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Comparative study of efficacy of Atorvastatin and Atorvastatin with Niacin in the management of Hyperlipidemia.

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ABSTRACT

The development of the "statins" class of drugs provided a momentual leap in the management by pharmacotherapy of hyperlipidemia and CHD risk reduction. Randomised clinical trials have provided strong evidence that lowering plasma cholesterol with statins reduces the risk of cardiovascular/CHD events. A total of 50 patients for Atorvastatin group and 50 patients for Atorvastatin and Niacin group were included in the study. The fasting blood samples were taken and serum (I°) were stored frozen until analysed for TG, TC, LDL-C, HDL-C, and Lp (a). Blood samples were taken again at follow up and serum (II°) was stored frozen until analysed for lipids by biochemical methods. In atorvastatin group, the mean total cholesterol level before treatment was 231.26 mg/dl and after treatment , it reduced to 198.9 mg/dl (P value < 0.001). In atorvastatin plus niacin group, the mean cholesterol before treatment was 224.45 mg/dl and after treatment it was 192.14 mg/dl (p value< 0.001). The effects of combination therapy of the two drugs were much higher than their effects alone and therefore, can be adopted in hyperlipidemia patients.

Key words: Atorvastatin, Niacin, Efficacy

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INTRODUCTION

Hyperlipidaemia is a major cause of atherosclerosis and atherosclerosis associated conditions such as coronary artery diseases, Ischemic cerebrovascular diseases and peripheral vascular diseases. Atherosclerosis remains the major cause of death and premature disability in developed societies.

World health Organization has drawn attention to the fact that coronary heart disease as our modern epidemic i.e a disease that affects population not an unavoidable attribute of ageing [1]. Coronary heart disease is the commonest cause of cardiovascular disability and death. In India, it is the fast becoming major killer. It is estimated that there are more than 30 million patients with coronary heart disease in India [2].

Compared to Europeans, Americans and other Asians the prevalence, incidence, hospitalization and mortalty from coronary heart disease in India is 2 – 4 fold higher at all ages and 5 – 10 fold higher in those above 40 years of age.

Hyperlipidemia is a major modifiable risk factor in primary and secondary prevention of coronary artery disease. However the term dyslipidaemia is preferred to to hyperlipidaemia because low levels of plasma HDL – C levels can be harmful [3].

Low HDL which is a powerful predictor of the occurrence and recurrence of myocardial infarction and stroke and is associated with premature and severe CAD[4] can be raised using fibrates or niacin. Raising HDL cholesterol (as a secondary target) in addition to lowering LDL has been shown to confer additional benefits in patients with CAD (slowing of progression or regression of atherosclerosis and protection against MACE). Among the currently available HDL raising agents, nicotinic acid (or niacin) is not only effective but niacin 1-3 g/day has been shown to reduce major coronary events by 25%, stroke by 26%, and any other cardiovascular events by 27%[5]. Moreover, niacin exerts beneficial effects on all atherogenic lipid and lipoprotein subclasses, including total cholesterol, non-HDL-C, LDL-C, triglycerides, apolipoprotein B, lipoprotein-a, and significantly raises levels of HDL-C and apolipoprotein A. It is also the only agent that reduces Lp (a) levels. Niacin reduces Lp (a) by up to 30–40% in a dose-dependent manner. A recently introduced formulation of nicotinic acid, niacin extended-release (ER), has superior tolerability to the immediate-release formulation and an added advantage of once daily dosing. Considering the potential of combining a statin with niacin ER, we speculated that a combination of niacin ER and atorvastatin would have wide-ranging lipid modifying properties, the ability to treat all aspects of dyslipidemia, the potential to achieve target LDL levels and additional benefits on premature CAD by reducing Lp (a) levels. Thus, this combination would be suitable to treat Indian dyslipidemic patients with mixed or combined dyslipidemias as well as patients with or at a risk of premature CAD. This study was therefore planned as a preliminary investigation to assess the safety and efficacy of a fixed dose combination of atorvastatin and niacin ER (Niacin ER/Atorvastatin) in the Indian dyslipidemic population.

METHODOLOGY

This study was comparative and randomized, performed in 126 patients for 6 weeks duration attending the cardiology outpatient department, Government general hospital, Guntur. All patients were both men and women aged 20 -7- years with previous history of acute MI or unstable angina. Before starting the study, the ethical committee approved the protocol. Written and informed consent was obtained from each patient.

