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Comparative Study of Efficacy and Safety of Atorvastatin Co-administered with Ezetimibe versus Atorvastatin Monotherapy in Newly Diagnosed Patients with Dyslipidemia

Rasika Khobragade* and Vijay Ramkrishna Zad

Department of Pharmacology, Dr. V. M. Government Medical College, Solapur, Maharashtra, India

Abstract

Introduction: Coronary heart disease (CHD) refers to a narrowing of the coronary arteries. It accounts for nearly 30 percent of all deaths. Guidelines from the National Cholesterol Education Program (NCEP), the American Heart Association and American stroke association all support recommendations to lower LDL to at least under 100mg/dl with recommendations to lower LDL < 70mg/dl as a 'therapeutic option'. Ezetimibe is a novel drug in a class of lipid-lowering compounds. Added to a statin, Ezetimibe further decreased LDL to a significantly greater extent. Studies have shown that Atorvastatin and Ezetimibe combination therapy achieves greater reduction in LDL levels and greater increase in HDL levels than Atorvastatin monotherapy.
Objective: To compare the efficacy and safety of Atorvastatin co- administered with Ezetimibe versus Atorvastatin alone.
Material & Methods: This was a prospective, randomized, parallel-group, open labelled study. Sample size was 50 per group. The quantitative variables will be evaluated using unpaired t-test or chi square test. The qualitative variables will be compared using Chi-square test and mean variables by T or Anova test.
Results: A total 100 patients were enrolled. 50 patients were allocated to Atorvastatin group and 50 patients to Atorvastatin and Ezetimibe group. They had received either Atorvastatin (20 mg) or combination of Atorvastatin plus Ezetimibe (10 mg + 10 mg). Administration of Ezetimibe with Atorvastatin resulted in significantly greater percentage reduction in LDL as compared to that achieved with Atorvastatin alone. Also there was greater reduction in the levels of TC, TG, VLDL in Atorvastatin plus Ezetimibe combination group as compared with Atorvastatin alone.
Conclusion: Atorvastatin co-administered with Ezetimibe offers more effective and equally tolerated option than Atorvastatin alone for the patients with newly diagnosed dyslipidemia having LDL levels of > 100 mg/dl as it significantly lowers the LDL, TG, TC and VLDL along with significant increase in HDL.
Keywords: CHD, Atorvastatin, Ezetimibe.

***Correspondence Info:**
Dr. Rasika Khobragade,
Department of Pharmacology,
Dr. V. M. Government Medical College,
Solapur, Maharashtra, India

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1. Introduction

Coronary heart disease (CHD) refers to a narrowing of the coronary arteries, the blood vessels that supply oxygen and blood to the heart. It is also known as coronary artery disease. Coronary heart disease is one of the leading causes of death worldwide. Coronary heart diseases have assumed epidemic proportions worldwide. [1] CHD is responsible for more than 75% of death occurring in developing countries. Studies have shown that in developed countries mortality of CHD is rapidly declining at the same time it is increasing in developing countries.[2,3] CHD is not only responsible for increased number of deaths but also for disability in low- and middle-income countries, such as in India, where it accounts for nearly 30 percent of all deaths.[4]

Various risk factors responsible for coronary heart disease are diabetes, hypertension, atherogenic dyslipidemia,

smoking, central obesity and physical inactivity. [5] Rapid change in the lifestyle for past few decades has increased the frequency of CHD in country like India. Studies in the past have shown that laboratory, experimental and epidemiologic data identify dyslipidemia as a pivotal CHD risk factor. [6-8]

Dyslipidemia is a group of disorders of lipoprotein metabolism regarded as primary risk factors for atherosclerotic disease, especially CHD.[9] Studies have suggested that as such, LDL reduction is the guideline-recommended treatment target for primary and secondary prevention of cardiovascular events.[10-12] Guidelines from the National Cholesterol Education Program (NCEP)[7] , the American Heart Association[8] and American stroke association[9] all support recommendations to lower LDL to at least under 100mg/dl with recommendations to lower LDL < 70mg/dl as a 'therapeutic option'. Statins are 3-hydroxy-3-methyglutaryl coenzyme A (HMG-CoA) reductase inhibitors, which are prescribed extensively for cholesterol lowering in the primary and secondary prevention of cardiovascular disease.[13,14] A meta-analysis of primary and secondary prevention trials of statin therapy demonstrated a 20% reduction of major cardiovascular events and stroke per 1-mmol/L reduction in LDL.[12]

Ezetimibe is a novel drug in a class of lipid-lowering compounds that selectively inhibits the intestinal absorption of cholesterol and related phytosterols. Ezetimibe reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine.[15] Added to a statin, Ezetimibe further decreased LDL to a significantly greater extent and produced better attainment of pre-specified LDL levels than a statin alone in hypercholesterolemic patients.[16,17] Studies have shown that Atorvastatin and Ezetimibe combination therapy achieves greater reduction in LDL levels and greater increase in HDL levels than Atorvastatin monotherapy, including doubling the statin dose.[18] So we thought it is worthwhile to evaluate lipid lowering ability of combination of Atorvastatin and Ezetimibe compared with Atorvastatin alone in double dose .

