ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 03 | March - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EVALUATION OF THE EFFECT OF ATORVASTATIN ON INSULIN SENSITIVITY

General Medicine

Dr Shaik Zubair Ahamed Postgraduate, Department of General medicine, Narayana medical college, Nellore-524003

Dr V Mahesh* Associate Professor department of General medicine, Narayana medical college, Nellore– 524003 *Corresponding Author

ABSTRACT

Background and Objectives: 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. statins have clinical benefits that appear to be greater than those onewould expect from improvement in the lipid profile alone .Objective of the study is to evaluate the effects of Atorvastatin on insulin sensitivity. **Methodology:** The study deals with the effect of Atorvastatin on insulin sensitivity conducted at Hypertension outpatient department of Narayana Medical College Hospital, Nellore. 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 Narayana Medical College Hospital are chosen as volunteers and are compared with another group of 34 hypertensive patients receiving atenolol 50 mg/day only. **Results:** It has been suggested that HMG Co-A reductase inhibitors ('statins') may reduce the risk of developing type 2 Diabetes mellitus., Statin use was associated with a 10-month delay before newly treated diabetic subjects needed to start insulin treatment. This study suggest that statins increase insulin sensitivity even in normoglycemic patients. **Conclusion:** 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.

KEYWORDS

1. 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 pleotrophic 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. Diabetes affected 194 million people worldwide in 2003 and is estimated to affect 299 to 333 million by 2025, according to International Diabetes Federation. The South Asian population is known to be at risk of a atherosclerosis, even though the subject does not have clinical evidence of coronary heart disease.

In India, population is vast, and there is heterogenecity of origin or race, geography and habit, socioeconomic status, dietary habits, methods of cooking and preservation, use of pesticides etc. These factors along with known variables like age, sex etc. influence lipid profile of individuals. India is facing a diabetic explosion.

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 (invivo and invitro) 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. 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.

2.METHODOLOGY :

The study deals with the effect of Atorvastatin on insulin sensitivity conducted at Hypertension outpatient department of Narayana Medical College Hospital.

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 Narayana 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.

2.1 Inclusion Criteria

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

2.2 Exclusion Criteria

Those patients not satisfying the inclusion criteria are excluded.

Statistical Analysis

The statistical analysis is done based on paired t-test, and p-value is calculated using paired t-statistic.

3 .OBSERVATIONS AND RESULTS

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 3: Values of Blood parameters of Control Group

	0 mon	1 mon	2 mon	3 mon	4 mon	5 mon	6 mon	7 mon	8 mon	9 mon	10 mon	11 mon	12 mon
T. cholesterol	140 ± 20	138 ± 8	136 ± 16	134 ± 15	132 ± 15	130 ± 16	128 ± 8	125 ± 10	123 ± 8	120 ± 12	117 ± 6	115 ± 6	112 ± 18
HDL	40 ± 10	40 ± 8	41 ± 9	41 ± 7	41 ± 7	42 ± 6	42 ± 7	42 ± 7	42 ± 6	43 ± 8	43 ± 9	43 ± 8	44 ± 9
LDL	110 ± 30	110 ± 12	108 ± 18	108 ± 16	108 ± 14	106 ± 12	106 ± 13	106 ± 13	102 ± 11	100 ± 18	98 ± 16	97 ± 10	95 ± 13
VLDL	35 ± 15	35 ± 9	35 ± 8	35 ± 7	35 ± 8	35 ± 10	35 ± 10	35 ± 8	35 ± 12	35 ± 14	35 ± 11	35 ± 6	35 ± 8
TGL	120 ± 20	120 ± 11	120 ± 8	119 ± 12	120 ± 14	118 ± 12	119 ± 8	116 ± 17	118 ± 8	118 ± 11	119 ± 12	116 ± 12	116 ± 13
FBS	96 ± 10	96 ± 8	94 ± 6	94 ± 5	92 ± 8	94 ± 8	94 ± 5	92 ± 6	92 ± 9	92 ± 8	96 ± 7	94 ± 8	94 ± 6

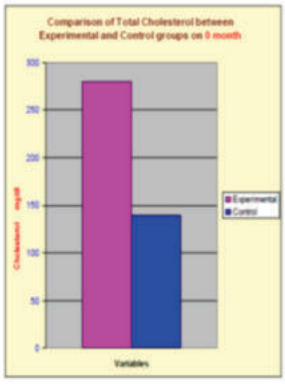
Table 2: Values of Blood parameters of Experimental Group

