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Original Research Article

Efficacy and safety of atorvastatin and rosuvastatin in ischemic heart disease patients: A prospective study

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Abstract

Purpose: *To compare the safety and efficacy of two commonly used statins namely; atorvastatin and rosuvastatin, and determine the efficiency of CoQ10 in the reversal of statin-induced myopathy.*
Methods: *An investigational study design was adopted using randomized trials involving patients suffering from ischemic heart disease and receiving either atorvastatin or rosuvastatin. The study was conducted at Punjab Institute of Cardiology, Lahore, Pakistan during the period, November 2016 - February 2017. A total number of 95 male and female patients, between the ages of 40 and 80 years, were selected. Their blood samples were analyzed for lipid profile, total cholesterol, serum high-density lipoprotein-cholesterol (HDL-C), serum triglycerides, low-density lipoproteins-cholesterol (LDL-C) and total cholesterol/HDL-C ratio.*
Results: *Gender and dose showed significant correlation with creatine phosphokinase (CPK) levels, ($p = 0.001$) and ($p > 0.001$), respectively. The patients using rosuvastatin 20 mg had a higher risk of developing myopathy than those treated with atorvastatin 40 mg ($p = 0.023$), while atorvastatin 20 mg patients were more prone to induce myopathy than 10 mg ($p = 0.001$) recipients. Atorvastatin 20 mg produced higher CPK levels than rosuvastatin 10 mg ($p = 0.002$). A substantial increase in CPK levels was found with rosuvastatin 20 mg and atorvastatin 20 mg usage ($p > 0.001$). It was observed that rosuvastatin 20 mg significantly increased the risk of myopathy compared to atorvastatin 10 mg ($p > 0.001$). However, rosuvastatin 20 mg/day considerably reduced the blood cholesterol as compared to atorvastatin 10mg/day ($p = 0.001$). CPK levels reduced significantly following treatment with CoQ10 ($p = 0.022$).*
Conclusion: *Rosuvastatin users are more prone to the risk of myopathy, myalgic symptoms and rise in CPK levels than atorvastatin users, and these effects are dose related. CoQ10 is effective in lowering CPK levels and reversing myalgia.*

Keywords: *Statin, Myalgia, CoQ10, CPK, Atorvastatin, Rosuvastatin*

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INTRODUCTION

Cardiovascular diseases are considered to be the primary cause of disability and death in the entire world; however, Asian countries are amongst the highest at risk, threatened by this disease [1]. It is estimated that one third of the adults in US are suffering from cardiovascular

diseases and hyperlipidemia [2]. It is a fact that Statins have been used to treat hypocholesteremia since 1987. As a result, it is reported that statins are prescribed in over 100 million prescriptions per year [3]. These medicines act by lowering the levels of low density lipoproteins-cholesterol (LDL-C).

Statins are considered to be very effective in lipid lowering but unfortunately, they have side effects. The commonly known side effect is myopathy which is a common worldwide problem [4]. The biochemical marker for the evaluation of statin induced myopathy is the elevation in creatinine kinase (CK) levels.

Glueck and colleagues evaluated the effectiveness, acceptability, and safety profile of rosuvastatin and other statins. They established that 5mg and 10mg/day doses of rosuvastatin were well tolerated, effective and had a good safety profile [5].

Backes and colleagues determined the tolerance and effect of medicating (EOD) of rosuvastatin every alternative day. They concluded that EOD of rosuvastatin therapy was effective in most of the patients and was quite beneficial to the patients who were intolerant to once a day dose of statins [6]. It was also determined that rosuvastatin was more efficacious in reducing LDL-Cholesterol levels as compared to atorvastatin [7,8]. Baner and colleagues established that the most effective statin, in reducing total cholesterol and serum lipid in patients, was rosuvastatin 10 mg [8]. The risk over benefit ratio also indicated that rosuvastatin was more efficient than atorvastatin [9,10]. A number of treatments for managing statin induced myopathy are used but CoQ10 supplementation is considered to be the final and quite common in almost all patients [11].

This study aimed to compare the safety profile, efficacy of atorvastatin, rosuvastatin, and the effectiveness of CoQ10 in managing statin-induced myopathy.

METHODS

A prospective study design was carried out at Punjab Institute of Cardiology, Lahore, Pakistan from November 2016 - February 2017. A total number of 95 patients were selected between the ages of 40 and 80 years. For safety profile and comparative efficacy of atorvastatin and rosuvastatin, both male and female subjects were included in the study. All the selected patients suffered from ischemic heart disease. However, for determining the efficacy of the treatment with CoQ10, the additional criterion of muscle problems with elevated levels of CPK was included.

