A comparative study of efficacy of atorvastatin, rosuvastatin, and atorvastatin + fibrates as lipid lowering agents

Karunasree Nagarur1*, Yamini Vadlamannati1, Narasimha Rao Raja2

INTRODUCTION

Hypercholesterolemic patients are at a high risk for coronary heart disease. The National Cholesterol Eradication Programme (NCEP) Adult Treatment Panel III (ATP III) guidelines provide the option of aggressively lowering low density lipoprotein cholesterol (LDL-C) in hypercholesterolemia patients.1 LDL-Cholesterol is associated with an increased risk of atherosclerosis and coronary heart disease.2 In contrast, higher levels of HDL-Cholesterol are protective.3

Presently the standard therapy of hypercholesterolemia is HMG Co A reductase inhibitors. The aim of the present study is to compare the efficacy of Atorvastatin and Rosuvastatin and Atorvastatin monotherapy with combination of Atorvastatin with Fibrate as the lipid lowering agents.

METHODS

The study was conducted for a period of 18 months during the period of December 2013 to June 2015, on patients suffering from hyperlipidemia attending the medical and surgical OPD’s of Government medical college, Nizamabad. The approval of Institutional Ethics committee (IEC) was taken before the start of the study.

Total 150 patients of both sexes, of age between 18-75 years and who were already on treatment for hyperlipidemia for more than 1 year were included in our study. Patients who are using injectable lipid lowering...
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Drugs and with serious acute conditions were excluded from the study.

After taking written consent form they have been clinically examined the general parameters are noted. Then the laboratory investigations like TC (Total Cholesterol), HDL (High Density Lipoprotein), LDL (Low Density Lipoprotein), TG (Triglycerides) are recorded once during the study.

Data collected on drugs of study of prescribed hypolipidemic agents, Statins, Fibrates, and the combination regimens in subjects who were kept on such drugs. Data at the time of initiation of therapy is recorded and compared the same at the time of observation.

The optimal plasma lipid levels for treatment guidelines as per National Cholesterol Education Programme (2001), Risk of CAD: a) Optimal level -low risk, b) Borderline high-moderate risk, c) High level-high risk. Plasma lipid levels are as shown in Table 1.

The patients were divided into three groups. Group I: Atorvastatin (20 mg) (n=96; 64%); Group II: Rosuvastatin (10 mg) (n=41; 27.33%); Group III: Atorvastatin (20 mg) + Fibrates (145 mg) (n=13; 8.66%).

Statistical analysis

Using SPSS software version 16 statistical analysis was done.

The treatment groups were compared for efficacy using Students paired t Test.

RESULTS

At the end of the study the following observations and results were obtained:

Table 2 explains that there is a significant reduction in mean value of TC (22.98%, p <0.0001), LDL (33.8%, P <0.0001), TG (20.14%, p <0.0001) and significant increase in HDL (2.6%, p <0.0001) after treatment. There is a significant reduction in mean value of TC (25.66%, P <0.0001), LDL (39.59%, p <0.0001), TG (31.41%, P <0.0001), and significant increase in HDL (12.67%, P <0.0001) after treatment.

As given in Table 2, there is a significant reduction in mean value of TC (22.17%, P =0.0001), LDL (34.66%, p =0.0001), TG (30.36%, P =0.0001), and significant increase in HDL (3.05%, P =0.0001) after treatment.

Table 1: Plasma lipid levels.

| Parameters | Desirable | Borderline | High |
|------------|-----------|------------|------|
| TC         | <200 mg/dl| 200–239 mg/dl | > 240 mg/dl |
| LDL        | <130 mg/dl| 130-159 mg/dl | >160 mg/dl |
| TG         | <150 mg/dl| 150-199 mg/dl | >200 mg/dl |
| HDL        | >40 mg/dl for men, >50 mg/dl for women | - | >60 mg/dl |

Table 2: Lipid profile of Atorvastatin treated cases.

| Parameters | Group-I (Atorvastatin) | Mean | SEM | P value | % decrease |
|------------|------------------------|------|-----|---------|------------|
| TC         | Pre Rx                 | 248.13 | 0.79 | 0.0001 | 22.98      |
|            | Post Rx                | 191.35 | 0.38 |         |            |
| LDL        | Pre Rx                 | 170.8 | 0.78 | 0.0001 | 33.8       |
|            | Post Rx                | 113   | 0.30 |         |            |
| TG         | Pre Rx                 | 204.11 | 0.90 | 0.0001 | 20.14      |
|            | Post Rx                | 163   | 0.76 |         |            |
| HDL        | Pre Rx                 | 40.12 | 0.13 | 0.0001 | 2.6        |
|            | Post Rx                | 41.2  | 0.13 |         |            |

Table 3: Lipid profile of Rosuvastatin treated cases.