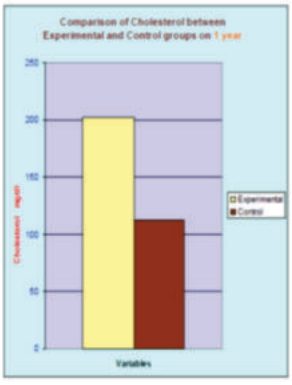
	0 mon	1 mon	2 mon	3 mon	4 mon	5 mon	6 mon	7 mon	8 mon	9 mon	10 mon	11mon	12 mon
T. cholesterol	280 ± 20	278 ± 18	276 ± 16	260 ± 18	256 ± 16	248 ± 18	240 ± 16	234 ± 12	226 ± 11	218 ± 13	212 ± 12	208 ± 10	202 ± 12
HDL	45 ± 10	45 ± 12	46 ± 12	46 ± 13	47 ± 12	48 ± 16	48 ± 8	49 ± 11	50 ± 14	50 ± 10	51 ± 13	51 ± 11	52 ± 12
LDL	180 ± 20	178 ± 18	176 ± 12	172 ± 11	172 ± 12	168 ± 18	166 ± 10	164 ± 8	160 ± 12	160 ± 8	159 ± 10	152 ± 8	148 ± 12
VLDL	40 ± 5	40 ± 3	40 ± 2	39 ± 6	39 ± 5	39 ± 6	39 ± 5	39 ± 4	39 ± 2	39 ± 4	39 ± 3	39 ± 4	39 ± 3
TGL	220 ± 20	218 ± 18	218 ± 16	214 ± 10	214 ± 9	216 ± 8	212 ± 10	210 ± 11	210 ± 12	206 ± 6	214 ± 8	208 ± 9	212 ± 6
FBS	106 ± 6	106 ± 8	108 ± 7	103 ± 4	101 ± 3	101 ± 4	98 ± 8	98 ± 6	96 ± 5	95 ± 4	92 ± 8	98 ± 3	98 ± 4

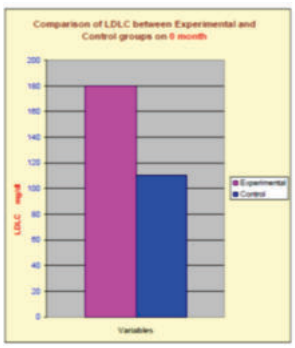
Table 4: Showing serum insulin and HOMA-IR 2 values of Different group

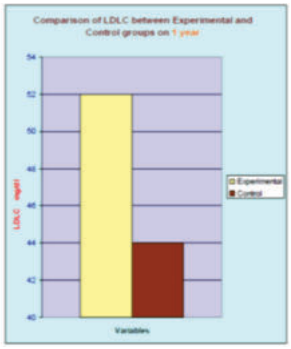
	S. insulin initial value	S. insulin end value	Homeostasis model assessment of insulin resistance 2-IR (initial value)	HOMA - 2 IR end value
Exp Group	20 ± 5	18 ± 3	4.3 ± 0.5	3.7 ± 0.4
Control Group	18 ± 5	18 ± 5	4.3 ± 0.3	4.3 ± 0.2

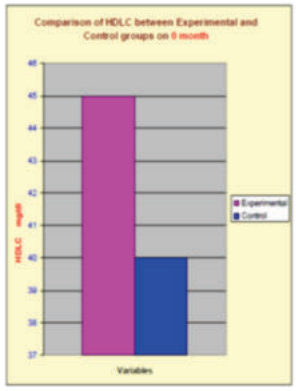
Comparison of different variables between experimental groups and Control Groups

