

Comparative Study on Effectiveness and Safety of Atorvastatin with Rosuvastatin in Hyperlipidemic Patients at a Tertiary Care Hospital in Nepal

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ABSTRACT

Introduction

Hyperlipidemia is one of the most contributing factors to coronary heart diseases. Statins have become standard medicine in clinical practice to reduce total cholesterol, low density lipoprotein and to increase high density lipoprotein cholesterol. This study is conducted to compare the effectiveness and safety of atorvastatin with rosuvastatin in hyperlipidemic patients.

Methods

This is a prospective observational study involving 150 patients conducted in the Department of Internal Medicine of Kathmandu Medical College and Teaching Hospital from July 2019 to March 2020. Patients newly diagnosed with hyperlipidemia were enrolled. Patients that were prescribed with 10 mg of atorvastatin and 5 mg of rosuvastatin by the treating physician once daily for 6 weeks were divided into two groups. Data was recorded in the customized proforma and the SPSS package version 20 was used for analysis.

Results

Patients that were prescribed with atorvastatin were put in group I and those prescribed with rosuvastatin were included in group II with 75 participants in each group. The mean age of the patients were 50.56 ± 10.08 years in group I and 52.45 ± 10.20 years in group II with male to female ratio of 3:1. The mean BMI of group I was 25.36 ± 1.74 and that of group II was 26.48 ± 2.21 before therapy. There was a significant main effect of duration ($F_{1,74} = 401.02$, $p < 0.001$) on the TG and TC levels ($F_{1,74} = 1134.23$, $p < 0.001$) as well as ($F_{1,74} = 614.99$, $p < 0.001$) on the LDL and HDL levels ($F_{1,74} = 146.38$, $p < 0.001$).

Conclusion

Rosuvastatin was significantly more effective than atorvastatin in reducing levels of TG, TC and LDL-C. Rosuvastatin also significantly increased the level of HDL.

Keywords

Atorvastatin, hyperlipidemia, rosuvastatin

INTRODUCTION

Cardiovascular diseases are the most common causes of morbidity and mortality in underdeveloped and developing countries and have direct impact in terms of health resources and loss of productivity.¹ Hyperlipidemia or dyslipidemia is one of the most contributing factors to coronary heart diseases. It has major role in causing atherosclerosis and atherosclerosis associated conditions, such as coronary heart disease (CHD), ischemic cerebrovascular disease and peripheral vascular disease.²

Study conducted in Nepal revealed that 56% of the population had dyslipidemia which accounts for 17% with elevated level of total cholesterol, 27% with raised triglyceride, 30% with decreased high density lipoprotein and 10% with raised low density lipoprotein.³

Many studies have established relationship between the raised level of total cholesterol (TC), and low density lipoprotein cholesterol (LDL-C) in the occurrence of coronary heart disease. In order to prevent occurrence of coronary heart disease the levels of TC and LDL-C should be reduced below 442.86 mg/dl and 116 mg/dl, respectively.^{4,5} Statins have become standard therapeutic medicine in clinical practice to reduce total cholesterol and low density lipoprotein to prevent cardiovascular diseases.⁶

They possess other important properties besides cholesterol lowering agents like antioxidant, anti-inflammatory effects and antithrombotic effects, they also improve the endothelial activities and reduce the growth of atherosclerotic plaques.⁷ Statins have another important properties besides lowering of low density lipoprotein cholesterol (LDL-C) and triglycerides; it also contributes in the increment of high density lipoprotein cholesterol (HDL-C) which is also known as beneficial cholesterol in preventing coronary heart diseases.⁸

The aim of this study is to compare the effectiveness and safety of lipid lowering agent atorvastatin and rosuvastatin in hyperlipidemic patients in order to prevent from the coronary heart diseases in tertiary care hospital.

METHODS

This prospective observational study involving 150 patients based on convenience sampling was conducted in the Department of Internal Medicine of Kathmandu Medical College Teaching Hospital from July 2019 to March 2020 after obtaining ethical approval from Institutional Ethical Committee. The study recruited patients that attended the outpatient of Internal Medicine Department and were diagnosed with dyslipidemia with any of the following - TC>200mg/dl, serum triglycerides (TGs)>150mg/dL, low density lipoprotein cholesterol (LDL-C) > 100mg/dL, and high density lipoprotein cholesterol (HDL-C) < 40mg/dL levels. Height and weight were also recorded for BMI scale and obesity. Before initiating the therapy, the baseline data of all patients were collected including lipid parameters with TC, TG, LDL-C an HDL-C (Table 1).