Initially 126 patients were taken into the study. Of these only 100 patients attended the outpatient department regularly till the end of the study.

These patients were selected and placed into two groups randomly. One group (group A) was treated with atorvastatin 10 mg once daily orally and another group (group B) was on atorvastatin with niacin combination (10 mg + 500 mg) once daily orally for 6 weeks.

Inclusion criteria

- Age 20 -70 years
- LDL-C > 100mg/dl

- HDL-C < 40 mg /dl
- Serum creatinine < 1.2 mg/dl
- Normal LFT

Exclusion criteria

- Acute illness
- Renal failure
- Hepatic dysfunction
- Diabetes mellitus
- Thyroid disease
- Alcoholics
- Gout
- Active peptic ulcer
- Pregnancy and lactation

Before starting the study the risk factors like smoking, hypertension, h/o unstable angina and MI were noted for each patient. All the patients underwent routine clinical examinations encompassing routine laboratory tests like Hb%, blood sugar, blood urea, serum creatinine, serum uric acid, liver function tests and lipid profile.

All the patients in two groups were advised to visit hospital every week. During the whole they were followed for any adverse effects.

The lipid profile and all the other investigations were done before starting the treatment and repeated after 6 weeks of follow up in all the patients.

Data was entered in Microsoft excel and analyzed using SPSS

RESULTS

Both regimes were well tolerated but the atorvastatin with niacin combination improved lipid profile better than atorvastatin monotherapy.

Among 100 patients, 1 patient (1%) was between 20 -30 years age group, 15 (15%) were between 31 – 40 years, 31 (31%) between 41 – 50 years, 34 (34%) between 51 – 60 years and 19 (19%) were between 61 – 70 years of age group. So the incidence of coronary heart disease with hyperllipidaemia was more at the age of 41 – 60 years.

Among total study subjects, 73 (73%) were males and 27 (27%) were females. So the incidence of coronary heart disease with hyperllipidaemia was more in males.

In atorvastatin group, the mean total cholesterol level before treatment was 231.26 mg/dl and after treatment, it reduced to 198.9 mg/dl (P value < 0.001). In atorvastatin plus niacin group, the mean cholesterol before treatment was 224.45 mg/dl and after treatment it was 192.14 mg/dl (p value< 0.001). the percentage decrease in total cholesterol levels in group A was 13.99% and in group B was 14.93%. the difference in reduction being 0.97% between group A and group B.

In group A, the mean HDL-C level before treatment was 39.22 mg/dl and after treatment it increased to 39.98 mg/dl (P value<0.05). In group B, mean value before treatment was 38.88 mg/dl and after treatment, it was 41.44 mg/dl. The percentage increase in HDL-C levels in group A was 1.93% and in group B was 6.58%. The difference in increase being 4.65% in between the two groups.

In group A, the mean LDL-C level before treatment was 154.03 mg/dl and after treatment it reduced to 122.86 mg/dl (P value<0.001). In group B, mean value before treatment was 144.93 mg/dl and after treatment, it was 115.60 mg/dl. The percentage decrease in LDL-C levels in both groups was same 20.23%

In atorvastatin group, the mean TG level before treatment was 200.52 mg/dl and after treatment, it reduced to 180.12mg/dl (P value < 0.001). in atorvastatin plus niacin group, the mean TG before treatment was 205.24 mg/dl and after treatment it was 174.78 mg/dl (p value< 0.001). The percentage decrease in TG levels in group A was 10.77% and in group B was 14.84%., the difference in reduction being 4.07% between group A and group B.

In atorvastatin group, the mean VLDL-C level before treatment was 40.10 mg/dl and after treatment, it reduced to 38.08 mg/dl (P value < 0.001). In atorvastatin plus niacin group, the mean was 39.06 mg/dl and after treatment it was 34.98 mg/dl (p value< 0.001). The percentage decrease in VLDL-C levels in group A was 5% and in group B was 10.5%., the difference in reduction being 5% between group A and group B.

In our study, during 6 weeks of treatment there were no serious side effects. However 4 patients complained of flatulence, 4 patients complained of constipation, one patient complained of epigastric pain and in one patient cutaneouis flushing was noted.

