COMPARISON OF SAFETY AND EFFICACY OF ROSUVASTATIN (10 MG) AND ATORVASTATIN (20 MG) IN CASES OF DYSLIPIDAEMIA OVER SIX WEEKS OF TREATMENT

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ABSTRACT

AIMS AND OBJECTIVES

To Compare the Safety and Efficacy of Rosuvastatin (10 Mg) and Atorvastatin (20 Mg) in Cases of Dyslipidaemia Over Six Weeks of Treatment.

MATERIALS AND METHODS

Inclusion Criteria: Both male and female (Excluding Pregnancy) above 18 years of age with hypercholesterolaemia, having LDL-C concentration of >159 and, 259 mg/dL and triglyceride concentration of <400 mg/dL, who had failed to have achieved LDL-C goals laid down by the NECP ATP-III guidelines after therapeutic lifestyle change (TLC): HDL-C level: <40 mg/dL for men and, <50 mg/dL for women. 60 cases of dyslipidaemia were selected and 30 were treated with rosuvastatin 10 mg (Study group 'A') and 30 of them were treated with atorvastatin 20 mg (study group 'B').

Exclusion Criteria

Use of lipid lowering agents within the past 6 months.
Any history of known familial hypercholesterolaemia.
Any history of serious or hypersensitivity reactions to other statins.
Uncontrolled hypothyroidism; uncontrolled hypertension.
Acute liver diseases or hepatic dysfunction.

After estimation of total cholesterol, triglycerides, HDL- cholesterol and LDL-c in a basal state, 30 patients were put on rosuvastatin 10 mg and 30 patients were put on atorvastatin 20 mg daily after night meals. After taking drugs, lipid fractions were re-estimated at the end of 4 weeks and 6 weeks. Clinical examination and questions about occurrence of side effects were carried out at interval of 2 weeks. Present study was conducted in the Department of Medicine and Pathology, of Katihar Medical College, Katihar, B. N. Mandal University, Madhepura; Bihar. Approval of the Institutional Ethical Committee was taken.

Study conducted by "Keith C et al (2006)" showed 37.1±1.3%, improvement in patients treated with RSV (10) and 38.5±1%, with (ATV 20), (ARIES TRIAL), "Cheng J. W. et al (2004)" found 43% improvement in levels of LDL-C, with RSV (10) and "Herregod et al (2008)" found that RSV (10) significantly reduced LDL level up to 47% in his study. In the "SOLAR TRIAL" conducted by "Insull W Jr. et al (2007)[1]", it was found that mean levels of LDL-C in patients taking RSV(10) over six weeks reached their target <100 mg/dL, which were comparable 100.43±2.93 to our study. The most frequent adverse effect in both the groups were myalgia with incidence of 3.33% in study. Group' A' (RSV 10 mg) and 6.66% incidence in study Group 'B' (ATV 20 mg), all adverse events were mild and had no action taken, and resolved spontaneously.

SUMMARY AND CONCLUSION

The present study "Comparison of Safety and Efficacy of Rosuvastatin (10 mg) and Atorvastatin (20 mg) in cases of Dyslipidaemia over six-week Treatment" was conducted amongst 60 diagnosed patients of dyslipidaemia. The result of this study shows that rosuvastatin 10 mg is more efficacious and safe in reducing the levels of TC, LDL, TC/HDL, TG and improving HDL levels as compared to Atorvastatin 20 mg.

KEYWORDS

Atorvastatin, Rosuvastatin, Dyslipidaemia Improvement, Efficacy.

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INTRODUCTION: Dyslipidaemia is a condition characterised by increased level of lipid rich lipoprotein circulating in peripheral blood. Dyslipidaemia covers a broad spectrum of lipid abnormalities, some of which are of great importance in CVD prevention. Dyslipidaemia may be related to other diseases (Secondary dyslipidaemias) or to the interaction between genetic predisposition and environmental factors.

Elevation of total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C) has received most attention, particularly because it can be modified by lifestyle changes and drug therapies. Also epidemiologically data has established low plasma high-density lipoprotein (HDL) cholesterol level is a major risk factor for cardiovascular disease[2].