Patients that were prescribed 10 mg atorvastatin once daily were included in group I and the patients that were prescribed with 5 mg of rosuvastatin once daily were included in group II. Patients were followed up after 6 weeks for assessment of lipid profile. Results were recorded and compared from the baseline at the start of the drug therapy. Safety and tolerability were evaluated throughout the study on the basis of reported adverse effects. At the end of 6 weeks, data related to lipid profile, compliance and side effects were recorded.

Data were recorded in the customized proforma from the patient record sheets and reports during the outpatient follow up after taking written consent from the patient. SPSS package version 20 was used for statistical analysis.

Table 1. Baseline characteristics of the study groups

Characteristics	Group I (Atorvastatin 10 mg)	Group II (Rosuvastatin 5 mg)
Number of patients	75	75
Age range (years)	34 to 72	28 to 72
Mean age (Years)	50.56±10.08	52.45±10.20
Sex (Male/Female)	59/16 (3:1)	55/20 (3:1)
Body mass index (BMI)	25.36±1.74	26.48±2.21
Lipid profile		
Triglyceride (TG) (mg%)	241.83±32.13	256.73±51.60
Total cholesterol (TC) (mg %)	254.55±24.38	270.27±21.06
Low density lipoprotein (LDL) (mg %)	149.39±17.17	165.25±13.85
High density lipoprotein (HDL) (mg %)	39.05±2.19	39.39±1.89

RESULTS

The total number of patients included was 150, with 75 in group I that prescribed with Atorvastatin and 75 in group II that were prescribed with Rosuvastatin. The age range of the patient was from 28 years to 72 years with mean age 50.56 ± 10.08 with male is to female ratio were 3:1 in group I and the age range was 28 to 72 years with 52.45 ± 10.20 years with male is to female ratio of 3:1 in group II. The mean body mass index (BMI) of group I was 25.36 ± 1.74 kg/m^2 and that of group II was 26.48 ± 2.21 kg/m^2 before drug therapy. Mean level of TG were 241.83 ± 32.13 and 256.73 ± 51.60 . Similarly the level of TC, were 254.55 ± 24.38 and 270.27 ± 21.06 , level of LDL were 149.39 ± 17.17 and 165.25 ± 13.85 and the level of HDL were 39.05 ± 2.193 and 39.39 ± 1.89 respectively in group I and group II before drug therapy (Table 1).

In group I the BMI of patients were change from 25.36 ± 1.74 to 24.64 ± 1.96 and the BMI of patients in group II were changed from 26.48 ± 2.21 to 26.55 ± 2.21 . Similarly the level of TG in group I were reduced from 241.83 ± 32.13 to 212.60 ± 30.33 in group I and from 256.73 ± 51.60 to 193.64 ± 36.75 in group II.

The level of TC was reduced from 254.23 ± 24.38 to 224.97 ± 21.40 in group I and from 270.27 ± 21.06 to 212.19 ± 18.15 in group II. The level of LDL was reduced from 149.39 ± 17.17 to 136.81 ± 18.97 in group I and from 165.25 ± 13.85 to 122.63 ± 12.25 in group II. There was slight increase in the level of HDL, from 39.05 ± 2.19 to 39.63 ± 1.95 in group I and from 39.39 ± 1.89 to 41.37 ± 1.45 in group II after drug therapy.

There was significant variation between the group I and group II after drug therapy with respect to TG, TC, LDL and HDL along with the test within subject's effects.

There was a significant main effect of duration ($F_{1,74}=401.02$, $p<0.001$) on the TG levels. The effect of drug choice on TG levels was not significantly different ($F_{1,74}=2.90$, $p<0.93$) which is not significant. Interaction between duration and drug choice has significant effect on TG levels ($F_{1,74}=10.20$, $p<0.002$).

There was a significant main effect of duration ($F_{1,74}=1134.23$, $p<0.001$) on the TC levels, however the effect of drug choice on TC levels was not significantly different ($F_{1,74}=0.33$, $p<0.57$). Interaction between duration and drug choice also had a significant effect on the TC levels ($F_{1,74}=172.27$, $p<0.001$).

