MEDICAL CHANNEL

Original Article

EFFICACY OF STATINS AND FIBRATES IN ALTERING THE LIPID PROFILE IN HYPERTENSIVE PATIENTS

1. **MADIHA SHAH**
2. **MAHBOOB AHMED WAGAN**
3. **SHAHEEN SHAH**
4. **ALI NAWAZ BHURGRI**

1. ***Student***
   Liaquat University of Medical Sciences Jamshoro, Hyderabad.
2. ***Associate Professor***
   Liaquat University of Medical Sciences Jamshoro, Hyderabad.
3. ***Professor of Pharmacology***
   Liaquat University of Medical Sciences Jamshoro, Hyderabad.
4. ***Student Pharmacology,***
   Liaquat University of Medical Sciences Jamshoro, Hyderabad.

Correspondence Address:
MADIHA SHAH
MBBS, FCPS- P-II
Student
Department of Pharmacology
Liaquat University of Medical Sciences Jamshoro, Hyderabad.

ABSTRACT

Lipid lowering drugs have become most powerful Pharmacological strategies in treatment of cardiovascular diseases. In our study of 100 patients having an age range from 35 to 65 years were enrolled. The antihypertensive used were Angiotensin Converting Enzym Inhibitors (Lisinopril 10mg / day) & Calcium channel blockers (Amdolipine 5 mg/ day). Lipid profile was done at base line and then repeated after 12 and 24 weeks Group A received Fenofibrate 40 mg/day and Group B received Atorvastatin 20 mg/day, group A showed fall in LDL-C, TG & TC and the percentage fall was 18%,35%, and 20% respectively, whereas the HDL-C levels were elevated by 16%. The fall was rapid during the 1st three months. And then slow in the last three months. The patients of group B on atorvastatin showed a fall of 35%, 28% and 26% in the levels of LDL-C, TG and TC respectively and the rise in HDL-C was 8%.

Our study showed a greater effect of fenofibrate in lowering TGs & raising HDL-C whereas Atorvastatin was more effective in lowering LDL-C and moderately lowered TGs.

Key words: Hyperlipidemia, Low density lipoprotein (LDL-C), High density lipoprotein (HDL-C), Total Cholesterol (TC) and Triglycerides (TGs).

INTRODUCTION

Hypertensive patients with a risk factor of hyperlipidemia are highly prone to cardiovascular event and need intervention in the form of lipid lowering drugs[1].

Primary and secondary prevention has contributed to the reduction in coronary heart disease mortality rates, many life style modifications are difficult to achieve & maintain. The causal relationship between atherosclerotic disease and hyperlipidemia is well documented[2]. Elevated LDL-C levels and reduced HDL-C levels are independent risk factors for the development of ischemic heart disease[3]

The "4S" study demonstrated that pharmacological intervention with statins lower total cholesterol and LDL-C, with beneficial effect on survival, the aim should be that TGs should be less than 192mg/dl.[4,5]

Hyperlipideima occurs in 50% of at risk coronary patients[6]. The most important risk factors contributing to the development of atherosclerosis include lipid disorder & pre disposition to early ischemic heart disease, atherosclerosis develops as a result of modification of vascular walls. Oxygen free radicals take part in the process, which may probably be opposed by anti oxidant system of the body[7]. The patients of hyperlipideima and hypertension are advised life style modifications & healthy eating plan to reduce fat in diet and maintain proper weight & appropriate pharmacotherapy. This includes statins, which lower the cholesterol and produce physiological effects within weeks, that also decrease LDL-C & improves endothelial function, decrease aggregation of platelets & thrombus deposition & reduce inflammation of vascular wall. They act by inhibiting Hydroxy methyl A glutaryl Coenzyme A reductase (HMG COA) and reduce mortality and recurrent infarction[8].

Elevated plasma LDL-C concentrations are highly atherogenic especially the small dense LDL species, Fenofibrate has been reported to shift the LDL profile by decreasing the small density LDL sub fraction and increasing larger LDL sub classes.