Study design

A convenience sampling technique was adopted. A total of 50 patients were included for efficacy purpose, out of which 40 patients participated in the safety evaluation and finally 5 patients were selected for the determination of efficacy of CoQ10.

Data was collected from patients visiting the outpatient department. The patients were divided into Group A and B. The patients in Group A were receiving atorvastatin while group B patients used rosuvastatin at different doses. These patients were further subdivided into three subgroups. In the first subgroup, comparison of the efficacy of the statins was determined, whereas, in the second subgroup safety comparison was evaluated while in the last subgroup the efficacy of the treatment recommended for the management of myopathy, that is CoQ10 supplementation, was determined.

In these subgroups, severity of the symptoms and total cholesterol levels were compared. Furthermore, CPK levels were also measured. The patients showing high levels of CPK were given CoQ10 supplementation and its effects were recorded.

Determination of efficacy of the statins

To compare the efficacy of atorvastatin and rosuvastatin, fifty (50) patients were selected who had been taking different doses (10, 20, and 40 mg) of these medications for more than one year.

Assessment of lipid profile

The blood samples were collected from the cubital vein of the patient and analyzed for lipid profile. For total cholesterol, serum HDL-C and serum triglycerides, Kit method (ADVIA Chemistry systems Siemens) was used to calculate LDL-C and total cholesterol/HDL-C ratio as in Eqs 1 and 2.

LDL-C = TC – HDL-C – (TG/5) ……. (1)

TC/HDL-C = TC/ HDL-C ……. (2)

Evaluation of safety profile

For safety profile the parameter evaluated was CPK which was done when myopathy was

present. Blood samples of 40 patients were drawn from the cubital vein and analyzed.

Assessment of effectiveness of CoQ10

To determine the effectiveness of CoQ10 in managing statin-induced myopathy, a randomized trial was conducted. When CK test was performed, 5 patients showed elevated levels of CK, therefore they were given 100 mg/day CoQ10 supplementation. After 30 days their blood CK levels were analyzed again and compared with the CK levels performed before the therapy.

The study design/protocol and the proforma were approved by the Ethical Committee of Punjab Institute of Cardiology (PIC), Lahore, Pakistan along with the patient's consent form, both in English and Urdu.

The ethical approval was obtained for human studies by Department of Research, Training and Post graduate Medical Education affiliated with PIC, Lahore, Pakistan under the approval number, RTPGME-Research-070. International guidelines for human studies were followed [12].

Study was conducted under the supervision of physicians and confidentiality of personal information was assured.

Data analysis

The data obtained was analyzed by SPSS version 21 and GraphPad Prism 7. Descriptive statistics (mean, standard deviation, frequency, percentage) were applied to summarize the data. Independent sample t-test was used for the comparison of safety and efficacy of the two statins, while paired t-Test was used to analyze the effect of CoQ10. The value of $P > 0.05$ was taken as statistically significant.

RESULTS

Demographics of the patients are depicted in Table 1. Amongst the Age ranges from 43-86 years, a total of 13 (32.5%) were female, while 27(67.5%) were male patients.

Association of levels of CPK with gender, age and duration of statin used is shown in Table 2. The results revealed that males, 142.59 ± 73.75 had significantly increased levels of CPK as compared to females, 65.17 ± 24.47 ($p = 0.007$).

Correlation of age, gender, dose and duration with CPK levels is illustrated in Table 3. Gender showed negative significant correlation with CPK ($p = 0.001$) while dose illustrated positive significant correlation ($p > 0.001$). Comparative effect of atorvastatin and rosuvastatin on CPK levels revealed that patients using rosuvastatin 20 mg, 139.6 ± 87.88 were significantly at higher risk of statin induced myopathy compared to those using atorvastatin 40 mg, 95.45 ± 38.52 ($p = 0.023$). The results further revealed that patients taking 20 mg rosuvastatin, 198.5 ± 78 were at higher risk of statin induced myopathy as compared to those using 10 mg rosuvastatin, 64.29 ± 23.19 ($p > 0.001$). Similarly, patients taking 20 mg atorvastatin, 110 ± 34.95 were more prone to induce statin induced myopathy compared to those taking 10 mg atorvastatin, 61.29 ± 20.13 ($p = 0.001$).