Aim*:* To compare the efficacy and safety of Atorvastatin co- administered with Ezetimibe versus Atorvastatin alone.

Objectives: To compare changes in levels of serum LDL, HDL, TG, Total cholesterol(TC), Very low density lipoprotein (VLDL) by Atorvastatin co-administered with Ezetimibe over Atorvastatin alone.

To compare adverse effects of Atorvastatin co-administered with Ezetimibe over Atorvastatin alone.

2. Material and methods

This study was conducted in medicine department with a 733 bedded district level tertiary care hospital in Western Maharashtra attached to medical teaching institute after getting approval from Institutional Ethics Committee (Letter no. IEC/Pharmac/Proposal No. 0916048-25 dated 05/10/2016). This was a prospective, randomized, parallel-group, open labelled study.

Patient recruitment started in the month January 2017 and continued till August 2018. Patients with type 2 diabetes mellitus (T2DM) or hypertension (HTN) were recruited from the medicine outpatient department (OPD) and cardiology OPD after initial screening for participating in the study.

Screening was based on following criteria:

2.1 Inclusion criteria

- Men and women in the age group of 18-60 years with newly diagnoseddyslipidemia.
- Patients with LDL levels $\geq$ 100mg/dl. This is according to NCEP ATP IIIguidelines.[19]

2.2 Exclusion criteria

Following patients were excluded from the study;

1) Patients with serum LDL levels > 190 mg/dl.
2) Patients suffering from active or chronic hepatic disease [Alanine Aminotransferase (ALT), Aspartate Transaminase (AST) elevations >3ULN].
3) History of serious adverse effects or hypersensitivity reactions to the drugs in the study, in particular any history of myopathy.
4) Coronary heart disease which includes history of myocardial infarction, unstable angina, stable angina, coronary artery procedures (angioplasty or bypass surgery) or evidence of clinically significant myocardial ischemia.
5) Fasting Triglyceride level>400mg/dl.
6) Patients with impaired renal function.
7) Pregnant and lactating women.

Sample size was calculated using following formula [20]: $N = (Z_{\alpha/2})^2 \, s^2 / d^2$

Where N denotes sample size, s is the standard deviation obtained from previous study, and d is the accuracy of estimate or how close to the true mean. Zα/2 is normal deviate for two- tailed alternative hypothesis at a level of significance.

S– Standard deviation = From previous study = $5.5 Z_{@/2} = Z_{0.05/2} = Z_{0.025} = 1.96$ at type 1 error of 5%

d = 1.8

$N = (1.96)^2 \, 5.5^2/1.8^2 = 35.85$

So the minimum sample size for the present study for each group willbe 36, but considering the error and drop out of 40%, the sample size will be increased to 50 per group.

2.3 Statistical methods

The quantitative variables will be evaluated using unpaired t-test or chi square test. The qualitative variables will be compared using Chi-square test and mean variables by T or ANOVA test. A p-value <0.05 will be assumed

statistically significant. Statistical Package for Social Sciences (SPSS) version 22.0 will be used for analysis.

Patients who were found fit to be included in the study were explained the aim and objectives of the study in detail. They were informed about the benefits of the study along with the possible risk. After explaining the entire scope of the study, a written informed consent was obtained from them. The patients were randomly allocated to group A or group B treatment group based on chit method.

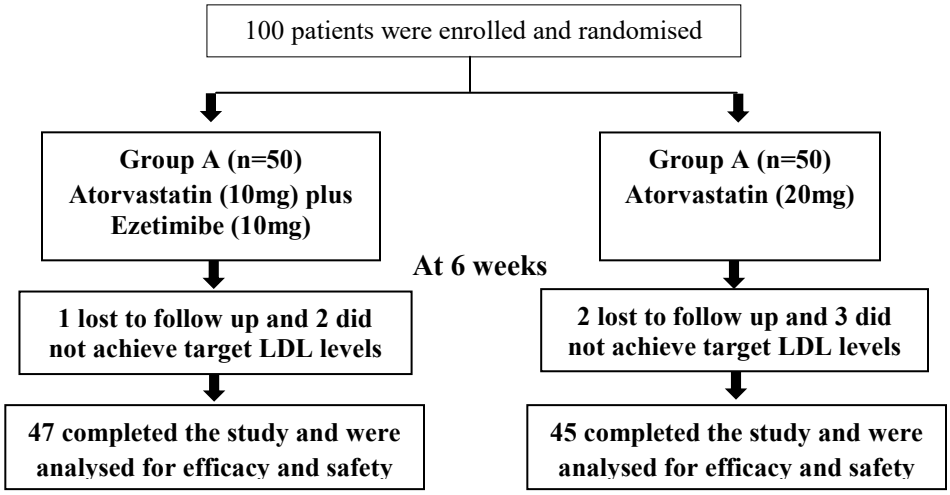
On first visit (0 week) patient's characteristics such as age, sex, registration no., and brief medical history was noted in record form Baseline investigations such as serum total cholesterol (TC), serum low density lipoprotein (LDL), serum very low density lipoprotein (VLDL), serum high density lipoprotein (HDL), serum triglycerides (TG) levels, serum glutamate oxalate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum creatine phosphokinase (CPK) levels, serum creatinine, blood urea nitrogen (BUN) were recorded. Patients were provided with a drug diary to record consumption of medicine and any adverse effect Patients from group A received tablet Atorvastatin (10 mg) and tablet Ezetimibe (10 mg) orally once a day at bedtime and group B received tablet Atorvastatin (20 mg) orally once a day at bedtime. All the patients were instructed to take the medicine orally once a day with glass of water at bedtime.