Atorvastatin has been reported to reduce plasma total cholesterol (TC) and triglyceride (TG) concentrations and thus could modify the LDL profile.[9]

Fibrates cause a decrease in plasma triacyl glycerol level by stimulating lipoprotein lipase activity, this results in hydrolyses of triacyl glycerol in chylomicrons & VLDL & thus removal of these particles from plasma, HDL levels are increased moderately.

Treatment of hypercholesterolemia seems to decrease the rate of coronary events, the magnitude of the preventive effect being proportional to the degree of LDL cholesterol reduction.[10]

Data from Framingham Heart Study showed that the optimal HDL cholesterol level for men & women are more than 45mg/dl & 55mg/dl respectively. The risk of CAD increases by 25 percent for every 5mg/dl.[11] A drug that can produce a large increase in HDL cholesterol and at the same time reduce LDL cholesterol may be a valuable treatment.

Fibric acid derivatives are hypolipidimic drugs that decrease total cholesterol & triglyceride concentrations and increase in HDL-cholesterol.

AIMS AND OBJECTIVES

A prospective study was carried out to evaluate the efficacy of two groups of drugs i.e Atorvastatin 20 mg/day and fenofibrate 40 mg/day in altering the lipid profile in hypertensive patients attending cardiac & medical OPD.

METHODOLOGY

This was prospective interventional study, a written consent was taken and the patients were included according to the inclusion criteria results were expressed as percentage alteration of various parameters from the base line level.

INCLUSION CRITERIA.

All adult patients (both sexes)
Systolic BP > 139 mm of Hg
Diastolic BP > 89 mm of Hg
Total cholesterol > 200 mg /dl

EXCLUSION CRITERIA

Pregnant females, Diabetes Mellitus, Lactating mothers, Congestive cardiac failure, Severe anemia, Renal failure, Hepatic dysfunction Myocardial infarction, Smoking more then 10 cigarettes
Women on HRT (hormone replacement therapy)

The patients were enrolled from cardiac & medical OPD and were randomly selected. This study was approved by ethical committee, the antihypertensive used were ACE inhibitors (Lisinopril 10 mg/day) and calcium channel blockers (Amlodipine 5 mg/day). The demographic details were collected on predesigned proforma. Baseline investigation included CBC, Urine DR, Blood Sugar, X-ray chest, lipid profile was done after 14 hours of fasting. The patients were divided into two groups A and B. Each group comprising of 50 patients Group A was given Fenofibrate 40 mg/day and Group B was given Atorvastatin 20 mg/day, the patients were advised to visit after 12 weeks and after 24 weeks and lipid profile was done on these two visits. They were advised to report any time due to any side effect. Patients were monitored during treatment for IHD, MI, CCF and stroke.

RESULT

The study was conducted from June 2009 to July 2010. Two thousand & seventy eight patients were screened and 100 patients were selected according to inclusion criteria. Table I shows age and gender of the patients selected for the study. After treatment the patient on fenofibrate i.e A group showed fall in LDL-C, TG & TC and the percentage fall was 18%, 35%, and 20% respectively, whereas the HDL-C levels were elevated by 16%. The fall was rapid during the 1st three months. And then slow in the last three months.

The patients of group B on atorvastatin showed a fall of 35%, 28% and 26% in the levels of LDL-C, TGs and TC respectively and the rise in HDL-C was 8%.Table II & III

DISCUSSION

There is overwhelming evidence of prognostic and clinical end point benefit from lipid lowering therapy in both sexes by using

TABLE NO. 1
Age distribution among the gender

	35 – 45 years n= 16	46 – 55 years n=27	56 – 65 years n= 57	Total
Male	9 (56.25%)	13 (48.14%)	30 (52.63%)	52
Female	7 (43.75%)	14(51.85%)	27 (47.36%)	48

TABLE NO. 2
Net Changes in Lipid levels after 03 & 06 months of treatment

	Base line	Fenofibrate		Atorvastatin	
		03months	06months	03months	06months
LDL-C mg/dl	175.00	157.50	132.50	140.00	124.00
HDL-C mg/dl	37.00	40.33	42.92	38.85	39.96
TG mg/dl	263.00	197.25	170.95	200.40	179.34
TC mg/dl	278 .00	236.30	212.40	230.74	205.72