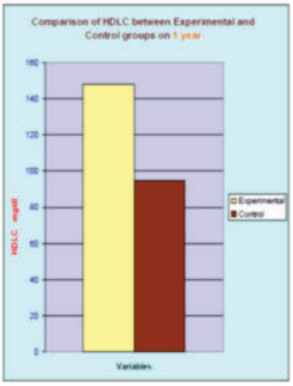


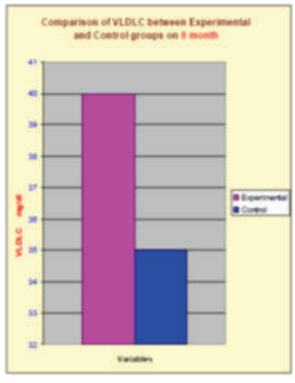


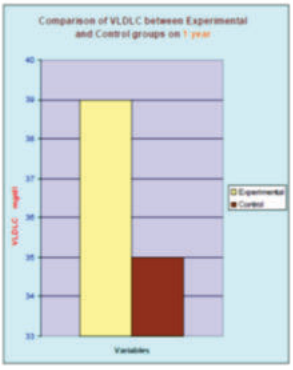


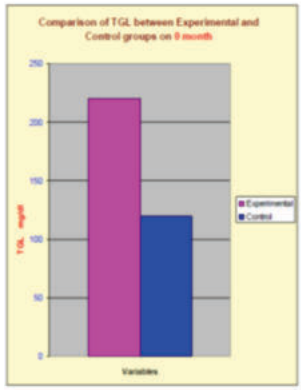


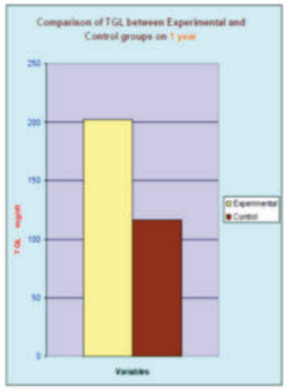


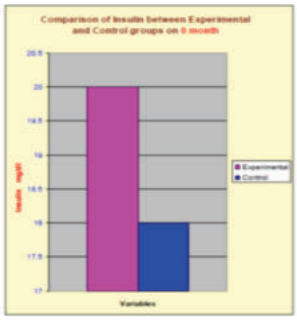


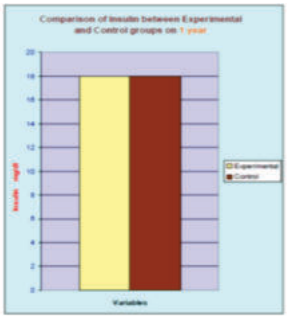






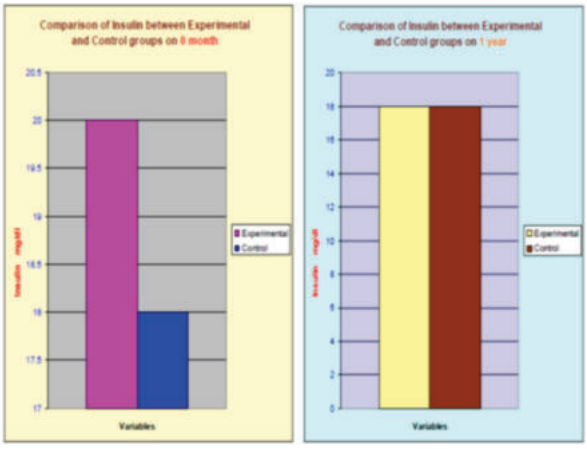






4.DISCUSSION

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.



4.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 ensures to maintain normal blood glucose levels. In epidemiological studies, fasting insulin level is commonly used as a surrogate marker of 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 ensures 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 co-workers, have been more widely used to assess insulin resistance in clinical and population based studies.

Although the role of insulin resistance in the pathophysiology of type 2 diabetes mellitus is well accepted, the relationship between insulin resistance and blood pressure remains controversial. 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.

It has been suggested that HMG Co-A reductase inhibitors ('statins') may reduce the risk of developing type 2 Diabetes mellitus. Yee et al. designed to evaluate whether use of statins would also delay progression to insulin therapy. After multivariate adjustment, however, statin use was associated with a 10-month delay before newly treated diabetic subjects needed to start insulin treatment. This study suggest that statins increase insulin sensitivity even in normoglycemic patients.

5. CONCLUSION

1. Statins improve insulin sensitivity even in normoglycemics and prevent the progression of IGT to type 2 diabetes.
2. Statins reduce levels of interleukin 6 and TNF through its anti-inflammatory 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.
3. Impaired endothelial function has been shown to correlate with insulin resistance. Atorvastatin by restoring endothelial function, may beneficially affect glucose and insulin transport.
4. 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.

REFERENCES

1. Mcfarlane S et al. Pleotropic effects of statins: Lipid reduction and beyond. Journal of clinical endocrinology 2002;879(4); 1451-1458
2. Wolfrum et al. Endothelium dependent effects of statins . Arterioscler Thromb Vasc Biol;2003;23(5).729-736
3. Freeman et al. Pravastatin and development of diabetes.West of Scotland Coronary Prevention Study .Circulation.2001;103;(3);357-362
4. Ikeda et al. Pleotropiceffects of statins on vascular tissue. Current Drug Targets Cardio Haematology Disorder.2001;1(1);51-58
5. Waldman et al . Pleotropic effects of statins. Drugs. 2003;63(2);139-152
6. Shepherd et al.Prevention of coronary artery disease with pravastatin in hypercholesterolemia.1995 NEJM303.1301-1307.
7. Tonolo et al .Additive effects of simvastatin beyond its effect on LDL cholesterol in hypertensive type 2 diabetic patients.2000 Eur J Clin 30;980-987
8. Tedgui et al .Anti-inflammatory mechanisms in vascular wall. Circulation. 2001. 88:877– 887