All the patients also received other concurrently required medications such as advised, antihypertensive or antidiabetic drug etc. No patient used any other lipid lowering agent like bile acid sequestrants, fibrates or niacin.

Study treatment was started on the day of randomization and continued for 12 weeks. Follow up visits were scheduled on 6th and 12th week and at each follow up the patients were advised to bring blisters of the tablet. Compliance to study medicine was measured by pill count during each follow up. The effect of the drugs in both the groups was assessed by changes in the lipid profile (TC, TG, VLDL, LDL, HDL) at 6th week and 12th week. To check for the hepatotoxicity or myopathy that may be caused by statins, SGOT, SGPT, CPK, BUN, serum creatinine were assessed at 6th week and 12th week for both the groups. During each follow up, patients were interviewed and examined for occurrence of myalgia, jaundice or any other adverse effect.

Those patients in both the groups in whom target LDL levels (<100 mg/dl) was not attained at 6th week, were excluded from the study and referred to the physician for further management. Such patients were excluded from statistical analysis.

The study profile according to CONSORT guidelines shown in the figure:



2.4 Efficacy assessment:

The effects of the drugs in both the groups will be assessed by changes in the Lipid profile (TC, LDL, VLDL, HDL, TG) at baseline, 6th week and 12th week.

The percentage of patients who achieved NCEP ATP III[36] target levels for LDL (≤100 mg/dl and ≤ 70 mg/dl) at 6th week and 12th week of treatment was calculated and percentage of patients who achieved ≥ 30 % reduction in LDL at 6th week and 12th week of treatment was also calculated.

2.4 Safety assessment

At each visit patients were interviewed for occurrence of any adverse effect and physically examined during the study period. Patients were informed to contact immediately if they experience muscle aches for further evaluation. Patients were also encouraged to enter any side effect they experienced in the drug diary provided to them. These drug diaries were also evaluated for occurrences of side effects.

The safety of the drugs in both the groups was assessed by liver function tests [SGOT, SGPT], CPK, BUN, serum creatinine done at baseline, 6thweek and 12th week.

Clinically significant laboratory abnormalities included elevations in levels of SGOT and SGPT to at least 3 times the upper limit of normal (ULN) [21] and increase in levels of CPK ≥ 10 times ULN[22], in an asymptomatic patient. In symptomatic patient who had abdominal pain, SGOT and SGPT were estimated when they were symptomatic. Such patients were excluded from the study and were asked to consult physician for further management.

2.5 Laboratory investigations

All analysis was conducted on fasting venous blood sample (5ml) at central biochemistry laboratory of the hospital at 6th and 12th week.

TC, HDL and TG were measured using enzyme method. LDL and VLDL were calculated using Friedewald equation [23] according to which:

LDL=TC-HDL-(TG/5)VLDL= (TG/5).

Table 1: Methods of estimation of serum lipid level

Lipids	Method of estimation
Total cholesterol	Roeschlau's method[24]
Triglycerides	Method of Wakomodified by McGowan[25]
HDL-C	Phosphotungstic acid method[26]

SGOT, SGPT, CPK, BUN, serum creatinine was examined.

2.6 Statistical analysis [20]

Categorical data in demographic parameters at baseline was analyzed by using 'Z' test for difference between two proportions. Continuous variables between the two treatment groups were analyzed by unpaired t-test. Efficacy endpoints within the group were analyzed by using paired t-test. A '*p*' value < 0.05 was considered statistically significant.

3. Observations and results

A total 100 patients were enrolled for the study. 50 patients were allocated to Atorvastatin group and 50 patients to Atorvastatin and Ezetimibe group. During the study period, 2 patients were lost to follow up and 3 patients did not achieve target LDL levels at 6th week in Atorvastatin group. 1 lost to follow up and 2 did not achieve target LDL levels at 6th week in Atorvastatin and Ezetimibe group and hence excluded from analysis. Thus 45 patients from Atorvastatin group and 47 patients from Atorvastatin and Ezetimibe group were considered for analysis of data.