TABLE NO.3
Lipid profile after 06 months of treatment

	Fenofibrate	Atrovastatin
LDL-C mg/dl	-42.30 (18%)	-51.00 (35%)
HDL-C mg/dl	+5.92 (16%)	+2.96 (8%)
TG mg/dl	-93.05 (35%)	-83.60 (28%)
TC mg/dl	-55.60 (20%)	-72.28 (26%)

LDL-C = Low density Lipoprotein Cholesterol
HDL-C = Low density Lipoprotein Cholesterol
TG = Triglycerides
TC = Total Cholesterol

statins, fibrates and antioxidants. In our study the LDL-C levels were 175mg/dl & HDL levels37mg/dl. These are independent risk factors for coronary artery diseases. Primary and secondary trials have shown relevance of lowering LDL-C to reduce coronary artery disease (CAD) risk. Dyslipidemia is a risk factor for ischaemic stroke & therefore an indication for the use of statins for the prevention of stroke. Statins act on atheromatic plaque and they have antithrombotic & neuroprotective properties.[12, 13] Statins reduce the risk of death or CV events across a wide range of cholesterol levels, whether or not patients have a history of coronary Artery disease.[14]

The reduction in cholesterol was 25-35% & the current guidelines recommended a target LDL cholesterol level of less than 100mg/dl for patients with CAD or diabetes.[15, 16]

In our study LDL-C decrease was 35% with atorvastatin and this is in accordance with findings of Nichholls in decreasing LDL-C levels with statins. CARE study demonstrates a relationship of lowering LDL-C and decreasing coronary events. (De Becker.[17]) The value of lowering low density lipoprotein (LDL) cholesterol level in preventing major cardiovascular events & stroke has been well documented. Recent studies have raised the issue of optimal treatment targets for patients with coronary heart disease. [18, 19, 20]

The Third Report of National Cholesterol Education Program Adult Treatment Panel & the most recent guidelines of the Third Joint Task force of European and other societies on cardiovascular disease prevention in clinical practice have recommended an LDL cholesterol level of less than 100mg/dl as the goal of therapy for patients at high risk for CHD.

In a study by John et al the LDL-C was reduced by 35%, Total cholesterol levels & triglycerides decrease significantly from base line to week 12 in patients receiving 80mg of Atorvastatin and a non-significant increase in HDL-C. The level of HDL-C was low in our study group it was 37mg/dl it has been reported that a reduced plasma HDL cholesterol was found to have greater impact than raised LDL-C on Atherogenic index (Total cholesterol / HDL-C ratio) Despres in the Quebec study[21].

It is therefore recommended that we need to go beyond LDL-C measurement and lowering therapy, besides LDL-C lowering, raising HDL-C by weight loss, healthy diet & increase physical activity and proper Pharmacotherapy should be a target for high risk patients.

In Heart Protection Study Statin Treatment resulted in LDL-cholesterol level that was 40mg/dl lower than the value in placebo group. The total cholesterol was 278 mg/dl at the base line level, after treatment with atorvastatin the levels were decreased by 17% after 3 months & then further decreased by 9% after next 3 months, so the overall fall in cholesterol was 26% at the end of 6 months .and with fenofibrate the decrease was 20%.

A study conducted by Roy Blank[22] in his Gemini study demonstrated that treatment with amlodipine atorvastatin single pill enabled many patients to attain hypertension and dyplipidemia treatment goal. Our study showed a greater effect of fenofibrate in lowering the TGs and it has been reported that fibrates are generally more effective than statins in lowering triglycerides in patients with elevated TG level Deuz et al 2005.[23]

CONCLUSION

It is concluded that statins are effective in lowering TG and LDL-C and Fibrates have good effect in elevating HDL-C levels in patients at moderate to high cardiovascular risk. Innovative approaches are needed to promote appropriate, more aggressive use of lipid lowering drugs and these should be the integral part of multi-factorial management of hypertensive dyslipidemic patients.

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