There was a significant main effect of duration ($F_{1,74}=614.99$, $p<0.001$) on the LDL levels, however the effect of drug choice on LDL levels was not significantly different ($F_{1,74}=0.13$, $p<0.71$). Interaction between duration and drug choice also had a significant effect on the LDL levels

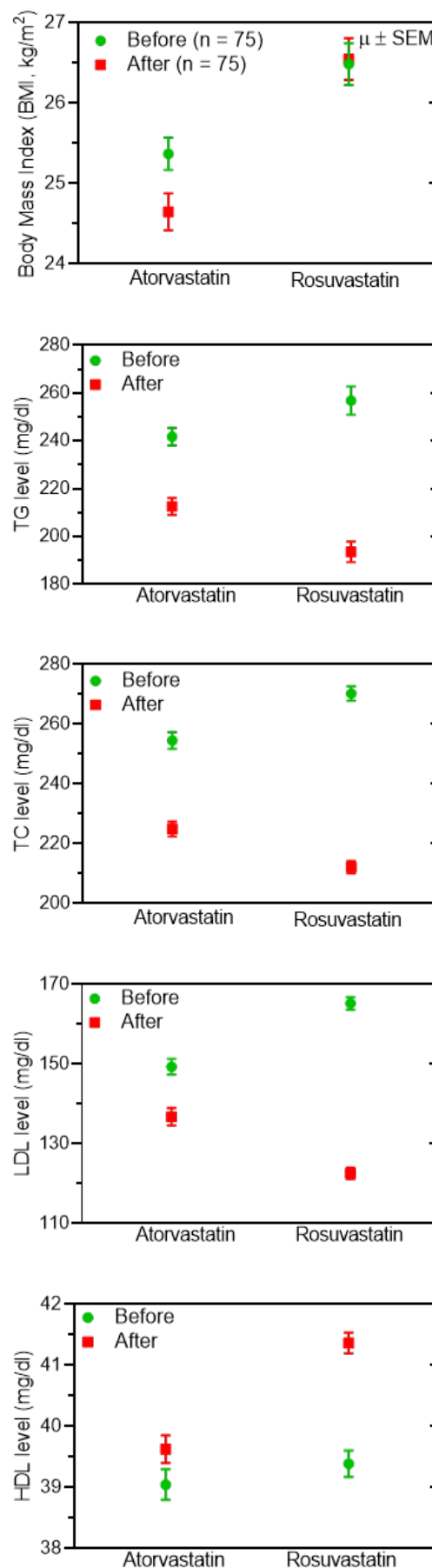


Fig 1. Changes in BMI, TG, TC, LDL and HDL after 6 weeks of drug therapy

Table 2. Adverse effects in the study groups

Adverse effects	Group I (Atorvastatin 10 mg)	Group II (Rosuvastatin 5 mg)
Headache	10 (13.3%)	4 (5.3%)
Allergy	6 (8%)	3 (4%)
Gastritis	8 (10.6%)	7 (9%)
Insomnia	5 (6.6%)	3 (4%)
Fatigue	12 (16%)	6 (8%)
Total occurrence	54.66%	30.66%

($F_{1,74}=266.44, p<0.001$).

There was a significant main effect of duration ($F_{1,74}=146.38, p<0.001$) on the HDL levels, the effect of drug choice on HDL levels was significantly different ($F_{1,74}=15.93, p<0.001$). Interaction between duration and drug choice also had a significant effect on the HDL levels ($F_{1,74}=60.85, p<0.001$).

Occurrence of adverse effects in atorvastatin (group I) was 54.66% while that in rosuvastatin (group II) was 30.66%, of which the most common adverse effects were fatigue, headache, gastritis, allergic rashes and insomnia (Table 2).

DISCUSSION

In the present prospective, comparative 6 week follow up observational study in dyslipidemic patients using two regimens of Atorvastatin 10 mg once daily in group I and Rosuvastatin 5 mg once daily in group II, we found that both the regimens were effective in improving the various parameters of lipid profile. When we compared the two regimens to determine the superiority of one therapy regime over the other; rosuvastatin has better effect with respect to Total cholesterol, LDL-C and HDL-C.

