COMPARATIVE STUDY TO EVALUATE LIPID-LOWERING EFFECT OF FENOFIBRATE VERSUS ATORVASTATIN IN PATIENTS WITH HYPERTRIGLYCERIDAEMIA

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ABSTRACT

BACKGROUND

Dyslipidaemia is a widely established risk factor for coronary artery disease. As Asians differ in pattern of various lipid abnormalities than non-Asians, this study was undertaken to compare efficacy of commonly administrated drugs, atorvastatin and fenofibrate.

MATERIALS AND METHODS

The present study was carried out in 100 diagnosed cases of hypertriglyceridaemia divided into two groups, A and B. The mean, standard deviation, standard error of mean and t value were calculated following 12 weeks of therapy of atorvastatin 10 mg in group A and micronized fenofibrate in group B.

RESULTS

Our study showed that fenofibrate is more efficacious in reducing the levels of triglycerides and rising level of HDL cholesterol, while atorvastatin is more efficacious in reducing LDL cholesterol.

CONCLUSION

Micronized fenofibrate has more efficiency in reducing triglycerides and raising HDL. Atorvastatin is more efficacious in reducing LDL levels.

KEYWORDS

Dyslipidaemia, Atorvastatin, Fenofibrate.

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BACKGROUND

Coronary artery disease is a major killer in the present lifestyle of India.[1] Dyslipidaemia is an important risk factor in acute coronary events including myocardial infarction.[2]

Three decades back American Heart Association stressed upon control of high cholesterol and LDL to prevent acute coronary disease. It recommended dietary control and discontinuing the use of animal fat and use of statins in these patients.[3] 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors or statins were shown to reduce the level of LDL cholesterol in both the animal and human studies. Result from statin trials have established that decrease in rate of coronary events was only 30% to 35%. This implies that a greater improvement could be achieved, though further interventional methods including therapy that modifies lipids other than LDL.[4]

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Although, some investigators have shown some strong association of total cholesterol and LDL with coronary artery disease, other findings suggest that this disease arises at lower lipid concentrations in people from south Asia, then in those from other region.

Lipid abnormalities such as high triglycerides and low HDL with normal LDL levels are common in people from south East Asian region. Hence, European/American recommendation of use of statins as first line agents may not entirely are applicable to all populations.[5]

The prevalence of coronary heart disease in India sharply rising from 4% in 1960 to 11% in 2001 between the age group of 30% to 70%.[6]

Raised LDL and total cholesterol are common findings in western countries on contrary characteristic lipid abnormalities in Indian are following-

- High triglyceride levels.
- Low levels of HDL.
- High level of small dense LDL.
- Atherogenic lipoprotein phenotype.
- Moderately increased LDL levels.[7,8,9]

Every one mmol/L (88.5 mg/dL) increase in triglyceride increases risk of coronary disease by 32% in men and 76% in women.[10]

In an 8-year study conducted on 2906 males at Copenhagen cumulative incidence of CHD was compounded to be 4.6% in patients with TG range from 39-97 mg/dL (n-982), 7.7% in patients with TG range from 98-140 mg/dL (n-973) and 11.5% in patients with TG range from >140 mg/dL (n-951).[11]

In a PROCAM study, patients with serum LDL-C >190 mg/dL and triglyceride concentration <200 mg/dL, incidence of coronary heart disease events was 107 cases per 1000 in 8 years, whereas it increased to 255 cases/1000 in patients with LDL >190 mg/dL and triglyceride >200 mg/dL.[12]

The fibric acid derivatives continues to have a place in the management of hypertriglyceridaemia. The third generation of these drugs particularly fenofibrate appears to offer some advantage over others. Studies demonstrate fenofibrate treatment effectively lower plasma triglyceride and total cholesterol increases HDL-C. Extensive European experience with fenofibrate, 6 million patient years indicate that severe side effects are unlikely.[13]

A comparative study between atorvastatin and micronized fenofibrate in the treatment of mixed hyperlipidaemia shows that fenofibrate was more effective at lowering levels of TG and rising levels of HDL-C.[14]

Aims and Objectives of Study

The present study is aimed to evaluate lipid-lowering effects of fenofibrate versus atorvastatin in patients of hypertriglyceridaemia.

MATERIALS AND METHODS

Both males and females excluding pregnancy aged between 20-80 yrs. with hypertriglyceridaemia having triglyceride concentration of more than 200 mg/dL who have failed to achieve normal triglyceride levels laid down by NCEP ATP III guidelines after therapeutic lifestyle changes were included in this study. 106 cases were selected and 53 of them were treated with atorvastatin 10 mg (study group A), while the rest were treated with micronized fenofibrate 160 mg (study group B). Exclusion criteria included history of sensitivity to statins or fenofibrate, secondary hypercholesteraemia, familial hypercholesteraemia, uncontrolled hypertension, hypothyroidism, serum creatinine above 2.5 mg/dL, LFT enzymes more than 3 times elevation. Six cases were dropped as they did not turned up for regular lipid profile test. After taking drugs, lipid fractions were re-estimated at the end 4 weeks and 12 weeks. The result of observation were analysed statistically. The mean, standard deviation, standard error of mean and t value were calculated. Probability p values were derived from t-test tables.