The results additionally revealed that the patients receiving atorvastatin 20 mg, 110 ± 34.95 showed higher levels of CPK as compared to those using rosuvastatin 10 mg, 64.29 ± 23.19 ($p = 0.002$). Substantial increase in CPK levels was also found in patients using rosuvastatin 20mg, 198.5 ± 78 compared to atorvastatin 20 mg, 110 ± 34.95 ($p > 0.001$). Rosuvastatin 20 mg, 198.5 ± 78 considerably increased the risk of myopathy compared to atorvastatin 10 mg, 62.71 ± 23.42 ($p > 0.001$). It was, likewise, observed that the effect of rosuvastatin 20 mg, 182.30 ± 54.66 was markedly lower than the effect of atorvastatin 20 mg, 177.0 ± 45.2 on the levels of cholesterol ($p = 0.032$). The result of rosuvastatin 20 mg, 28 ± 0.87 was noticeably lower than the effect of atorvastatin 10 mg, 5.89 ± 1.21 on the levels of Tchol/HDL-C ratio ($p = 0.001$). Atorvastatin 10 mg, 148.6 ± 57.36 was more efficacious than rosuvastatin 20 mg, 101.5 ± 43.26 when considering the levels of LDL-C ($p = 0.026$).

The results indicated that the levels of CPK, 122 ± 95.05 reduced, noticeably, after treatment with CoQ10 ($p = 0.022$). CPK values before and after taking CoQ10 are shown in Table 4. All the patients had normal values of lipid profile except one patient, who was taking 40mg of atorvastatin, but his symptoms were resolved and a reduction in CPK levels was also seen.

Table 1: Demographics of the patients (n=40)

Variable	Frequency (%)
Age range	43-86 years
Female patients	13(32.5)
Male patients	27(67.5)
Duration of taking statins	1-14years
Patients taking atorvastatin	22(55)
Patients taking rosuvastatin	18(43)

Table 2: Association of CPK levels with gender, age and duration of statin used

Variable	Asoociation of gender and CPK		Asoociation of age and CPK		Association of duration of statin use and CPK	
Group	Male	Female	≥6	< 56	≥5	< 5
N	27	12	17	22	12	27
Mean	149.6	65.2	121.6	116.6	121	16.1
SEM	14.2	7.1	19.1	116.6	117.8	15.3
P-value	0.007		0.592		0.351	

Table 3: Correlation of age, gender, dose and duration with CPK levels

Variable	CPK	
	Pearson correlation	*P*-value
Age	-0.075	0.325
Gender	-0.502**	0.001
Dose	0.601**	0.000
Duration	0.108	0.257

Table 4: Values of CPK before and after taking CoQ10(mg/dl) (P=0.022)

Before	After
283	83
305	312
303	82
212	77
231	169

DISCUSSION

While comparing efficacy and safety of atorvastatin and rosuvastatin, it was observed that the former induces significantly higher myalgic effect in females while later induces the same significant effect in males. Incidentally, no data is currently available in literature on this subject to confirm these findings. Hence further research is required. A number of reports have been published highlighting the effects of different statins to raise CPK levels [13].

In the present study, more than half of the patients were suffering from myopathy but only a few of them showed elevated levels of CPK. Paul and coworkers previously have reported that myopathic symptoms could appear in patients who had normal CPK levels. This concludes that myopathy can also occur with normal levels of CPK or those myalgias may be due to some other reason [14].

In the current study, statin induced myalgia and rise in CPK levels were compared based on the doses of atorvastatin and rosuvastatin. The results highlighted that the atorvastatin 20mg induced higher levels of CPK as compared to rosuvastatin 10mg. However, no significant difference was observed in the serum CPK levels of the patients who received 10 mg dose of either atorvastatin or rosuvastatin. This result was in agreement with the previous study [10]. However, other studies showed that statin induced myopathy was dose dependent [15,16].

Furthermore, it was observed that CPK levels were not duration dependent, but the extent of myalgia was duration dependent. Unfortunately, no supportive data is currently available to confirm these results, thus further research is required to endorse these findings. It was also reported that more rapid reduction in LDL-C levels was seen as the dose of the statin increased. The results of the study are in line with the previous studies [10,17,18].

The efficacy of CoQ10 in treating statin-induced myopathy is still debatable. CoQ10 has been reported to be useful for treating statin induced myopathy [21,22]. The use of CoQ10 supplementation was unable to reverse the statin induced myopathy in another study [23]. In the present study 5 patients were given CoQ10 whereas 4 patients showed significant reduction in CPK levels and reversal of myalgia symptoms.

CONCLUSION

Lipid-lowering drugs have the potential of inducing myalgic pain in patients which can be identified by regular monitoring of CPK levels. Moreover, administration of CoQ10 has the

potential to reverse not only the myalgic pain but also the levels of CPK.

DECLARATIONS

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We acknowledge the cooperation of the management and the Ethical Committee of Punjab Institute of Cardiology, Lahore, Pakistan, for granting permission to conduct and complete this research work. We also acknowledge the patients who participated in this research work.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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