Low HDL cholesterol together with raised triglyceride level is an atherogenic lipid profile, frequently associated with metabolic syndrome. A number of angiographic trials like, Multicentre Anti Atheroma Study (MAAS), Multicentre Coronary Intervention Trial (CCAIT), Monitored Atherosclerosis Regression Study (MARS) have demonstrated that a radical alteration in the plasma lipids and lipoproteins can delay the appearance of new atherosclerosis lesion, retard the progression of pre–existing lesion and even lead to regression. HMG CoA reductase is the rate-limiting step in cholesterol biosynthesis, and inhibition of this enzyme (Statins) decreases cholesterol synthesis.

Statins, the Agent of this Class Includes: Rosuvastatin, Atorvastatin, Fluvastatin, Pravastatin and Simvastatin. Rosuvastatin is an effective, hydrophilic HMG CoA reductase inhibitor, licensed for the treatment of hypercholesterolaemia and mixed dyslipidaemia. Rosuvastatin has demonstrated high efficacy for reduction in LDL, TG and has shown to have a greater HDL cholesterol raising effect than other statins.
The incidence of adverse drug reaction with statins is dose dependent: Most common adverse effects reported are headache, dizziness, gastrointestinal effects, myalgia and asthenia.

DISTRIBUTION: Extensive in Liver, 90% Bound to Plasma Protein, Mainly Albumin.

Metabolism: It is mainly metabolised to the N-desmethyl metabolite and the lactone metabolite. The N-desmethyl metabolite is an active metabolite and accounts for greater than 90% of the circulating HMG-CoA reductase inhibitor activity.

Excretion: About 90% of rosuvastatin is excreted as unchanged in faeces and remaining in urine, Plasma elimination half-life is 19 hours.

Atorvastatin: Mechanism of action is same as explained above, exclusively taken up by liver 98% bound is bound plasma protein.

Metabolism: Atorvastatin is extensively metabolised by cytochrome P-450, 3A4 is the principle isoenzyme involved and it is active metabolite, this accounts for about 70% of the circulating HMG-CoA reductase inhibitor activity. Excretion: Metabolites are eliminated primarily in bile following hepatic and extrahepatic metabolism.

MATERIALS AND METHODS: Both male and female (Excluding Pregnancy) above 18 years of age with hypercholesterolaemia, having LDL-C concentration of >159 and 259 mg/dL and triglyceride concentration of <400 mg/dL, who had failed to have achieved LDL-C goals laid down by the NECP ATP-III guidelines after therapeutic lifestyle change (TLC): HDL-C level: <40 mg/dL for men and, <50 mg/dL for women. 60 cases of dyslipidaemia were selected and 30 were treated with rosuvastatin 10 mg (Study Group 'A') and 30 of them were treated with atorvastatin 20 mg (study group 'B').

EXCLUSION CRITERIA INCLUDED:

1. Use of lipid lowering agents within the past 6 months.
2. Any history of known familial hypercholesterolaemia.
3. Any history of serious or hypersensitivity reactions to other statins.
4. Uncontrolled hypothyroidism; uncontrolled hypertension.

Acute liver diseases or hepatic dysfunction.

After estimation of total cholesterol, triglycerides, HDL-cholesterol and LDL-c in a basal state, 30 patients were put on rosuvastatin 10 mg and 30 patients were put on atorvastatin 20 mg daily after night meals.

After taking drugs, lipid fractions were re-estimated at the end of 4 weeks and 6 weeks. Clinical examination and questions about occurrence of side effects were carried out at interval of 2 weeks. Present study was conducted in the Department of Medicine and Pathology of Katihar Medical College, Katihar, B. N. Mandal University, Madhepura; Bihar. Approval of the Institutional Ethical Committee was taken.

OBSERVATION

Age: Maximum number of patients were in the age group of 51-60 years in both the study groups, 11 number of cases (37%) in study Group 'A' and 10 number of cases (34%) in study Group 'B', least number of cases were in the age group of 20-30 years, 01 number of cases (3%) in both the study groups.

Sex Ratio: In Group 'A', there was male predominance number of cases 19 (63%), and females were 11 (37%) and ratio of male and female was 1.72:1. In study Group 'B', male predominance with 16(53%) number of cases and female cases were 14(47%). The male female ratio was 1.14: 1.