RESULTS

Age	Study Group A		Study Group B	
	Number of Cases	Percentage	Number of Cases	Percentage
20-30	2	4	1	2
31-40	2	4	2	4
41-50	8	16	9	18
51-60	17	34	17	34
61-70	15	30	14	28
71-80	6	12	7	14
Total	**50**	**100**	**50**	**100**

Table 1. Age Distribution

Lipid Profile	Prior to Therapy			After 4 Weeks of Therapy			T value	P value	Remarks
	Mean	±SD	±SEM	Mean	±SD	±SEM			
TC	240.94	43.14	6.07	200.32	45.97	6.47	4.55	<0.001	Highly significant
LDL	143	39.59	5.58	100.14	36.06	5.1	5.66	<0.001	Highly significant
TG	309.08	99	13.94	276.16	90.50	12.75	2.68	<0.01	Highly significant
HDL	43.76	19.80	2.79	45.6	21.20	2.98	2.08	<0.05	Significant

Table 2. Statistical Comparison of Mean Level of Lipid Profile in Study Group A between the Level Prior to Therapy and After 4 Weeks of Therapy

Lipid Profile	Prior to Therapy			After 12 Weeks of Therapy			T value	P value	Remarks
	Mean	±SD	±SEM	Mean	±SD	±SEM			
TC	240.94	43.14	6.07	192.9	43.84	6.17	4.98	<0.001	Highly significant
LDL	143	39.59	5.58	94.04	41.71	5.87	5.14	<0.001	Highly significant
TG	309.08	99	13.94	262.6	115.25	16.23	3.18	<0.01	Highly significant
HDL	43.76	19.80	2.79	46.66	21.21	2.99	2.11	<0.05	Significant

Table 3. Statistical Comparison of Mean Level of Lipid Profile in Study Group A between the Level Prior to Therapy and After 12 Weeks of Therapy

Lipid Profile	Prior to Therapy			After 4 Weeks of Therapy			T value	P value	Remarks
	Mean	±SD	±SEM	Mean	±SD	±SEM			
TC	241.4	61.52	8.66	203.38	62.22	8.76	3.47	<0.001	Highly significant
LDL	138.76	56.56	7.97	124.18	50	7.04	2.96	<0.01	Highly significant
TG	304.78	111.01	15.63	184.8	84.85	11.95	6.06	<0.001	Highly significant
HDL	41.8	17.67	2.49	42.68	18.38	2.59	2.15	<0.05	Significant

Table 4. Statistical Comparison of Mean Level of Lipid Profile in Study Group B between the Level Prior to Therapy and After 4 Weeks of Therapy

Lipid Profile	Prior to Therapy			After 12 Weeks of Therapy			T value	P value	Remarks
	Mean	±SD	±SEM	Mean	±SD	±SEM			
TC	241.4	61.52	8.66	192.04	67.17	9.46	3.81	<0.001	Highly significant
LDL	138.76	56.56	7.97	110.92	40.41	5.69	3.13	<0.01	Highly significant
TG	304.78	111.01	15.63	169.62	82.73	11.65	6.9	<0.001	Highly significant
HDL	41.8	17.67	2.49	47.24	17.67	2.49	2.68	<0.01	Significant

Table 5. Statistical Comparison of Mean Level of Lipid Profile in Study Group B between the Level Prior to Therapy and After 12 Weeks of Therapy

Lipid Profile	Study Group A				Study Group B				T value	P value	Remarks
	Range	Mean	±SD	±SEM	Range	Mean	±SD	±SEM			
TC	160-222	193	43.84	6.17	143-238	192	67.17	9.46	0.07	>0.05	Not significant
LDL	59-118	94	41.71	5.87	56-157	111	40.41	5.69	3.05	<0.01	Highly significant
TG	192-355	263	115.25	16.23	113-230	170	82.73	11.65	4.65	<0.001	Highly significant
HDL	40-70	46.66	21.21	2.99	40-65	47.24	17.67	2.49	2.76	<0.01	Highly significant

Table 6. Statistical Comparison of Mean Level of Lipid Profile in Study Group A and Study Group B After 12 Weeks of Therapy

