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

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 drugs⁴. 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. Elevated LDL-C levels and reduced HDL-C levels are independent risk factors for the development of ischemic heart disease.⁵ 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.⁶,⁷ Hyperlipidemia occurs in 50% of at risk coronary patients. 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. The patients of hyperlipidemia 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 | 46 – 55 years | 56 – 65 years | Total |
| 35 – 45 years | n= 16 | n= 27 | n= 57 | n= 100 |
| 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 |
cholesterol level that was 40mg/dl lower than the value in placebo

In Heart Protection Study Statin Treatment resulted in LDL-

and proper Pharmacotherapy should be a target for high risk

HDL-C by weight loss, healthy diet & increase physical activity

measurement and lowering therapy, besides LDL-C lowering, raising

It is therefore recommended that we need to go beyond LDL-C

treatment targets for patients with coronary heart disease. 18, 19,

well documented. Recent studies have raised the issue of optimal

level in preventing major cardiovascular events & stroke has been

C ratio) Despres in the Quebec study 21.

than raised LDL-C on Atherogenic index (Total cholesterol / HDL-

in our study group it was 37mg/dl it has been reported that a

non-significant increase in HDL-C. The level of HDL-C was low

line to week 12 in patients receiving 80mg of Atorvastatin and a

cholesterol levels & triglycerides decrease significantly from base

In a study by John et al the LDL-C was reduced by 35%, Total

patients at high risk for CHD.

Joint Task force of European and other societies on cardiovascular

of cholesterol levels, whether or not patients have a history of

Artery disease.14

The reduction in cholesterol was 25-35% & the current guidelines

In our study LDL-C decrease was 35% with atorvastatin and this

was 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.

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 for patients with CAD or diabetes.15, 16

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treatment targets for patients with coronary heart disease. 18, 19.

The study conducted by Roy Blank22 in his Gemini study

of 6 months. and with fenofibrate the decrease was 20%.

3 months, so the overall fall in cholesterol was 26% at the end

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 Blank22 in his Gemini study

demonstrated that treatment with amlodipine atorvastatin single

pill enabled many patients to attain hypertension and dyslipidemia
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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<table>
<thead>
<tr>
<th>TABLE NO.3</th>
<th>Lipid profile after 06 months of treatment</th>
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<tbody>
<tr>
<td></td>
<td>Fenofibrate</td>
</tr>
<tr>
<td>LDL-C mg/dl</td>
<td>-24.30 (18%)</td>
</tr>
<tr>
<td>HDL-C mg/dl</td>
<td>+5.92 (16%)</td>
</tr>
<tr>
<td>TG mg/dl</td>
<td>-93.05 (35%)</td>
</tr>
<tr>
<td>TC mg/dl</td>
<td>-55.00 (20%)</td>
</tr>
</tbody>
</table>

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

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