Research Article

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COMPARATIVE EVALUATION OF HYPOLIPIDEMIC ACTIVITY OF EZETIMIBE AND ATORVASTATIN IN CORONARY ARTERY DISEASE PATIENTS

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Abstract: Statins are the first line drugs for the treatment of hypercholesterolemia patients. In the treatment of hyperlipidemia combination therapy has showed significant results. This study was conducted to find the efficacy of hypolipidemic drugs in cardiovascular diseases. 75 patients were included in the study. Randomly all the patients were divided in to three groups. Group-I (Ezetimibe 10mg/day), Group-II (Atorvastatin 10mg/day), Group-III (Ezetimibe 10mg/day+Atorvastatin 10mg/day) given for 4 weeks. Blood samples were collected from all the patients before and at the end of study to estimate lipid profile. Mono therapy with drugs decreased the lipid levels but combination therapy significantly showed 33.75% reduction in LDL-cholesterol level. Ezetimibe showed 21.9%, Atorvastation 31.54 reduction in LDL-cholesterol levels. There was significant reduction in other lipids and increase the HDL levels. Co-administration of Ezetimibe with statins shows significant results with less adverse effects. More studies required to find safety, efficacy of Ezetimibe with other hypolipidemic drugs.

Keywords: Atherosclerosis, Atorvastatin, Ezetimibe, Hypolipidemia, Lipid Profile, Sclerosis.

INTRODUCTION

Atherosclerosis is a major cause to develop coronary artery diseases. This is associated with increase in the lipids like LDL-C (Low density lipoprotein- cholesterol) and decreased HDL-C (High density lipoprotein-cholesterol) in blood[1]. Life style modification and change in the food consumption can reduce the cholesterol level by 10%. Lifestyle modification and decrease in the risk factors can slow down the progression of lipid deposition in arteries leads to slow down the atherosclerotic process.[2] Increase in the cholesterol levels is one of the most risk factor to develop cardiovascular diseases. Targeting the cholesterol biosynthesis is the major approach to reduce the hyperlipidemia. Statins are the class of drugs inhibit the HMG-CoA enzyme and decrease the cholesterol biosynthesis but clinical results still below acceptable stage.[3] Several other class of hypolipidemic drugs have less efficacy and safety. Natural products also are widely used to treat the hyperlipidemia. Their use is limited and can reduce the effect of other drugs by inhibiting absorption or increase the metabolism.[4] Ezetimibe is the drug inhibit the cholesterol absorption from small intestine without affecting the absorption of fat-soluble vitamins and other fat soluble agents. According to review of literature ezetimibe and its metabolite localized at the intestinal wall and prevents the cholesterol absorption.[5] In the human body there are two important sources for cholesterol one is absorption from intestine and second one is synthesis. Administration of synthesis inhibitors or absorption inhibitors may not show better results.[6] The present study was conducted to find the combined effect of Ezitimibe with statin on lipid profile in coronary artery disease patients.

MATERIALS AND METHODS

It is a randomized open label prospective hospital based study.

Drugs Studied:
Ezetimibe (EZEDOC, REDDY LABS), Atorvastatin (ATOCOR, REDDY LABS), Lipid profile kits (AUTOPAK CHOLESTEROL KIT):

Inclusion criteria:

- Patients aged between 34-74 years
- LDL- cholesterol more than 130mg/dl
- Patients not shown any response to after dietary modifications
- Patients not showed any response to after life style modifications.[7]

Exclusion criteria:

- Active arterial diseases.
- Hypothyroidism
- Peptic ulcer
- Hepatic insufficiency
- Renal disease
- Alcoholism
- Breast feeding women
- Oral Contraceptive medication
- Steroid medication[8,9]

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Study design:

Group-I: Ezetimibe (10mg/day/orally/4 weeks)[10]
Group-II: Atorvastatin (10mg/day/orally/4 weeks)[11]
Group-III: Ezetimibe (10mg/day/orally/4 weeks) + Atorvastatin (10mg/day/orally/4 weeks)

The study was ethically cleared by Institutional Human Ethical Committee, Osmania Medical College, Hyderabad, Andhra Pradesh.

Procedure:

Based on the inclusion and exclusion criteria total number of 75 patients were selected from outpatient wing, Cardiology department, Osmania General Hospital, Hyderabad. All the patients were randomly divided in to three groups and each group contains 25 patients. Demographic, personal data was collected from the study population. Group-I patients were treated with Ezetimibe (10mg/day/orally), Group-II were administered Atorvastatin (10mg/day/orally) and Group-III were given combination of Ezetimibe (10mg/day/orally) + Atorvastatin (10mg/day/orally). Three group's patients were treated for 4weeks with respective drugs. After completion of total study duration of 4 weeks of treatment, the patients were asked to visit the hospital for the blood sample collection, to find any clinical improvement, development of any adverse effects. Following biochemical investigations done for all the patients to find the hypolipidemic efficacy of drugs. 3ml of blood was collected in anti-coagulant tubes and centrifuged at 2500RPM for 10 min. Serum was separated and used for the estimation of LDL- cholesterol (Total cholesterol-[HDL cholesterol-Triglycerides/5]" formula method), Total cholesterol(Oxidase Peroxidase method), Triglycerides(GPO-PAP methodology), HDL-cholesterol (Phosphotungstate Magnesium acetate precipitation method), VLDL- cholesterol (Triglycerides/5) by standard methods.[12,13,14] All the parameters were estimated before the start of the experiment and at 4 weeks by fully automated auto analyzer (_HITACHI 7070 (911) - model analyzer, JAPAN CARE CO., LTD., Japan).