Table 2: baseline characteristics of patients in both

Variables	Atorvastatin(20 mg) N=45	Atorvastatin (10 mg) plus Ezetimibe(10mg) N=47	p value
Age in years (Mean)	51.84	49.70	> 0.05*
Sex distribution			
Male	20 (44.44%)	24 (51.06%)	
Female	25 (55.56%)	23 (48.94%)	>0.05**
Co-morbidities			
DM	10	13	>0.05**
HTN	16	18	>0.05**
HTN and DM	19	16	>0.05**
Concurrent			
Drug Therapy			
Enalapril	22	20	>0.05**
Atenelol	16	15	>0.05**
Calcium Channel Blockers	3	2	>0.05**
Oral antidiabetic drugs	9	10	>0.05**

unpaired 't' test*, z test**

Table 2 Shows baseline characteristics including age, sex, clinical features and concurrent drug therapy of both treatment groups. As regard to age, sex, co-morbidities, concurrent drug therapy there was statistically no significant difference between the two groups when analysed by unpaired 't' test (p>0.05) and z test (p>0.05).

Table 3: Baseline mean lipid values (mg/dl)

Baseline lipid values	Atorvastatin (20 mg)N=45 Mean±SD	Atorvastatin (10 mg) plus Ezetimibe (10mg) N=47 Mean±SD	p value*
LDL	139.34±13.96	139.24±13.10	> 0.05
TC	226.78±10.98	228.62±11.96	> 0.05
TG	218.51±15.16	205.68±6.69	> 0.05
HDL	43.73±7.35	48.28±7.19	> 0.05
VLDL	43.70±3.03	41.10±1.41	> 0.05

*Unpaired t test, Values are expressed as Mean ± SD

Table 2 shows the baseline mean and standard deviation of lipid values in two treatment groups. Baseline mean lipid values showed statistically no significant difference between the two groups when analysed by unpaired 't' test. (p>0.05).

3.1 Efficacy of treatment in Atorvastatin and Atorvastatin plus Ezetimibe combination groups

Table 3: changes in mean values of lipids in atorvastatin group (mg/dl)

Lipid	Baseline	6^{th} week Mean±SD	12^{th} week Mean±SD	p value# 6^{th} week and12^{th} week
LDL	139.34	125.41±13.73	113.44±12.29	< 0.01
TC	226.78	212.6±11.85	199.98±10.29	<0.01
TG	218.51	209.49±14.47	198.78±12.73	<0.01
HDL	43.73	45.29±6.98	46.78±6.85	<0.01
VLDL	43.70	41.90±2.89	39.76±2.54	<0.01

#paired 't' test.

Table 3 shows mean values of lipid in Atorvastatin group at baseline, 6^{th} week and 12^{th} week. At 6^{th} and 12^{th}week, the levels of LDL, TC, TG, VLDL showed statistically significant decrease (p<0.01) and HDL levels showed statistically significant increase (p<0.01) as compared to the baseline levels when analysed by paired 't' test.

Table 4: Changes in mean values of lipids in atorvastatin plus ezetimibe group (mg/dl)

Lipid	Baseline	6^{th} week Mean±SD	12^{th} week Mean±SD	p value# 6^{th} week and12^{th} week
LDL	139.24	114.30±13.10	107.90±12.39	<0.01
TC	228.62	204.83±13.12	190.32±12.12	<0.01
TG	205.68	186.09±7.55	170.04±9.15	<0.01
HDL	48.28	52.34±6.59	54.62±6.50	<0.01
VLDL	41.10	37.09±1.58	35.35±3.87	<0.01

#paired 't' test.

Table no. 4 shows mean values of lipid in Atorvastatin and Ezetimibe combination group at baseline, 6^{th} week and 12^{th} week. At 6^{th} and 12^{th} week, the levels of LDL, TC, TG, VLDL showed statistically significant decrease (p<0.01) and HDL levels showed statistically significant increase (p<0.01) as compared to the baseline levels when analysed by paired't' test.

3.2 Mean reduction (percentage) in serum lipid parameters

Table 5: Mean reduction (percentage) in levels of LDL in both treatment groups

Group	Mean reduction (percentage)		p value*
	Atorvastatin (20 mg)N=45 Mean in mg/dl (%)	Atorvastatin (10 mg) plus Ezetimibe (10mg)N=47 Mean in mg/dl (%)	
6^{th} week	13.93 (9.99%)	24.94 (17.91%)	< 0.05
12^{th} week	25.90 (18.58%)	31.34 (22.50%)	< 0.05

*Unpaired t test

Table 5 shows mean reduction (percentage) in levels of LDL in the two treatment groups. There was greater reduction in levels of LDL in patients treated with Atorvastatin plus Ezetimibe combination as compared to those patients treated with Atorvastatin alone. This difference in mean reduction (percentage) in LDL levels in between two groups was significant at 6th and 12th week when analysed by unpaired 't' test ($p<0.05$).

