Original article:

Various statin combinations in dyslipidemias

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Abstract:
The majority of people with hyperlipidaemia have plasma lipid concentrations that are only mildly or moderately elevated and they exhibit no clinical symptoms. The current NCEP GUIDELINES FOR MANAGEMENT of patients with lipid disorders is of two types. One is population based approach, which is intended to lower blood cholesterol by dietary recommendations; reduce total calories from fat less than 30% and from saturated fat to be less than 10%; consume less than 300 mg of cholesterol per day; and maintain desirable body weight. The second is the patient based approach described in the 2001 of NCEP Adult Treatment Panel III which continuous to focus on lowering LDL-C levels as the primary goal of therapy.

New guidelines and trails highlighting the need for a more aggressive approach to dyslipidaemia. Intense competition from generic statins including Simvastatin, Pravastatin, and later Atorvastain. The arrival of new so called “super statins”. Impact of alternative treatments' including cholesterol absorption inhibitors and PPAR agonists. Entry of combination therapies offering targeted forms of treatment. (IMS Health Aug 2004 pages 250) In this present study 106 patients who were hyperlipidemiac between thirty to eight years of age were taken. Out of 106, 49 were given Atorvastatin plus Fenofibrate (Group A) and 57 patients were given Atorvastatin and Ezetimibe (Group B). Measurements of HDL, LDL, VLDL, Triglycerides and total cholesterol were performed in both the groups. The results of this study were analyzed using SPSS software (statistical package of social studies). Data was expressed as mean values ± standard deviation (SD). Standard deviation has been taken to indicate whether the variation of difference of an individual from the mean is by change. Statistical analysis was performed applying independent sample “ANOVA” test to the data of independent samples for Equality of variances within the group. The probability value (P) < 0.05 was considered as statistically significant because such a difference could commonly occur due to change and the factor under study may have no influence on the variables.

Out of 106 patients in the present study 63 were males and 43 were females with a male: female ratio of 1:0.99 in Atorvastatin plus Fenofibrate and with a male: female ratio of 1:3 in Atorvastatin and Ezetimibe.

Introduction:
The majority of people with hyperlipidaemia have plasma lipid concentrations other only mildly of moderately elevated and they exhibit no clinical symptoms. The current NCEP GUIDELINES FOR MANAGEMENT of patients with lipid disorders is of two types. One is population based approach, which is intended to lower blood cholesterol by dietary recommendations; reduce total calories from fat less than 30% and from saturated fat to be less than 10%; consume less than 300 mg of cholesterol per day; and maintain desirable body weight. The second is the patient based approach described in the 2001 of NCEP Adult Treatment Panel III which continuous to focus on lowering LDL-C levels as the primary goal of therapy.

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New guidelines an trails highlighting the need for a more aggressive approach to dyslipidaemia. Intense competition from generic statins including Simvastatin, Pravastatun, and later Atorvastain. The arrival of new so called “super statins”. Impacto of alternative treatments’ including cholesterol absorption inhibitors and PPAR agonists.Entry of combination therapies offering targeted forms of treatment. (IMS Health Aug 2004 pages 250). The aim of the present study is to compare the clinical effects and biochemical parameters, Atorvastatin in combination with Ezetimibe and Fenofibrate in dyslipidaemias attending outpatient department of Internal Medicine, GSL Medical College and Hospital, Rajahmundry.

Materials and methods
This study involved 120 patients (both male and female) aged between 30 to 80 years, presenting for treatment in the medical outpatient department of GSL General Hospital. The patients were divided into two groups namely Group A and Group B. Group A patients are those who are taking atorvastatin 10mg with Fenofibrate 160mg and group B patients aree those who are taking Atrovastatin 10mg and Ezetimibe 10mg as Fixed dose Combinations. The study was conducted over a period of one year i.e. from July 2008 to August 2009. An informed consent was taken from all the patients and an approval from the ethical committee of the institution.