The age range of the patient was from 28 years to 72 years with mean age 50.56 ± 10.08 with male is to female ratio were 3:1 in group I and the age range was 28 to 72 years with mean age of 52.45 ± 10.20 years with male is to female ratio of 3:1 in group II which is similar with the prevalent age and also represent the sex distribution in study conducted in Nepal⁹ which suggest that on the increasing age and in male sex the prevalence of dyslipidemia is high due to decrease physical activity and uncontrolled dietary habits. The mean body mass index (BMI) of group I was $25.36 \pm 1.74 \text{ kg/m}^2$ that of group II was $26.48 \pm 2.21 \text{ kg/m}^2$ before drug therapy which is similar with the prevalence of obesity in Nepalese population¹⁰ the reason could be due to the enrollment of the maximum patients of urban region.

The level of TG in group I were reduced from $241.83 \pm 32.13 \text{ mg/dl}$ to $212.60 \pm 30.33 \text{ mg/dl}$ and

from $256.73 \pm 51.60 \text{ mg/dl}$ to $193.64 \pm 36.75 \text{ mg/dl}$ in group II which was 12% and 24.60% respectively indicates that the patient under rosuvastatin therapy have reduced more TG compare to atorvastatin similar study concluded that triglyceride levels were reduced by a (median reduction -33.0% on atorvastatin and -27.6% on rosuvastatin.¹¹ the reason could be the better metabolism of cholesterol by rosuvastatin with its long half life. Another study found reduction of TGs by 15.2% ($p<0.001$), with the use of rosuvastatin.¹² Similarly the level of TC was reduced from $254.23 \pm 24.38 \text{ mg/dl}$ to $224.97 \pm 21.40 \text{ mg/dl}$ in group I and from $270.27 \pm 21.06 \text{ mg/dl}$ to $212.19 \pm 18.15 \text{ mg/dl}$ in group II after drug therapy which is 11.8% and 21.48% respectively which resemble with another similar study where TC levels were reduced by 35.1% ($p<0.001$).¹²

The level of LDL-C was reduced from 149.39 ± 17.17 to 136.81 ± 18.97 in group I and from 165.25 ± 13.85 to 122.63 ± 12.25 in group II which is 8.7% and 26% respectively in another study it was found that LDL cholesterol was reduced by more than 50% versus baseline by both statins¹³ similarly in another study with the use of rosuvastatin it was found that the mean low density lipoprotein cholesterol (LDL-C) level decreased significantly from 108.9 ± 16.5 to $91.6 \pm 24.5 \text{ mg/dL}$ ($p < 0.001$) there was significant reduction which resembles with our finding.¹⁴ Another study found LDL-C by 48.5% ($p<0.001$),¹² In the LUNAR study, while the atorvastatin 80 mg provided a 42% reduction in LDL-C levels, rosuvastatin 40 mg provided a 46.8% reduction in LDL-C levels at the end of 6 weeks.¹⁵ One of the review study on atorvastatin has concluded that based on dose range of 10 to 80 mg/dl has found that the reduction of LDL-C was by 37.1% to 51.7% which is quite high compared to our study the possible reason behind this decrease was due to inhibition of (HMG-COA) reductase by one third to one half of the dose range and LDL-C is only one of the important biochemical product produced by HMG-COA reductase pathway and same study also resembles our finding which states that having similar dose response effect of both atorvastatin and rosuvastatin, atorvastatin is atleast three fold less potent than rosuvastatin in reducing total and LDL-cholesterol.¹⁶ Similarly another study conducted by Marias et al.¹⁷ also concluded with 19% reduction of LDL-C with the use of rosuvastatin, Teramoto et al.¹⁸ concluded 42-52% reduction in LDL-C with the use of rosuvastatin, the difference was significantly higher compare to our study which could be due to difference in the variation of patient profile as well as dietary intake, social and cultural variation.

In this study, there was slight increase in the level of HDL which was $39.05 \pm 2.19 \text{ mg/dl}$ to $39.63 \pm 1.95 \text{ mg/dl}$ in atorvastatin group I and from $39.39 \pm 1.89 \text{ mg/dl}$ to $41.37 \pm 1.45 \text{ mg/dl}$ in rosuvastatin group

II which was similar with another study in which both do not show significant increase in HDL level it was increased by small fold which was 4.1% in case of atorvastatin and 7.3% with rosuvastatin. Rosuvastatin has been approved for use at doses of 5 – 40 mg to improve HDL and other parameters in dyslipidemic patients.^{19,20} Study conducted by Farnier et al.²¹ also concluded that there was only 3% increment in HDL level with the use of rosuvastatin for weeks which resembles our study, similarly Marias et al.¹⁷ also showed an increment of 5% with the use of Rosuvastatin for six weeks. Juszczek et al.²² showed improvements of 11% with the use of Rosuvastatin. This finding suggests that there was no significant increment of HDL levels.