Comparison of Weight: The maximum numbers of patients were in the weight range of 71-80 kg, in study Group 'A' and study Group 'B', with mean weight of patients in group 'A' is 73.9±8.8 and in group 'B' is 73.9±9.3.

Body Mass Index: In study Group 'A', 57% of cases had BMI >25-30 and 30% had BMI >30-35. In study Group, 'B' 54% of cases had BMI>25-30 and 33% had BMI >30-35. With mean BMI in Group 'A' of 28.3±2.9 and in Group 'B; mean BMI was 27.1±5.8.

Mean level of LDL: The mean level of LDL in study Group A (Rosuvastatin 10 mg), prior to therapy was 186.10±5.28%. Four weeks after treatment with rosuvastatin 10 mg, the level decreased to 107.46±3.02%; and after six weeks of therapy, mean level further decreased to 100.43±2.93%.

In Group 'B' (Atorvastatin 20 mg) mean level also showed improvement. Prior to therapy, the mean level of LDL was 187.6±3.73%. After 4 weeks of therapy, it was 122.5±3.93%; and after completion of six weeks of therapy, the mean level decreased to 119.7±3.86%. This showed that there was a percentage improvement of 45.4% with Rosuvastatin 10 mg therapy, and 36.06% improvement in patients treated with Atorvastatin 20 mg over six weeks.

Mean Level Changes of Total Cholesterol in Study: The Mean levels of Total Cholesterol studied in Group 'A' and group 'B' showed levels of 271.03±4.28 in Group 'A' and 274.03±4.62 in Group 'B' prior to therapy. After four weeks of therapy, the mean levels of TC decreased to 192.0±2.95 in Group 'A' and 207.0±3.95 in Group 'B'. At the end of study that is at 6 weeks, the mean levels in Group 'A' and Group 'B' were 184.86±2.84 and 204.0±3.93.

Mean Level Changes in Triglyceride Levels: The mean level of Triglyceride in study Group 'A' prior to therapy was 183±8.47, after 4 weeks of therapy was 153±8.98 and after completion of therapy that is after six weeks treatment mean levels were 149.9±8.47. In study Group 'B', mean levels of triglycerides were 183.10±8.27, 153±8.98 and 149.9±8.47, prior to therapy, after 4 weeks and after end of six weeks respectively. Overall improvement in Group 'A' was 18.9% and Group 'B' was 17.09%.

Mean Level Increase in High Density Lipoproteins Level: Mean levels of HDL in Group 'A' study, prior to therapy were 50.83±1.03, after 4 weeks the levels increased to 53.83±1.02 and at the end of six weeks, the HDL levels increased to 56.26±1.78. In study Group 'B', the levels of HDL were 51±1.285, 53.6±1.28 and 53.9±1.28 prior to therapy, after 4 weeks of therapy and after 6 weeks of treatment respectively. There was overall 11.19% increase in Group 'A' and 5.86% in Group 'B'.

Mean level of TC/HDL Ratio: In study Group 'A', patients treated with Rosuvastatin 10 mg showed improvement of 36.64% and in Study Group 'B' patients treated with Atorvastatin 20 mg showed 29.63% improvement after six weeks of treatment.

Percentage Improvement in Lipid Profile in both the Study Groups: There was a marked improvement of 11.19% in HDL levels in study Group 'A' (Rosuvastatin 10 mg), than in study group 'B' (Atorvastatin 20 mg) which was only 5.86% respectively. In case of LDL levels, also there was decrease in the levels of LDL-C more in Group 'A' (Rosuvastatin) than in Group 'B' (Atorvastatin) which were 45.4% and 36.6% respectively.

Adverse Effects Seen: Both drugs were well tolerated with similar incidence of adverse events. During treatment period, 2 patients in study Group 'A' and 3 patients in study Group 'B' respectively reported adverse events. The most frequent adverse effect in both the groups were myalgia with incidence of 33.3% in study Group 'A' and 6.6% incidence in study Group 'B' respectively.