Table 6: Mean reduction (percentage) in levels of TC in both treatment groups

Group	Mean reduction (percentage)		P value*
	Atorvastatin (20 mg)N=45 Mean in mg/dl (%)	Atorvastatin (10 mg) plus Ezetimibe (10mg)N=47 Mean in mg/dl (%)	
6th week	9.23 (6.25 %)	23.79 (10.40 %)	<0.05
12th week	21.51 (11.81 %)	38.30 (16.75 %)	<0.05

*Unpaired t test

Table 6 shows percentage mean reduction in levels of TC in the two treatment groups. There was greater reduction in levels of TC in patients treated with Atorvastatin plus Ezetimibe combination as compared to those patients treated with Atorvastatin alone. This difference in percentage mean reduction in TC levels in two groups was significant at 6thand 12th week when analysed by unpaired 't' test ($p<0.05$).

Table 7: Mean reduction (percentage) in levels of TG in both treatmentgroups

Group	Mean reduction (percentage)		P value*
	Atorvastatin(20 mg) N=45 Mean in mg/dl (%)	Atorvastatin (10 mg) plus Ezetimibe (10mg) N=47 Mean in mg/dl (%)	
6th week	9.02 (4.12 %)	19.59 (9.52 %)	<0.05
12th week	19.73 (9.02 %)	35.65 (17.33 %)	<0.05

*Unpaired t test

Table 7 shows mean reduction (percentage) in levels of TG in the two treatment groups. There was greater reduction in levels of TG in patients treated with Atorvastatin plus Ezetimibe combination as compared to those patients treated with Atorvastatin alone. This difference in mean reduction (percentage) in TG levels in two groups was significant at 6th and 12th week when analysed by unpaired 't' test ($p<0.05$).

Chart 1: Mean reduction (percentage) in levels of VLDL in bothtreatment groups

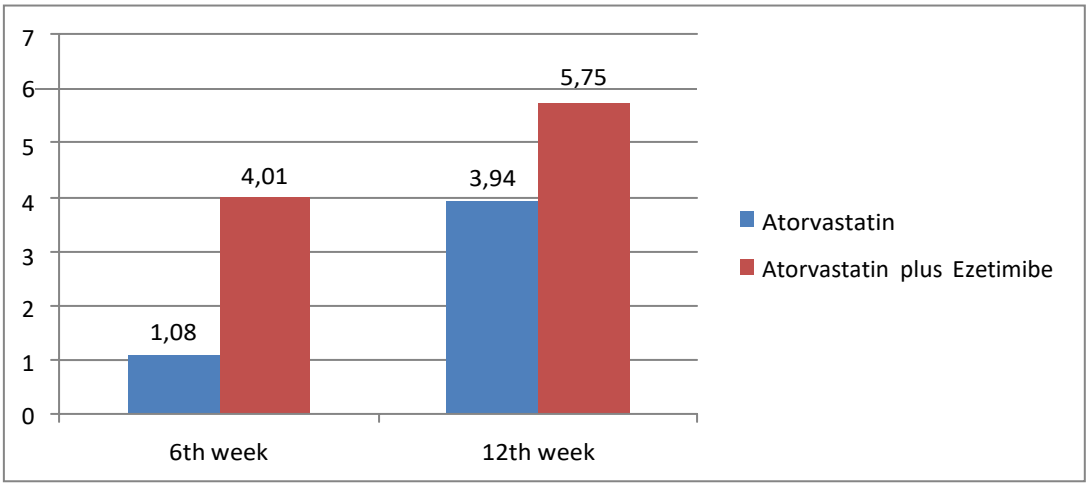


Chart 1 shows mean reduction (percentage) in levels of VLDL in the two treatment groups. There was greater reduction in levels of VLDL in patients treated with Atorvastatin plus Ezetimibe combination as compared to those patients treated with Atorvastatin alone. This difference in mean reduction (percentage) in VLDL levels in two groups was significant at 6th and 12th week when analysed by unpaired 't' test ($p<0.05$).

Chart 2: Mean increase (percentage) in levels of HDL in bothtreatment groups.