Table 1: Profile of patients

Profile	Atorvastatin group (n=50)	Atorvastatin and Niacin group (n=50)
Age:		
20 – 30 years	01 (02.0%)	00
31 – 40 years	10 (20.0%)	05 (10.0%)
41 – 50 years	12 (24.0%)	19 (38.0%)
51 – 60 years	15 (30.0%)	19 (38.0%)
61 – 70 years	12 (24.0%)	07 (14.0%)
Gender		
Male	39 (78.0%)	34 (68.0%)
Female	11 (22.0%)	16 (32.0%)
Hypertension		
Yes	33 (66.0%)	36 (72.0%)
No	17 (34.0%)	14 (28.0%)
MI		
Yes	35 (70.0%)	41 (82.0%)
No	15 (30.0%)	09 (18.0%)
Unstable angina		
Yes	15 (30.0%)	09 (18.0%)
No	35 (70.0%)	41 (82.0%)

Table 2: Comparison of Mean Lipid levels before and after treatment

Lipid profile	Atorvastatin group			Atorvastatin and Niacin group		
	Baseline	End of 6 weeks	% change	Baseline	End of 6 weeks	% change
TC (mg/dl)	231.2+/-15.5	198.9+/-16.1	13.99%	224.4+/-17.2	192.1+/-13.6	14.9%
LDL-C(mg/dl)	154.0+/-22.1	122.8+/-16.9	20.23%	144.9+/-16.6	115.6+/-13.7	20.23%
HDL-C(mg/dl)	39.2+/-1.7	39.9+/-1.7	1.93%	38.8+/-1.8	41.4+/-1.7	6.58%
TG(mg/dl)	200.5+/-16.4	180.1+/-16.8	10.7%	20-5.2+/-15.5	174.7+/-14.2	14.84%
VLDL-C(mg/dl)	40.1+/-3.0	38.0+/-3.7	5%	39.0+/-3.7	34.9+/-2.9	10.5%

DISCUSSION

The results in the present study suggested that the combination of atorvastatin and niacin was more effective than atorvastatin alone in improving the HDL-C and triglyceride levels from the base line. The combination group improved the lipid profile particularly HDL-C levels very significantly with mean percentage difference of 4.65%. These results were consistent with those of Bay HE et al [6]. In their study it was concluded that statin with niacin combination was more effective in increasing HDL-C levels than with statin monotherapies.

The combination of statin and niacin in group B showed significant decrease in triglyceride levels and increase in HDL-C levels than the statin group. These results were consistent with the study of JM Morgan et al [7]. In their study, they concluded that combination therapy of statin with niacin significantly increased HDL-C levels and reduced triglyceride levels from the base line.

In our study, in atorvastatin group the difference between the mean LDL-C levels before and after treatment was 31.17 mg/dl and in combination group it was 29.3mg/dl. The difference between the mean HDL-C levels before and after treatment was 0.72 mg/dl in atorvastatin group and 2.56 mg/dl in the combination group. These results were similar to other studies [8]. They concluded that atorvastatin had a preferred LDL-C effect where as niacin had preferred HDL-C effect.

In our study, during 6 weeks of treatment there were no serious side effects. However 4 patients complained of flatulence (two from each group), 4 patients complained of constipation two from each group), one patient complained of epigastric pain and in one patient cutaneous flushing in group B was noted.

CONCLUSION

The coherence of our data on lipid profile with the use of statins and niacin suggest that coimbination therapy by adding niacin to statins could reduce triglyceride levels, VLDL-C levels and increase HDL-C levels more effectively. The other parameters like total cholesterol and LDL-C levels showed les significant changes

REFERENCES

[1] K Park; Text Book of Preventive and Social Medicine;18th edition;2005;Banarasidas Bhanoth publishers, Jabalpur, ch.6: pages 286-287.
[2] Editorial; Cardiology Today; Nov- Dec 1997: vol 1
[3] HP Rang, MM Dale et al; 5th edition pharmacology;2005; Elsevier publications; chapter 19; pages 306 – 313.
[4] Pearson TA, Bulkley BH, Achuff SC, Kwiterovich PO, Gordis L. Am J Epidemiol 1979; 109:285-95.
[5] Bruckert E, Labreuche J, Amarenco P. Atherosclerosis 2010; 210:353-61.
[6] Bays H E, Mc Govern ME. Prev Cardiol 2003 fall;6(4):179-88
[7] Morgan JM, Carey et al. Prev Cardiol 2004;7(4):176-81.
[8] Mc Kenny JM, Mc Cormic LS, Schaefer EJ, Black DM, Watkins ML. Am J Cardiol 2001;88(3):270 – 4.