| Parameters | Group-II (Rosuvastatin) | Mean | SEM | P value | % decrease |
|------------|------------------------|------|-----|---------|------------|
| TC         | Pre Rx                 | 272  | 0.77 | 0.0001 | 25.66      |
|            | Post Rx                | 202.2 | 0.46 |         |            |
| LDL        | Pre Rx                 | 190.7 | 0.82 | 0.0001 | 39.59      |
|            | Post Rx                | 115.2 | 0.21 |         |            |
| TG         | Pre Rx                 | 233.3 | 1.08 | 0.0001 | 31.41      |
|            | Post Rx                | 160   | 1.35 |         |            |
| HDL        | Pre Rx                 | 44.02 | 0.36 | 0.0001 | 12.67      |
|            | Post Rx                | 49.6  | 0.34 |         |            |
Comparison of changes in lipid profile between Atorvastatin and Rosuvastatin group after treatment showed significant reduction in TC (22.98% vs 25.66%, P <0.0001), LDL (33.8% vs 39.59%, P <0.0001), increase in HDL which was significant (2.6% vs12.67% P <0.0001), but the reduction in TG level was insignificant (20.14% vs 39.59%, P <0.3789).

Comparison of changes in lipid profile between Atorvastatin and combination of Atorvastatin and Fibrate showed significant reduction in TC (22.98% vs 22.17%, P <0.0001), LDL (33.8% vs 34.66%, P <0.0001), TG (20.14% vs 30.36%, P <0.0001) and increase in significant increase in level of HDL (3.05% vs 0.002%, P <0.0001) after treatment.

Comparison of changes in lipid profile between Rosuvastatin and combination of Atorvastatin and Fibrate after treatment showed significant decrease in TC (25.66% vs 22.17%, P <0.0001), LDL (39.59% vs 34.66%, P <0.0001), TG (31.41% vs 30.36%, P <0.0001) and significant increase in HDL (12.67% vs 3.05%, P <0.0001) after treatment.

**DISCUSSION**

Table 2 shows the pre-treatment and post treatment values after 20 mg Atorvastatin. This table shows the difference in the lipid profile after treatment with Atorvastatin. There is a significant reduction in mean value of TC (22.98%, P <0.0001), Our study is similar to Meenakshi et al TC (28%, P <0.001), Maruti et al TC (25.5%, P <0.001), Bener et al (15.5%, P <0.001) 4,5. There was a significant decrease in the mean LDL (pre-treatment =248.13 mg/dl vs post treatment =191.35 mg/dl; P <0.0001) with a mean reduction of 33.8%. This finding related to the study conducted by Maruti et al showed 35%, (P <0.001) reduction in LDL after Atorvastatin treatment and Meenakshi et al 37% (P <0.001) reduction in LDL. 4,5

There was a significant decrease in the mean value of TG after Atorvastatin treatment (pre-treatment =204.11 mg/dl

Table 3: Lipid profile of Atorvastatin + Fibrates treated cases.

| Parameters | Group-III (Atorvastatin+Fibrates) | Mean | SEM | P value | % decrease |
|------------|-----------------------------------|------|-----|---------|------------|
| TC         | Pre Rx                            | 231.3| 1.25| 0.0001  | 22.17      |
|            | Post Rx                           | 180  | 0.71|         |            |
| LDL        | Pre Rx                            | 150  | 1   | 0.0001  | 34.66      |
|            | Post Rx                           | 98   | 0.75|         |            |
| TG         | Pre Rx                            | 190  | 1.23| 0.0001  | 30.36      |
|            | Post Rx                           | 132.3| 1.43|         |            |
| HDL        | Pre Rx                            | 42.5 | 0.33| 0.0001  | 3.05       |
|            | Post Rx                           | 43.8 | 0.27|         |            |

Table 5: The post treatment values between Group I and II, Group I and III, Group II and III.

|       | TC | LDL | TG      | HDL |
|-------|----|-----|---------|-----|
| Groups       | I  | II  | I      | II  |
| Mean         | 191.35 | 202.2 | 113 | 115.2 | 163 | 160 | 41.2 | 49.6 |
| SEM          | 0.38 | 0.46 | 0.30 | 0.21 | 0.76 | 1.35 | 0.13 | 0.34 |
| % decrease   | 22.98 | 25.66 | 33.8 | 39.59 | 20.14 | 31.41 | 2.6 | 12.67 |
| P value      | 0.0001 | 0.0001 | 0.3789 | 0.0001 |
| Groups       | I  | III | I     | III |
| Mean         | 191.35 | 180 | 113 | 98 | 163 | 132.3 | 41.2 | 43.8 |
| SEM          | 0.38 | 0.71 | 0.30 | 0.75 | 0.76 | 1.43 | 0.13 | 0.27 |
| % decrease   | 22.98 | 22.17 | 33.8 | 34.66 | 20.14 | 30.36 | 2.6 | 3.05 |
| P value      | 0.0001 | 0.0001 | 0.0001 |
| Groups       | II | III | II    | III |
| Mean         | 202.2 | 180 | 115.2 | 98 | 160 | 132.3 | 49.6 | 43.8 |
| SEM          | 0.46 | 0.71 | 0.21 | 0.75 | 1.35 | 1.43 | 0.34 | 0.27 |
| % decrease   | 25.66 | 22.17 | 39.59 | 34.66 | 31.41 | 30.36 | 12.67 | 3.05 |
| P value      | 0.0001 | 0.0001 | 0.0001 |