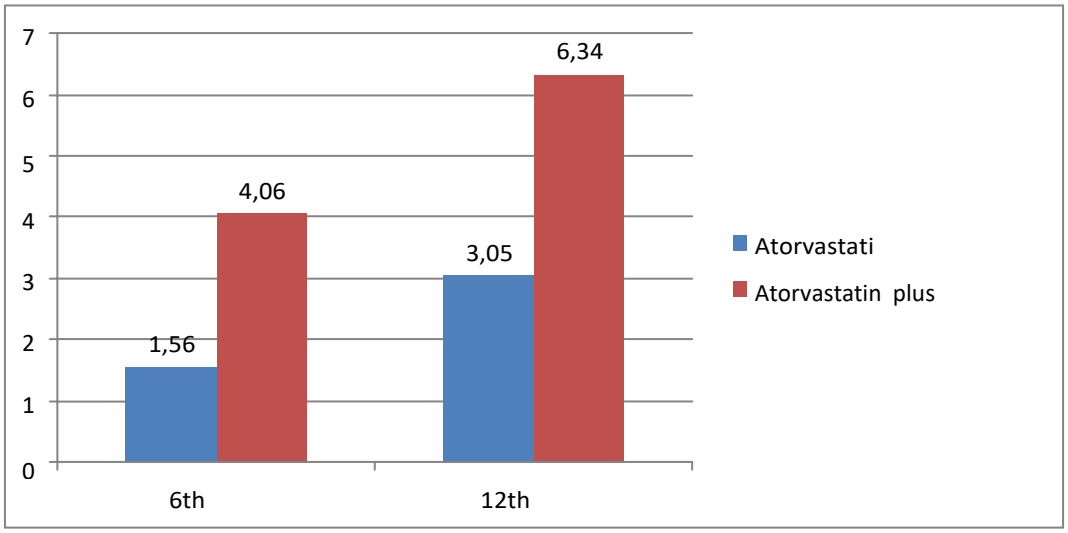


Chart 2 shows mean increase (percentage) in levels of HDL in the two treatment groups. There was higher increase in levels of HDL in patients treated with Atorvastatin plus Ezetimibe combination as compared to those patients treated with Atorvastatin alone. This difference in mean increase (percentage) in HDL levels in two groups was significant at 6th and 12th week when analysed by unpaired 't' test ($p<0.05$).

Chart 3: Percentage of patients who achieved target levels of LDL ≤ 100 mg/dl

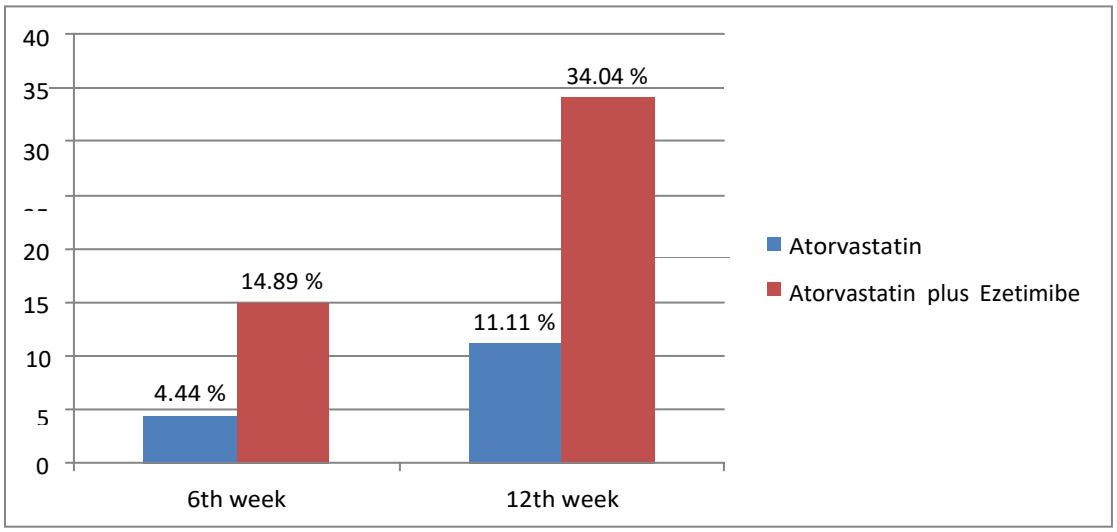


Chart 3 shows percentage of patients who achieved target levels of LDL ≤ 100 mg/dl at 6th week and 12th week in the two groups. It was seen that significantly higher percentage of patients from Atorvastatin plus Ezetimibe group achieved the target level of ≤ 100 mg/dl LDL as compared to Atorvastatin alone group at 6th week and 12th week when analysed by 'z' test ($p<0.01$).

