the anthropometric and biochemical characteristics of the subject in the control and Atorvastatin treated groups at the start of the study. The proportion of the male & female in both the groups was similar. Proportion of subjects having positive family history of diabetes and blood pressure in both the groups were also similar.

It is found that in the group receiving atenolol and atorvastatin (experimental group), TC is reduced from initial values of 280 ± 20 mg/dl to 202 ± 12 mg/dl ($p = 0.05$). HDLC is increased from 45 ± 10 mg/dl to 52 ± 12 mg/dl ($p = 0.04$). LDLC reduced from 180 ± 20 mg/dl to 148 ± 12 mg/dl ($p = 0.05$). VLDLC, Triglycerides values remain almost same, and changes are statistically insignificant. FBS values changed from initial 106 ± 6 mg/dl to 88 ± 4 mg/dl ($p = 0.04$). In the control group receiving atenolol only, it is observed that TC is from initial values of 140 ± 20 mg/dl to 112 ± 8 mg/dl. HDLC changes from 40 ± 10 mg/dl to 44 ± 9 mg/dl. LDLC changes from 110 ± 30 mg/dl to 95 ± 13 mg/dl. VLDLC, TG and FBS values remain almost same, and all the value changes are statistically insignificant.

Table 2 Showing serum insulin and HOMA-IR 2 values of Different group

(HOMA 2-IR) values of different groups, in order to determine insulin sensitivity. It was observed that in the experimental group, serum insulin value initially is 20 ± 5 microU/ml and finally is 18 ± 3 microU/ml ($p = 0.03$), and in the control group, serum insulin value initially is 18 ± 5 microU/ml and finally is 31 ± 2 microU/ml. HOMA 2 values (insulin resistance or IR) of the two groups of patients show that in the experimental group it was 4.3 ± 0.5 microU/ml initially and 4.3 ± 0.3 microU/ml finally, showing increase in insulin sensitivity by atorvastatin.

TABLE 1: Anthropometrical, Clinical and Biochemical characters of volunteers

	Experimental Group (34)	Control Group (34)
AGE	45 ± 4	43 ± 3
MALES	21	21
FEMALES	13	13
BMI	27.3 ± 12	27.5 ± 2.1
SBP	154 ± 16	146 ± 24
DBP	100 ± 12	94 ± 8
T. CHOLESTEROL	280 ± 20	140 ± 20
LDL	180 ± 20	110 ± 20
HDL	45 ± 10	40 ± 10
VLDL	40 ± 5	35 ± 15
TGL	220 ± 20	120 ± 20
FBS	106 ± 6	96 ± 6
FASTING INSULIN	20 ± 5	18 ± 5

Table 2: Showing serum insulin and HOMA-IR 2 values of Different group

	S. INSULIN INITIAL VALUE	S. INSULIN END VALUE	HOMA – 2 IR INITIAL VALUE	HOMA- 2 IR END VALUE
EXPERIMENTAL GROUP	20 ± 5	18 ± 3	4.3 ± 0.5	3.7 ± 0.4
CONTROL GROUP	18 ± 5	31 ± 2	4.3 ± 0.3	4.3 ± 0.2

DISCUSSION:

The study shows that atorvastatin increases insulin sensitivity in normal subjects. Compared with placebo, treatment with atorvastatin (10 mg/day) resulted in significant reduction in the HOMA index. In addition, significant reductions in total and LDL cholesterol

concentrations were observed in the atorvastatin group. It thus corroborates previous findings that though uncertain, statin therapy can affect insulin resistance syndrome. Insulin Resistance refers to the reduction in insulin mediated glucose uptake in insulin sensitive tissues, specifically in the skeletal muscles. As a compensatory response, hyperinsulinemia ensues to maintain normal blood glucose levels.

In epidemiological studies, fasting insulin level is commonly used as a surrogate marker of insulin resistance. In normoglycemic subjects, fasting insulin correlated well with whole body glucose uptake. Although fasting insulin is a reasonable measure of insulin resistance, it is potentially confounded by variability in insulin secretion. Thus the indexes derived from fasting insulin and glucose, such as Homeostasis Model Assessment (HOMA), the Quantitative Insulin Sensitivity Check Index (QUICKI), and the Insulin Sensitivity Index (ISI) developed by Gutt and coworkers, have been more widely used to assess insulin resistance in clinical and population based studies.

Statins are the more effective LDL – cholesterol-lowering drugs by about 25% to 60%. In addition, they also increase HDL-cholesterol by about 5% to 10% and decrease triglycerides by about 10% to 30%. The effect on triglycerides is proportional to the decrease in LDL-cholesterol. Pre diabetes and type 2 diabetes are characterized with low grade inflammation.

Aggressive lowering of LDL-cholesterol by atorvastatin decreases hsCRP by 42% vs 9.6% with placebo. Several studies have proved that LDL reduction by statins is associated with improved endothelial function due to enhanced NO release. Besides these actions, the reduction in risk of development of diabetes is due to improved insulin sensitivity by statins.

CONCLUSION:

Statins improve insulin sensitivity even in normoglycemics and prevent the progression of IGT to type 2 diabetes. Statins reduce levels of interleukin 6 and TNF through its antiinflammatory activity.

These cytokines inhibit lipoprotein lipase activity and to stimulate lipolysis in adipose tissue.

Atorvastatin may therefore interrupt the progression from central obesity to insulin resistance mediated by the adipose tissue derived cytokines.

Impaired endothelial function has been shown to correlate with insulin resistance.

Atorvastatin by restoring endothelial function, may beneficially affect glucose and insulin transport.

Since statins are used for the treatment of hypercholesterolemia in clinical practice, it is important to know their effect on insulin sensitivity.

If further studies confirm the observation that statins improve insulin sensitivity and reduce the onset of type 2 diabetes, the perceived benefit of cardiovascular intervention in clinical trials could be greatly increased and the long term cost-benefit analysis of those interventions may be more positive than previous studies have estimated.

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