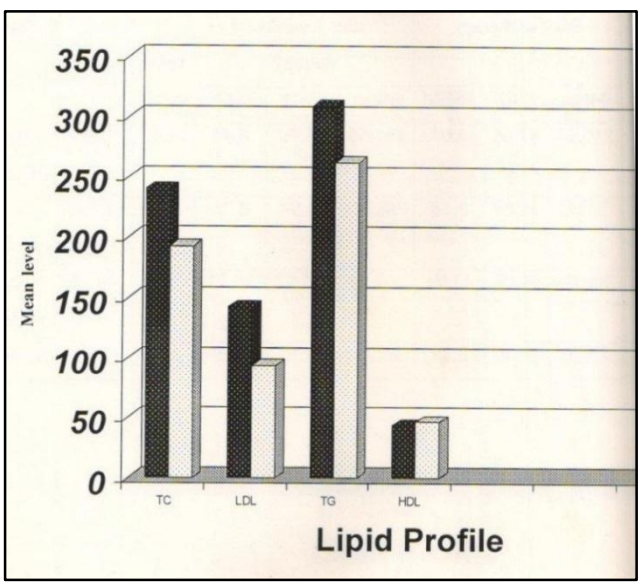

Figure 1. Statistical Comparison of Mean Level of Lipid Profile in Study Group A between the Level Prior to Therapy and After 12 Weeks of Therapy

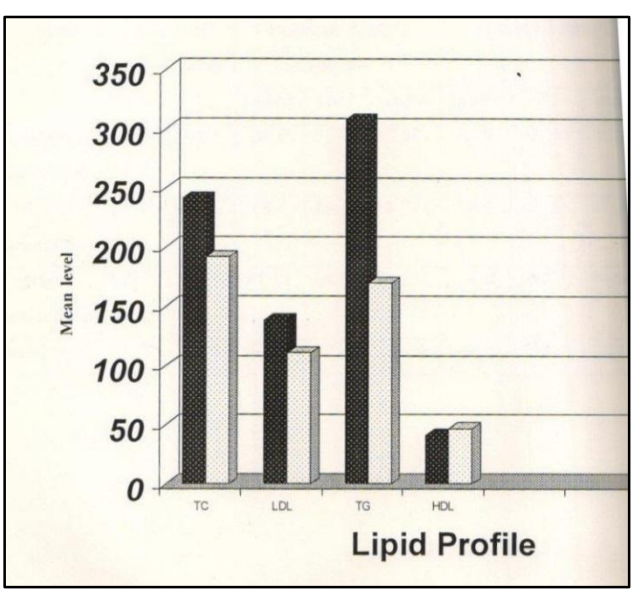

Figure 2. Statistical Comparison of Mean Level of Lipid Profile in Study Group B between the Level Prior to Therapy and After 12 Weeks of Therapy

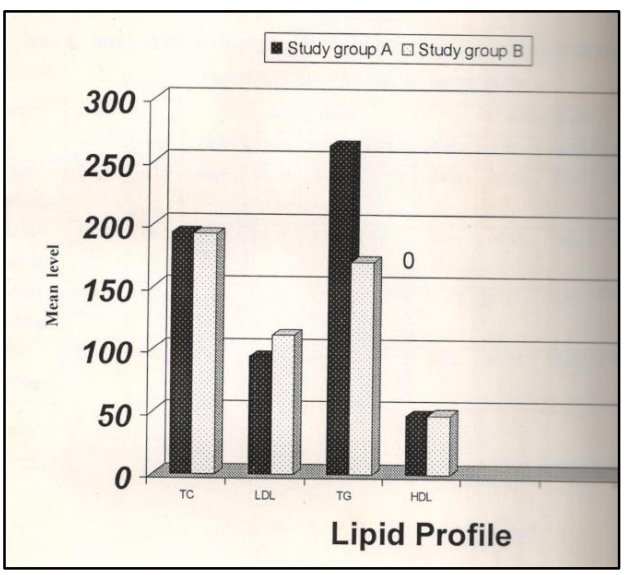

Figure 3. Statistical Comparison of Mean Level of Lipid Profile in Study Group A between the Level Prior to Therapy and After 4 Weeks of Therapy

DISCUSSION

The study group 'A' comprised of 50 patients of hypertriglyceridaemia between the age group of 20-80 years put on atorvastatin (10 mg) and study group 'B' comprised of 50 patients of hypertriglyceridaemia between the age group of 20-80 years, put on fenofibrate (160 mg) (Table 1). 44% cases were females and 56% were males in study group A, while 48% cases were females and 52% were males in Group B. BMI of group A, 54% of cases had BMI-25-30 and 34% had BMI 30-35. In group B, 56% had 25-30 and 32% had 30-35.

Lipid profile studies of both group were studied before starting the drugs. In group A, mean total cholesterol were 241 ± 6.07 mg%, LDL 143 ± 5.58 mg%, TG 309 ± 13.94 mg%, HDL 43.76 ± 2.79 mg%. In study group 'B', the mean level of lipids were following- TC 241 ± 8.66 mg%, LDL 139 ± 7.97 mg%, TG 305 ± 15.63 mg%, HDL 41.8 ± 2.49 mg%.