Inclusion Criteria:
- The patients included are above 18 years of age, any race, and any gender.
- The patients must have the following fasting parameters:
  - LDL-C> 100 mg/dL and <250 mg/dL.
  - TG level >=100 mg/dL and <400 mg/dL.
  - HDL-C<30 mg/dL (men) and <40 mg/dL (women).
- The patients must have one or more of the Following:
  - Treated or untreated hypertension defined as blood pressure (BP)
  - 130 mmHg >= 85 mmHg (systolic / diastolic).
  - Waist circumference > 88 cm (35 inches) for women or >102 cm (40 inches) for men.
  - Fasting glucose defined as >= 100 mg/dL but <=125 mg/dL.
- The patient has, in the opinion of the investigator, a life expectancy greater than 6 months.
- Female patients must have a negative pregnancy test prior to study enrollment.
- Female patients of child bearing potential must agree to practive an effective barrier method of birth control for the duration of the study.
- Patient must be willing to observe the Step I Diet recommended by the NCEP throughout the study.
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Exclusion Criteria:
- Patients has a known hypersensitivity to fenofibrate, exetimibe, or Atorvastatin
- Patient has a history of pancreatitis  or cholelithiasis or a history of gastric or duodenal ulcer within 3 months of study entry.
- Patient has hematologic, digestive, or central nervous system disorder including Cerrbrovascular diseae or degenerative disease that would limit study evaluation or participation.
- Patient has had a myocardial infarction, coronary bypass surgery, or angioplasty within 6 months of study entry.
- Patient has unstable or severe peripheral artery disease within 3 months of study entry.
Patient has unstable angina pectoris or uncontrolled cardiac arrhythmias.

Patient has coagulopathy (PT or PTT>1.25 times control).

Patient has known Impairment of renal function (serum creatinine >1.5 mg/dL), dysproteinemia, disease.

Patient has active or chronic hepatobiliary or hepatic disease (subjects with AST or ALT>2 times the upper limit of the central laboratory reference range).

Patient is pregnant or lactating.

Patient is receiving hormonal therapy.

Patient has a history of disanosed hereditary or acquired myopathy.

Patient is known to be HIV positive.

Patient has a history of mental instability, deug or alcohol (as defined by greater than 14 drinks per week) abuse, or subject has been treated for severe psychiatric illness, which, in the opinion of the investigator, may interfere with optimal participation in the study.

Patient has received a solid organ transplant.

Patient has a clinically significant, unstable, uncontrolled disease that could be adversely affecte by study participation.

Patient is unwilling or unable to consent to enter the study.

After a detailed history of signs and symptoms routine physical examination was done followed by routine investigation examination was done followed by routine investigations which included ECG, Chest X-Ray, Haemoglobin, TC, DC, ESR, RBS, Urine R/E and M/E.

5 ml of venous blood was collected for the biochemical analysis. 5 ml of venous blood was also collected from healthy controls after informed consent.

4. The VLDL and LDL fractions are calculated as below
   Friedwald WT et al ,1972
   VLDL = TGL/5
   LDL = Total cholesterol – (HDL + VLDL)

Statistical analysis:

The data was analysed by using student –t test for paired values. Prabability value was read from the available tables

Results

In this present study 106 patients who were hyperlipidiemic between thirty to eight years of age were taken. Out of 106, 49 were given Atorvastatin plus Fenofibrate (Group A) and 57 patients were given Atorvastatin and Ezetimibe (Group B). Measurements of HDL, LDL, VLDL, Triglycerides and total cholesterol were performed in both the groups. The results of this study were analyzed using SPSS software (statistical package of social studies).

Data was expressed as mean values ±standard deviation (SD). Standard deviation has been taken to indicate whether the variation of difference of an individual from the mean is by change. Statistical analysis was performed applying independent sample “ANOVA” test to the data of independent samples for Equality of variances within the group. The probability value (P) <0.05 was considered as statistically significant because such a difference could commonly occur due to change and the factor under study may have no influence on the variables.