RESULTS:

Time	Study Group 'A' Rosuvastatin 10 mg	Study Group 'B' Atorvastatin 20 mg
Prior to Therapy	186.10	187.63
After 4 weeks	107.46	122.50
After 6 weeks	100.43	119.70

Table 1: Mean Level of LDL in Study GROUP 'A' and GROUP 'B'

Time	Study Group 'A' Rosuvastatin 10 mg	Study Group 'B' Atorvastatin 20 mg
Prior to Therapy	271.03	274.03
After 4 weeks	192.00	207.00
After 6 weeks	184.86	204.00

Table 2: Mean Level Change of Total Cholesterol in Study GROUP 'A' and GROUP 'B'

Time	Study Group 'A' Rosuvastatin 10 mg	Study Group 'B' Atorvastatin 20 mg
Prior to Therapy	183.00	178.00
After 4 weeks	153.00	151.00
After 6 weeks	149.90	149.00

Table 3: Mean Level Change in Triglyceride in Study GROUP 'A' and GROUP 'B'

Time	Study Group 'A' Rosuvastatin 10 mg	Study Group 'B' Atorvastatin 20 mg
Prior to Therapy	50.83	51.00
After 4 weeks	53.83	53.60
After 6 weeks	56.26	53.90

Table 4: Mean Level Increase in HDL Levels in Study GROUP 'A' and GROUP 'B'

Time	Study Group 'A' Rosuvastatin 10 mg	Study Group 'B' Atorvastatin 20 mg
Prior to Therapy	5.43	5.47
After 4 weeks	3.61	3.94
After 6 weeks	3.42	3.85

Table 5: Mean Level of TC/HDL in Lipid Profile in Study GROUP 'A' and GROUP 'B'

Lipid Profile	Study Group 'A' Rosuvastatin 10 mg	Study Group 'B' Atorvastatin 20 mg
Total Cholesterol	31.61%	25.38%
LDL	45.40%	36.06%
Triglyceride	18.89%	17.09%
HDL	11.19%	05.86%
TC/HDL	36.64%	29.63%

Table 6: Percentage Improvement in Lipid Profile in Both Study Groups after 6 Weeks'

DISCUSSION: Cardiovascular diseases remain the leading cause of mortality and morbidity; statins have greatly improved the treatment of dyslipidaemias in primary and secondary prevention. The present study "Comparison of safety and efficacy of Rosuvastatin (10 mg) and Atorvastatin (20 mg) in cases of dyslipidaemia over six weeks treatment". The prevalence of dyslipidaemia is both age and gender dependent. The mean age of patients studied in study Group 'A' were 56.9±10.9 years and 56.83±12.1 years in the study Group 'B'. Maximum number of cases were in age group of 51-60 years in both study groups. There was male predominance in both the study groups with 63% and 53% in study Group 'A' and study Group 'B', female cases were in the range of 37% and 47% respectively.

In study done by 'Anjum Humayun et al (2009)[3]', it was observed that in females dyslipidaemia shows a gradual increase with age for all BMI categories. However, in males, the trend is different. It has been observed in our study that the percentage of females having dyslipidaemia was less as compared to males in the age between 20 and 59 years.

In both the study groups, maximum number of cases (37%) were in the weight range of 71-80 kg. Body Mass Index calculated in our study was in overweight category, which showed 57% of cases in study Group 'A' and 54% in study Group 'B' who were having BMI ~25-30. BMI ~30-35 observed in 30% cases in study Group 'A' and 33% cases in study Group 'B'.

The mean levels of BMI studied were 28.3±2.9 and 27.1±5.8 in study Group 'A' and study Group 'B' respectively which were found comparable in a study conducted by "Md. Faheem et al (2010)[4]" where he reported mean BMI of 26±4. Other studies conducted by "Hussain et al (2009)[5] reported a mean BMI of more than 28 in diabetics and nondiabetics.

In our study, the overall percentage improvement in the mean levels of Total Cholesterol was 31.61% in study Group 'A' (RVS 10 mg) and 25.38% in study Group 'B' (AVS 20 mg). Those levels found were comparable to the study conducted by "Jong-Seon Park et al (Korean J intern Med, 2010)[6]" where he found that Rosuvastatin (10 mg) reduced TC by 35.94±11.38% and Atorvastatin (10 mg) reduced TC by 30.07±10.46% respectively. In comparing the percentage decrease in the mean levels of Triglycerides in our study there was improvement of 18.9% and 17.09% in study Group 'A' (RVS 10 mg) and study Group 'B' (AVS 20 mg) respectively.

