ORIGINAL ARTICLE

Comparative Effectiveness of Atorvastatin (Low Vs High Dose) in Lowering Low-Density Lipoprotein Cholesterol in Intermediate Risk Cardiovascular Patients

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ABSTRACT

Background: Hyperlipidemia is a known risk factor for cardiovascular disease. Statins therapy greatly reduce the risk of cardiovascular events. The rationale of this study was to investigate the effectiveness of Atorvastatin (20mg vs. 40mg) in lowering LDL-C levels.

Aim: To determine the effectiveness of Atorvastatin (Low vs. High Dose) in terms of lowering LDL to < 100mg/dl in patients with Intermediate risk of cardiovascular disease by Framingham risk score.

Methodology: It was a randomized controlled trial and 140 patients, previously on no lipid lowering therapy, were divided into two groups by lottery method. This study was completed in 6 months after it was approved from IRB/ASRB.Baseline LDL cholesterol levels were recorded. One group was given low dose (20mg) atorvastatin while other was given high dose (40mg) atorvastatin for 6 months. LDL levels were again monitored after 6 months and efficacy of treatment was assessed.

Results: The mean age of the patients in group 1 was 61.67 years (SD 9.84) and group 2 was 66.7 years (SD 8.78), mean LDL-C levels were 149.24 mg/dl (SD 27.767). In group 1, 62.9% were males and 37.1% were females, whereas in group 2, 65.7% were males and 34.3% were females. Family history of cardiovascular disease was present in 61% of the patients, 41.43% were smokers, 59.3% were hypertensive and 45% were Diabetic. Chi square test revealed that both therapies had significant effect on lowering LDL-cholesterol and were equally effective.

Conclusion: Low dose Atorvastatin to reduce the LDL-C levels in Intermediate risk patients is equally effective and can help to get the same benefit from low dose preventing the side effects of high dose.

Key words: Cardiovascular disease, low density lipoprotein cholesterol, atorvastatin

INTRODUCTION

Hyperlipidemia is a well-established risk factor for cardiovascular disease[1] especially in high risk patients with cardio-metabolic syndrome. Statins have anti-atherosclerotic effects and reduce the levels of low density lipoprotein cholesterol (LDL-C) by inhibiting the synthesis of HMG-CoA Reductase[2]. This therapy significantly reduces the risk of primary and secondary cardiovascular events[3].

A study conducted on Japanese patients, revealed that strong intensity statins of 2nd and 3rd generation (Rosuvastatin, Atorvastatin and pitavastatin) are more effective in lowering the risk of cardiovascular disease as compared to standard-intensity statins of 1st generation (pravastatin, simvastatin and fluvastatin[3]. On contrary to this, some studies have shown that Asian patients require low-intensity statins because of lower body weight and Body Mass Index[4]. An experimental study was conducted in Korea and Singapore which revealed that low dose rosuvastatin (10mg) works well for Asian population as opposed to Atorvastatin (10-80mg) is similar in both Asian and Western populations[5-7].

The rationale of our study is to investigate the effectiveness of Atorvastatin (20mg vs. 40mg) in lowering LDL-C levels as there are controversies in the data of Asian and Western population available[6,7]. A study favors high dose (20mg) Rosuvastatin over low dose (10mg) Rosuvastatin in Western population[8]. Since there are no national guidelines available, physicians are compelled to follow international guidelines which recommend high dose statins but the trend in our population is to give low dose statins in the fear of development of side effects without any evidence or expert opinion. So, this study will may help the patients to get the same benefit from the low dose statins preventing the side effects of high dose statins.

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METHODOLOGY

This study was completed in 6 months after approval from IRB/ASRB and was conducted in the outpatient department of Medicine and Cardiology, Mayo Hospital Lahore. Patients of more than 50 years age and of both gender were included who fulfilled the criteria of Intermediate risk as per Framingham risk score operational definition i.e. patients with coronary artery disease who had:

- LDL-C ≥3.5 mmol/L (Strong, Moderate)
- For LDL-C <3.5 mmol/L consider if:Apo B ≥1.2 g/L OR Non-HDL-C ≥4.3 mmol/L (Strong, Moderate)
- Or were Men ≥50 and women ≥60 with 1 risk factor: low HDL-C, impaired fasting glucose, high waist circumference, smoker, hypertension

All Patients with chronic kidney disease (eGFR) determined by serum chemistry, pregnant females,

lactating mother, diabetics and smokers who were already on statins or other lipid lowering drugs were excluded from the study.

It was a Randomized controlled Trial. The participants (total 140) that were eligible were randomly assigned to 1 of the 2 treatment groups of equal ratio (70 patients in each group) for 6 months: one group was given atorvastatin 20mg/day and the other was given atorvastatin 40mg/day. Patients were assessed for a reduction in low density lipoprotein cholesterol levels after six months.

The randomization of participants was done through a lottery method so that the numbers of participants in each group could be approximately equalized. Assignment of patients into groups was done after all screening assessments were completed and being accepted into the study.