The study group 'A' was treated with atorvastatin (10 mg) at bedtime and study group B with micronized fenofibrate 160 mg at bedtime. Follow-up studies were done after 4 weeks and after 12 weeks of treatment. After 4

weeks in study group A, the mean level fell down to TC200 ± 6.17 mg%, LDL 100 ± 5.87 mg%, TG 276 ± 16.23 mg%, while HDL levels rise to 45.6 ± 2.99 mg%. After 4 weeks in study group B, the mean level fell down to TC 203 ± 8.76 mg%, LDL 124 ± 7.04 mg%, TG 185 ± 11.95 mg%, while HDL levels rise to 42.68 ± 2.59 mg%. Twelve weeks later, patients were called again. The serum lipid levels were studied. In group A, the mean level fell down to TC 193 ± 6.17 mg%, LDL 94 ± 5.87 mg%, TG 263 ± 16.23 mg%, while HDL levels rise to 46.6 ± 2.99 mg% (Figure 1). In group B, the mean level fell down to TC 192 ± 9.46 mg%, LDL 111 ± 5.69 mg%, TG 170 ± 11.65 mg%, while HDL levels rise to 47.24 ± 2.49 mg% (Figure 2).

Statistical comparison of mean level of lipid profile in study group A between the level prior to therapy and after 4 weeks of therapy found that there had been fall in the level of TC, LDL and TG ($p<0.001$, i.e. highly significant) and there had been rise of HDL, which was not statistically significant. Further studies, after 12 weeks shown that there was gradual decline in level of TC, LDL, TG, which was statistically highly significant ($p<0.001$) and rise in HDL, which was significant ($p<0.05$).

When lipids at the end of 4 weeks of therapy were compared to 8 weeks of therapy in a study group 'A' and between 8 weeks and 12 weeks, it was observed that fall of TC, LDL, TG and rise of HDL were almost equal at the end of 8 weeks and 12 weeks, i.e. they were not significant ($p>0.05$).

Statistical comparison of mean level of lipid profile in study group B between the level prior to therapy and after 4 weeks of therapy shows highly significant fall in the levels of TC, LDL, TG and rise in HDL, which was just significant ($p<0.05$). Statistical comparison of mean level of lipid profile in study group B between the level prior to therapy and after 4 weeks of therapy found that there had been fall in the level of TC, LDL and TG ($p<0.001$, i.e. highly significant) and there had been rise of HDL, which was statistically significant. Further studies after 12 weeks shown that there was gradual decline in level of TC, TG, which was statistically highly significant ($p<0.001$), LDL ($p<0.01$) and rise in HDL, which was significant ($p<0.01$).

Statistical comparison of mean level of lipid profile in study group A and study group B after 12 weeks of therapy showed that atorvastatin 10 mg in study group A reduced highly significant fall in the levels of LDL at the end of 12 week of therapy ($p<0.01$), while micronized fenofibrate 160 mg in study group B produced highly significant fall in TG levels at the end of 12 weeks of therapy. There was almost equal fall in TC in both study groups after the end of 12 weeks of therapy, i.e. $p>0.05$ (Figure 3).

Rise of HDL was highly significant in study group B compared to study group A after 12 weeks of therapy, i.e. $p<0.01$.

A comparison study between atorvastatin and micronized fenofibrate in the treatment of mixed hyperlipidaemia conducted by Bairaktari et al, University Hospital, Greece, concludes that atorvastatin was more effective at lowering levels of total and LDL cholesterol, whereas fenofibrate was more effective at lowering levels of triglycerides and raising the levels of HDL.[14] Studies conducted by Ellen RLB et al and Ruth MC Pherson with fenofibrate had similar results.[15,16] These studies prompted us to compare the atorvastatin and fenofibrate in Indian patients with hypertriglyceridaemia. The result of this present study has also shown that fenofibrate produces significant fall in the triglyceride levels within first four weeks of therapy and significant rise in HDL cholesterol after 12 weeks of therapy compared to atorvastatin and fall in total cholesterol level was almost identical in both study groups, but fall in the levels at LDL cholesterol was very much significant in atorvastatin users. Thus, micronized fenofibrate maybe recommended as a lipid-lowering agent in hypertriglyceridaemia and combined hyperlipidaemia.

CONCLUSION

Thus, the result of this study shows that fenofibrate is more efficacious in reducing the level of triglycerides and rising the level of HDL cholesterol compared to atorvastatin while later is more efficacious in reducing the level of LDL cholesterol. Thus, fenofibrate maybe recommended as lipid lowering agent in patients with hypertriglyceridaemia.

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