In a comparable study conducted by "Esther M. M. Ooi et al (2008) compared with placebo, both doses of rosuvastatin lowered triglycerides by 24%. "Michael B Clearfield et al (2006) did his study and concluded there is a decrease of 17.9% in triglyceride levels after 6 weeks of treatment with rosuvastatin 10 mg, 19.1% decreased in triglyceride with 6 weeks treatment of atorvastatin 20 mg.

Comparing the TC: HDL ratio, it was found that there was 36.64% improvement in study Group 'A' (RVS 10 mg) and 29.63% in study Group 'B' (ATV 20 mg). "Keith C Ferdinand et al (2006)[7] did his study and observed that there is a decrease in TC: HDL level by 30.6±1.1 after six weeks therapy of RVS 10 mg and almost similar reduction that is 30.5±1.1 with AVS 20 mg. In comparing the mean HDL levels prior to therapy in study Group 'A' (RSV 10 mg) & study Group 'B' (ATV 20 mg), after six weeks treatment showed a great improvement of 11.19% in study Group 'A' & 5.86% in study Group 'B', which was comparable to study conducted by "Robert S Rosenson et al (2009)[8]", where HDL-C concentration improved by 10% in RSV (10 mg) group and was comparable in ATV (20 mg) group over six weeks treatment.

Also "Keith C et al (2006, ARIES)", found in his study that in patient on RSV (10) had 7.0-9.6% improvement and in ATV (20) there was 3.7±1.0% and "Jones PH et al (2003)", studied that RSV (10) increased HDL-C by a mean of 7.7-9.6% compared with 2.1-6.8% in other groups, these studies were comparable to our study. In studying the mean levels of LDL in study Group 'A' (RSV 10 mg) and study Group 'B' (ATV 20 mg), we found that the mean levels of LDL after therapy were 100.43±2.93 and 119.7±3.86 respectively and the overall percentage improvement was 45.4% and 36.86% in study group 'A' and in study Group 'B'. Study conducted by "Keith C et al (2006)" showed 37.1±1.3%, improvement in patients treated with RSV (10) and 38.5±1%, with (ATV 20), (ARIES TRIAL). "Cheng J W et al(2004)" found 43% improvement in levels of LDL-C, with RSV (10) and "Herregod et al (2008)[9]" found that RSV (10) significantly reduced LDL level up to 47% in his study.

In the "SOLAR TRIAL" conducted by "Insull W Jr et al (2007)" found that mean levels of LDL-C in patients taking RSV (10) over six weeks reached their target <100 mg/dL, which were comparable 100.43±2.93 to our study. "PULSAR" Therapy conducted by "Michael B Clearfield et al (2006)[10]" concluded 44.6%, 30.8%, 6.4%, 17.9% and 34.6% improvement in levels of LDL-C, TC, HDL-C, TG and TC/HDL respectively after six weeks of treatment with Rosuvastatin 10 mg. Whereas the improvement was 45.4%, 31.61%, 11.19%, 18.89% and 36.64% in the levels of LDL-C, TC, HDL-C, TG and TC/HDL after six weeks treatment with Rosuvastatin 10 mg in our study. Also in our study, the improvement was 36.06%, 31.16%, 5.86% 17.09% and 29.63% in levels of LDL-C, TC, HDL-C, TG and TC/HDL, six weeks of treatment with Atorvastatin 20 mg.

Where as in "PULSAR" therapy, there was 42.7%, 30.7%, 3.1% 19.1% and 32.3% improvement in levels of LDL-C, TC, HDL-C, TG and TC/HDL. These findings are more or less similar and comparable to PULSAR therapy. The most frequent adverse effect in both the groups were myalgia with incidence of 3.33% in study Group 'A' (RSV 10 mg) and 6.66% incidence in study Group 'B' (ATV 20 mg), all adverse events were mild and had no action taken, and resolved spontaneously.

SUMMARY AND CONCLUSION: The present study "Comparison of Safety and Efficacy of Rosuvastatin (10 mg) and Atorvastatin (20 mg) in cases of Dyslipidaemia over six weeks Treatment" was conducted amongst 60 diagnosed patients of dyslipidaemia. The result of this study shows that Rosuvastatin 10 mg is more efficacious and safe in reducing the levels of TC, LDL, TC/HDL, TG and improving HDL levels as compared to Atorvastatin 20 mg.

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