Table 5 shows the post treatment values TC, LDL, TG, HDL compared in between groups i.e between Group I and Group II, Group I and Group III values, Group II and Group III.

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vs post treatment =163 mg/dl, P <0.0001) with a mean reduction of 20.14%. Our study was similar to Barakat et al TG (19.95%, P <0.01), Lella et al TG (20%, P <0.001), Benner et al TG 16.7% (P <0.01), Stalenhoef et al TG 25.2% (P <0.001).

There was significant increase in HDL level in our study (pre-treatment =40.12 mg/dl, post-treatment= 40.2 mg/dl) (P <0.0001) with mean reduction in 2.6%. This study correlates with Lella et al HDL 1.5%, Stalenhoef et al HDL 5.8%, P <0.01, Barakat et al HDL 5.5%.4,7,8

Table 3 shows a significant reduction in mean value of TC (pre-treatment =272 mg/dl, post treatment =202.2 mg/dl, p=0.0001) with a mean reduction of 25.66 with Rosuvastatin. Our study is similar to Bener et al, Barakat et al, and Arshad et al.6,7,9

Our study shows significant reduction in LDL in Rosuvastatin treated cases (pre-treatment = 190.7 mg/dl post treatment =115.2 mg/dl, P <0.0001) with reduction in 39.59%. This is similar to Maruti et al LDL 29.03% (P<0.001), Stalenhoef et al LDL 48.5%.5,8

In Rosuvastatin treated cases there was significant decrease in TG. (pre-treatment value =233.3 mg/dl post treatment value=160 mg/dl, P <0.0001), with mean reduction 31.41%. This correlates with Beneret al TG 25.2% (p <0.001) and Barakat et al TG (25.1, p <0.01).6,7

Our study showed significant increase in the mean value of HDL (pre-treatment =44.02 mg/dl, post treatment =49.6mg/dl, p <0.0001) 12.67% after treatment. This is similar to Marutil et al HDL-14% (P =0.001), Stalenhoef et al HDL-10,5,8

Table 4 shows the pre-treatment and post-treatment values after Atorvastatin and Fibrate combination. There is a significant reduction in mean value of TC (pre-treatment =231.3, post treatment= 180, P <0.0001), 22.17% reduction. This is similar to Lella et al TC 31%, P<0.001.4

LDL (pre-treatment =150, post treatment =98 P value 0.0001), 34.66% reduction, this is similar to Lells et al2 LDL 33% P<0.001. Similarly TG (pre-treatment =190, post treatment=132.3, P =0.0001) 30.36%, reduction after treatment. This is similar to Lella et al LDL 39%, P <0.001.4

There was significant increase in the mean value of HDL (pre-treatment=190 mg/dl, post treatment=132.3 mg/dl, P <0.0001; 3.05% increase. This is similar to study by Khan HDL 5.18%.10 Table 5 shows the post treatment values of lipid profile in between all the 3 groups. There is significant difference (P <0.0001) in TC, LDL, HDL between group I (Atorvastatin) and group II (Rosuvastatin). But there is insignificant decrease in TG level, P <0.3789).There is significant reduction in TC, LDL, TG, HDL between group I and group III after treatment and also between group II and group III. (P <0.0001).

In our study Rosuvastatin is best in decreasing LDL level to 39%. This is similar to Eliasson et al11 Rosuvastatin 67%. Clearfield et al12 (Rosuvastatin 10 mg reduced LDL-C levels significantly more than atorvastatin 20 mg at week 6 (44.6% vs. 42.7%, P <0.05).11,12

In our result Atorvastatin with Fibrates was better than Atorvastatin monotherapy in decreasing LDL (34.66% vs 33.85%) our result was similar to the results of Karalis et al (33% vs 35%).13 Michael et al showed reduction in HDL (40%) more in Atorvastatin and Fibrate combination than in Atorvastatin monotherapy.12 This is similar to our result (3%, P <0.0001) in lowering HDL in Group I (Atorvatatin) vs Group III (Atorvastatin and Fibrate).

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