Statistical analysis:

The data was analysed by SPSS (16.0) computer software. T-test and Dunnet's t test applied for the statistical significance. P value less than 0.05 considered statistically significant difference between groups.[15]

RESULTS

The study results showed significant reduction of base line lipid levels compared with after drug administration. Ezetimibe group results explain drug administration significantly reduce the LDL-cholesterol, Total cholesterol, Triglycerides but no significant difference on HDL cholesterol levels. Atorvastatin group also showed same results like Ezetimibe. The combination of two drugs showed more significant reduction in all the lipid profile compared to base line values with after 4 weeks treatment (Table.2). Ezetimibe showed less reduction of lipid levels compared to other drugs but combination of two drugs group showed more reduction in LDL-Cholesterol (111.72±5.45), Total cholesterol (176.76±6.19) and triglycerides (142.15±9.54) and increase in HDL-cholesterol (43.36±1.34) compared to Ezetimibe and Atorvastatin groups. It is observed that significant increase in HDL- cholesterol levels in two drug administered group compared to single drug administered group (Table.3).

Table.1: Demographic data of study population

Gender	Age (MEAN±SD)	Weight (MEAN±SD)	Body Mass Index (MEAN±SD)
Male	46.54±1.34	67.18±2.17	45.35±3.93
Female	49.33±1.85	70.11±3.25	41.03±2.45

Table.2: Pre and post treatment effect of drugs on lipid profile (mg/dl)

Lipid Profile	Group-I		Group-II		Group-III	
	Base line	End of the study	Base line	End of the study	Base line	End of the study
LDL- Cholesterol (MEAN±SD)	151.03±3.97	119.12±6.40*	149.14±8.65	102.45±5.91*	168.04±5.19	111.72±5.45*
Total Cholesterol (MEAN±SD)	248.52±9.58	215.45±9.86*	238.92±9.13	188.28±7.24*	236.52±6.01	176.76±6.19*
HDL- Cholesterol (MEAN±SD)	45.52±5.27	46.05±3.53	43.93±2.79	45.45±3.28	38.62±1.02	43.36±1.34*
Triglycerides (MEAN±SD)	260.91±9.34	252.03±8.23*	234.56±7.56	206.43±6.45*	196.17±9.23	142.15±9.54*

(*P<0.05 significant compared lipid profile levels before and after treatment with drugs within the groups)

Table.3: Multiple comparison of post treatment effect of hypolipidemic drugs on lipid profile (mg/dl)

Groups	LDL-Cholesterol (MEAN±SD)	Total Cholesterol (MEAN±SD)	HDL-Cholesterol (MEAN±SD)	Triglycerides (MEAN±SD)
Group-I	119.12±6.40	215.45±9.86	46.05±3.53	252.03±8.23
Group-II	102.45±5.91*	188.28±7.24*	45.45±3.28	206.43±6.45*
Group-III	111.72±5.45#	176.76±6.19*,#	43.36±1.34*	142.15±9.54*,#

(*P<0.05 significant compared lipid profile levels between group-I with group-II and III, #P<0.05 significant compared lipid profile levels between group-II with group-III)

DISCUSSION

Atherosclerosis is nearly always found in the epicardial portions of the vessels, while the intramural coronary vessels are spared. The degree to which the lumen is narrowed varies, but once the process is present, all the intimal of extramural portions of vessels is usually involved. A single tiny plaque occluding an otherwise normal coronary artery is rare. The world health organization predicts that deaths due to circulatory system disease are projected the double between 1985 and 2015. The major factor for this is increased lipid levels in the blood. Drugs have lipid lowering effect are the most valuable things to treat this disease. There are several drugs are used to treat hyperlipidemia. These drugs either inhibit the cholesterol synthesis or decrease the absorption of cholesterol from intestinal tract. The study was conducted to know the efficacy of newer hypolipidemic drug Ezetimibe mono therapy and combined with statins. 75 patients were included in this study. All the patients divided in to 3 groups and drugs were given to their respective groups for 4 weeks. At the end of 4 weeks blood lipid profile was estimated. Mono therapy with drugs decrease the serum lipid levels but combined therapy showed significant decrease in lipid profile and also increase the HDL levels.

CONCLUSION

The present study explained combination of Ezetimibe and Atorvastatin therapy significantly reduces the lipid levels compared to mono therapy. Combination of these two drugs showed more efficacy than other drugs. There is a requirement of more clinical studies to study effect of combination therapy on development of adverse effect, drug interactions and to find the effective dose. This study can give base to conduct single and multi-centric clinical trials in future.

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