Chart 4: Percentage of patients who achieved target levels of LDL ≤ 70 mg/dl

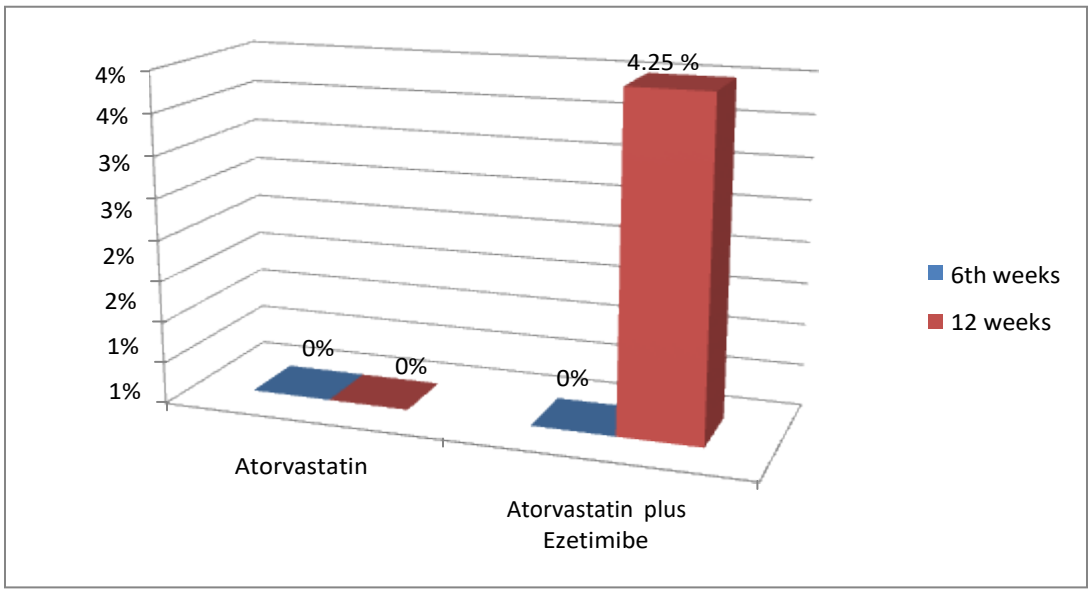


Chart 4 shows percentage of patients who achieved levels of LDL ≤ 70 mg/dl at 6th week, and at 12th week in the two groups. None of the patients from either treatment group reached levels of LDL ≤ 70 mg/dl at 6th week. At 12th week, 4% of patients in Atorvastatin plus Ezetimibe group attained LDL levels of ≤ 70 mg/ dl but no patient from Atorvastatin group could attain this level of ≤ 70 mg/ dl.

3.3 Safety and tolerability measures:

Chart 5: Incidence of adverse effects in both treatment groups

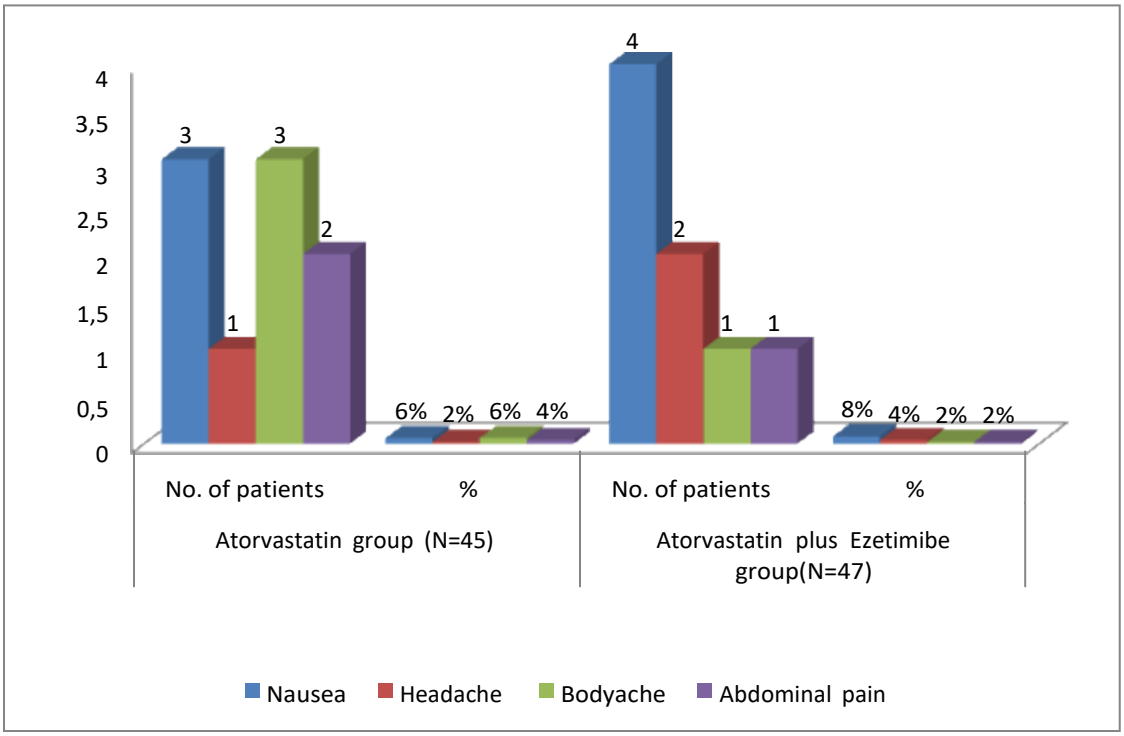


Chart 5 gives the comparative data regarding the percentage of patients who reported a particular adverse effect like nausea, headache, body ache or abdominal pain in the two treatment groups. There was no statistically significant difference in the incidence of these adverse effects in two treatment groups as analysed by z test ($p > 0.05$).