Out of 106 patients in the present study 63 were males
and 43 were females with a male: female ratio of 1:0.99 in Atorvastatin plus Fenofibrate and with a male: female ratio of 1:3 in Atorvastatin and Ezetimibe.

**Discussion:**
Alteration in the lipid profile pattern in both the groups with Atorvastatin plus Fenofibrate and Atorvastatin plus Ezetimibe are shown in Table-8.

**Table: Showing the alteration in Lipid Profile in Group A (A+F) and Group B(A+E):**

<table>
<thead>
<tr>
<th>Type</th>
<th>Group A (A+F)</th>
<th></th>
<th></th>
<th></th>
<th>Group B (A+E)</th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>3Months</td>
<td>6Months</td>
<td>Initial</td>
<td>3Months</td>
<td>6Months</td>
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<td></td>
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<tr>
<td>Tcho</td>
<td>238.2±5.89</td>
<td>226.1±5.37</td>
<td>210±4.91</td>
<td>237.8±5.03</td>
<td>222.4±4.55</td>
<td>201.2±3.95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGL</td>
<td>275.9±4.9999</td>
<td>243.5±5.52</td>
<td>225±4.86</td>
<td>181.5±6.14</td>
<td>169.2±5.4</td>
<td>156.4±4.80</td>
<td></td>
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<tr>
<td>HDL</td>
<td>30.9±0.82</td>
<td>33.1±0.71</td>
<td>35.4±0.64</td>
<td>39.2±1.27</td>
<td>40±1.04</td>
<td>42.5±1.01</td>
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<td></td>
</tr>
<tr>
<td>LDL</td>
<td>156.9±5.57</td>
<td>145.2±3.43</td>
<td>130.2±2.79</td>
<td>164.9±4.09</td>
<td>152.9±4.09</td>
<td>142.2±3.58</td>
<td></td>
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</tr>
<tr>
<td>VLDL</td>
<td>57.2±1.67</td>
<td>48.9±1.42</td>
<td>43.5±0.95</td>
<td>39.2±1.92</td>
<td>38±1.39</td>
<td>35±1.15</td>
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</tr>
</tbody>
</table>

The mean total cholesterol in Group A (A+F) at initial, 3months, and 6months was 238.2±5.89, 226.1±5.37, and 210±4.91 respectively, (p<0.05).

The mean total cholesterol in Group B (A+E) at initial, 3months, and 6months was 237.8±5.03, 222.4±4.55, and 201.2±3.95 respectively, (p<0.05).

The mean triglycerides in Group A (A+F) at initial, 3 months, and 6 months was 275.9±4.99, 243.5±5.52 and 225±4.86 respectively, (p<0.05).

The mean triglycerides in Group B (A+E) at initial, 3months, and 6months was 181.5±6.14,169.2±5.4 and 156.4±4.79 respectively, (p<0.05).

The mean HDL in Group A (A+F) at initial, 3months, and 6 months was 39.2±1.27,40±1.04 and 42.5±1.01 respectively, (p<0.05).

The mean LDL in Group A (A+F) at initial, 3 months, and 6months was 156.9±5.57, 145.2±3.43, and 130.2±2.79 respectively, (p<0.05).
The mean LDL in Group B (A+E) at initial, 3 months, and 6 months was 164.9±4.79, 152.9±4.09, and 142.2±3.58 respectively, (p<0.05).

The mean VLDL in Group A (A+F) at initial, 3 months, and 6 months was 57.2±1.67, 48.9±1.42, and 43.5±0.95 respectively, (p<0.05).

The mean VLDL in Group B (A+E) at initial, 3 months, and 6 months was 39.2±1.92, 38±1.39, 35±1.15 respectively, (p>0.05).

**Conclusion:**
From the above data it is evident that mean serum total cholesterol, triglycerides, LDL, VLDL shows significant decrease in case of group A and in group B, but HDL levels shows increase in both groups. In group B the VLDL level shows statistically insignificant figures.

**Bibliography:**