Detailed history and physical examination was taken to satisfy the inclusion and exclusion criteria. Group A patients received low dose (20mg) and group B with high dose (40mg) of Atorvastatin for 6 months. All basic demographic information of each patient (name, sex, height, weight, waist circumference, contact, address) were also recorded on pre-designed performa. Predefined diet and exercise plan were given to all the patients, in which statins are indicated. Baseline investigations like Fasting lipid profile (LDL-C), CBC, serum chemistry profile was done before the study and LDL-C was done at 03 & 06 months after starting statins. End point was LDL level after 06 months of treatment. All information was recorded through pre-designed performa. Effectiveness of statins was determined by achieving LDL-C levels as ≥30% reduction from baseline.

All the collected data was entered into SPSS version 26 and analyzed. The qualitative data like demographics (gender; male or female) were presented by frequency and percentage. Quantitative data like age (years), LDL-C level were presented by means and standard deviations. Comparison of efficacy of Low and high intensity therapy was assessed by Chi square test. P-value ≤0.05 was taken as significant.

RESULTS

A total of 140 patients were enrolled and were divided into two groups of 70 patients each. One group received low dose atorvastatin and the other one received high dose atorvastatin. The mean age of the patients in group 1 was 61.67 years with a standard deviation of 9.84, whereas in group 2 was 66.7±8.78. The mean LDL-C levels were 149.24 gm/dl with a standard deviation of 27.767. In group 1, 62.9% were males and 37.1% were females and in group 2, 65.7% were males and 34.3% were females.

Among the participants, family history of cardiovascular disease was present in 61% of the patients. Out of 140 participants, 58 (41.43%) were smokers. Hypertension was present in 83 (59.3%) of the patients. Diabetes was present in 63 (45%) of the patients.

Mean LDL-C levels were decreased by both treatment to a value of less than 100mg/dL. Chi square test was applied to look for the effect of low dose vs high dose atorvastatin in patients and it was found that low dose atorvastatin was equally effective in lowering LDL-C as compared to high dose atorvastatin as indicated by a p value of >0.05 for both groups when the means were compared.

Table 1: Age, gender of the participants and the efficacy of treatment

Parameters	**Group A (Low Dose LDL-C) (n=70)**	**Group B (High dose LDL-C) (n=70)**	**P value**
Age (in years)	61.67±9.84*	66.5±8.78*	
LDL-C (mg/dl):			
Baseline	148.19±28.235*	150.3±27.452*	0.576
At the end of treatment	96.51±20.849*	82.7±12.55*	0.859
Gender:			
Male	44 (62.9%)	46 (65.7%)	
Female	26 (37.1%)	24 (34.3%)	
Treatment efficacious:			
Yes	49 (70%)	54 (77.1%)	0.338
No	21 (30%)	16 (22.9%)	0.448

P-value of ≤0.05 is considered as significant
*mean and standard deviation

DISCUSSION

In this study comparing the two different intensities of lipid lowering drug i.e. atorvastatin, in individuals with intermediate risk of cardiovascular disease, it was found that both intensities that is of 20mg and 40mg were equally effective in lowering down the low density lipoprotein cholesterol levels to less than 100mg/dL in a timeframe of 9 to 12 months. In previous placebo controlled trials comparing the different intensities, similar results were obtained i.e. Standard doses of atorvastatin were more beneficial compared to intensive doses.

The current study did not considered the effects of statin therapy on the outcomes of intermediate risk cardiovascular disease. Previous studies comparing the intensities also studied the effects of statin therapy, specifically atorvastatin, on the outcomes specifically mortality. A study done by Christopher P. Cannon et. al, revealed that high intensity statin therapy was effective in lowering the risk of mortality from any major cardiac issue or other cause in patients who were hospitalized for an acute cardiac emergency.

Other risk factors that were considered in this study were diabetes, hypertension, smoking and family history of cardiovascular disease. However, though there were many

individuals with multiple risk factors the effect of these risk factors on the overall results was not studied and it was not revealed if they had any influence on the low density lipoprotein levels.

Previous trials had been comparing different statins therapy at various doses, however, there are limited trials comparing the efficacy of a single statin at different doses. Due to different trials of statins, there was difference in the extent of lowering low density lipoprotein cholesterol levels. However, those trials could not exclude the possibility that the difference in the outcomes was related to non-lipid pleiotropic effects of statins, which may differ from each other and suggested that further trials should be based on different doses of a single statin drug can address such possibility. This possibility was assessed in the current study and we revealed that there was no difference in terms of dose of atorvastatin in lowering down the levels of low density lipoprotein cholesterol, both low and high doses were equally efficacious in intermediate risk cardiovascular disease.

The current study had certain limitations. The trial included only atorvastatin, so the results cannot be generalized to the other statins.There was no comparison with more potent newer statins.The study was conducted for a short duration, when atherosclerosis is a very chronic disease.The efficacy of atorvastatin at low and high dose was only assessed in intermediate risk group, however, the effect of two intensities in low and high risk cardiovascular disease was not studied.Lastly, the cost benefit analysis was not seen in the current study.

CONCLUSION

The statistical distribution of effectiveness of Atorvastatin (Low Vs High Dose) to reduce the LDL-C levels in Intermediate risk patients was elaborated through the results of this study on basis of dose of respective drug which can help patients to get the same benefit from low dose preventing the side effects of high dose, as the results turn out to be favorable for low dose.

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