There was no occurrence of any serious adverse event in any patients during this study. Minor adverse effects in form of nausea, headache, body ache or abdominal pain were encountered in both groups. These adverse events were mild and self-limiting, hence did not require discontinuation of the study drugs.

4. Discussion

A total 100 patients were enrolled for the study. 50 patients were allocated to Atorvastatin group and 50 patients to Atorvastatin and Ezetimibe group. During the study period, 2 patients were lost to follow up and 3 patients did not achieve target LDL levels at 6th week in Atorvastatin group. 1 lost to follow up and 2 did not achieve target LDL levels at 6th week in Atorvastatin and Ezetimibe group and hence excluded from analysis. Thus, 45 patients from Atorvastatin group and 47 patients from Atorvastatin and Ezetimibe group were considered for analysis of data. Both the groups were comparable as regards to age, sex distribution, comorbidities, concurrent drug therapy as there was no statistically significant difference found.

Patients enrolled in the study received either Atorvastatin (20 mg) or combination of Atorvastatin plus Ezetimibe (10 mg + 10 mg). Similar doses have been used in several studies comparing efficacy and safety of Atorvastatin plus Ezetimibe combination therapy with Atorvastatin alone.[27-29] González *et al* in their study used statin therapy plus Ezetimibe 10 mg/day for 6-8 weeks.[30] In some previous studies such as Goldberg *et al*, T. Pearson *et al* investigators had used Simvastatin instead of Atorvastatin.[31,32] Jacques Genest studied combination of statin and Ezetimibe for the treatment of dyslipidemias and the prevention of coronary artery disease.[33]

Study reported by Goldberg *et al* evaluated the efficacy of Ezetimibe/Simvastatin and Atorvastatin in patients with Type II Diabetes mellitus and hypercholesterolemia, the percentage reduction of LDL from baseline in Ezetimibe/Simvastatin (10mg/20mg) was 53.6% and Atorvastatin (40mg) was 50.9%. They reported higher percentage reduction in LDL with Atorvastatin alone (50.9%) than that of our study (19%), this may be because they had used Atorvastatin in dose of 40 mg while we used a dose of 20 mg.[32]

Foody *et al* in their study found that LDL reductions from baseline and goal attainment improved substantially in patients treated with Ezetimibe added onto simvastatin, Atorvastatin, or rosuvastatin therapy (n=2,312) versus those (n=13,053) who titrated these statins. In multivariable models, percent change from baseline in LDL was -13.1% to -14.8% greater for those who added Ezetimibe onto simvastatin, Atorvastatin, or rosuvastatin versus those who titrated.[34]

Studies in the past have demonstrated similar percentage reduction in LDL than result obtained in our study. Evan Stein *et al*, reported that at the end of 14 weeks, Atorvastatin plus Ezetimibe combination therapy resulted in 33.2 % reduction in LDC as compared to 20.5 % with Atorvastatin alone. Azar *et al* reported a 24% reduction in LDL with combination therapy and 14% reduction in LDL with Atorvastatin alone in cardiovascular patients.

In present study, most commonly reported adverse effect were nausea, headache, bodyache or abdominal pain in the two treatment groups. No musculoskeletal adverse effects like myalgia, rhabdomyolysis were encountered in either of the groups. There was no statistically significant difference in the incidence of these adverse effects in two treatment groups. Similar findings were reported by Ballantyne *et al*[27], González *et al*[35] and Jacques Genest *et al*.[33]

At the end of 6th week and 12th week, administration of Ezetimibe with Atorvastatin resulted in significantly greater percentage reduction in LDL as compared to that achieved with Atorvastatin alone. Also there was greater reduction in the levels of TC, TG, VLDL in Atorvastatin plus Ezetimibe combination group as compared with Atorvastatin alone. This difference in percentage reduction in TC,TG, VLDL in two groups was significant at 6th and 12th week ($p<0.05$). There was greater increment in HDL in Atorvastatin plus Ezetimibe combination group as compared with Atorvastatin alone. This difference in percentage increment in HDL in two groups was statistically significant at 6th and 12th week ($p<0.05$). Similar observations were reported by Ballantyne *et al* [27].

5. Conclusion

We conclude that Atorvastatin co-administered with Ezetimibe offers more effective and equally tolerated option than Atorvastatin alone for the patients with newly diagnosed dyslipidemia having LDL levels of > 100 mg/dl as it significantly lowers the LDL, TG, TC and VLDL along with significant increase in HDL.

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