There was a significant main effect of duration ($F_{1,74}=401.02$, $p<0.001$) on the TG levels. The effect of drug choice on TG levels was not significantly different ($F_{1,74}=2.90$, $p<0.93$) which is not significant. Interaction between duration and drug choice has significant effect on TG levels ($F_{1,74}=10.20$, $p<0.002$). Similarly another similar study found that the level of TG decreased within both groups, but this decrease was not statistically significant [from 116.00 (87.00–182.00) mg/dL to 110.00 (89.00–154.00) mg/dL in the atorvastatin group; $p=0.532$, and from 154.50 (125.75–215.75) mg/dL to 135.00 (91.00–182.50) mg/dL in the rosuvastatin group, $p=0.052$, respectively.¹⁵ In contrast with our finding they concluded the level of significance with TGs by 15.2% ($p<0.001$), with the use of rosuvastatin.¹² There was a significant main effect of duration ($F_{1,74}=1134.23$, $p<0.001$) on the TC levels, however the effect of drug choice on TC levels was not significantly different ($F_{1,74}=0.33$, $p<0.57$). Interaction between duration and drug choice also had a significant effect on the TC levels ($F_{1,74}=172.27$, $p<0.001$) in patients in another study also it was found significant effects in respect to TC (from 181.64 ± 35.42 mg/dL to 138.36 ± 34.08 mg/dL in the atorvastatin group, $p<0.001$, and from 206.33 ± 36.00 mg/dL to 143.27 ± 39.95 mg/dL in the rosuvastatin group, $p<0.001$, respectively.²³

There was a significant main effect of duration ($F_{1,74}=614.99$, $p<0.001$) on the LDL levels, however the effect of drug choice on LDL levels was not significantly different ($F_{1,74}=0.13$, $p<0.71$). Interaction between duration and drug choice also had a significant effect on the LDL levels ($F_{1,74}=266.44$, $p<0.001$). Another study concluded with similar finding where LDL-C (from 120.08 ± 27.68 mg/dL to 72.22 ± 25.09 mg/dL in the atorvastatin group, $p<0.001$, and from 131.69 ± 24.61 mg/dL to 69.06 ± 26.62 mg/dL in the rosuvastatin group, $p<0.001$, respectively) were significantly reduced within atorvastatin and rosuvastatin.²³ In similar study it was found that both atorvastatin and rosuvastatin were effective in reducing LDL-C level

after 6 weeks of treatment but in comparison to both of them rosuvastatin was more effective than atorvastatin ($p<0.001$).²⁴ There was a significant main effect of duration ($F_{1,74}=146.38$, $p<0.001$) on the HDL levels, the effect of drug choice on HDL levels was significantly different ($F_{1,74}=15.93$, $p<0.001$). Interaction between duration and drug choice also had a significant effect on the HDL levels ($F_{1,74}=60.85$, $p<0.001$). In similar study it was found rosuvastatin was more effective than atorvastatin in increasing level of HDL ($p\leq 0.002$).²⁴ The effect of rosuvastatin on HDL, 7.3% (95%CI 7.1 to 7.6) is significantly greater than the effect of atorvastatin on HDL, 4.1% (95%CI 3.9 to 4.2).²⁵ Based on reported adverse effects in comparison to both groups of drugs common adverse effects were fatigue, headache, gastritis, allergic and insomnia in which the incidence was less in rosuvastatin group than atorvastatin group with 30.66% and 54.66% respectively. Similar study also concluded with the experience of adverse effects like myopathy, myalgia, rhabdomyolysis, abdominal pain and headache.²⁶ So considering the results with minimum adverse effects the drug reflects safe.

CONCLUSION

This study demonstrated that rosuvastatin 5 mg is significantly more effective than atorvastatin 10 mg in reducing TC, TG, LDL-C levels. It also significantly increases the level of HDL. The reported adverse effects are also lesser with rosuvastatin, so it can be considered safe and effective in dyslipidemic patients.

CONFLICT OF INTEREST

None declared.

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