Original article:

Various statin combinations in dyslipidemias

Dr. K.Sivaji[1], Dr. G.V.Benerji[1], M. Farid babu[1] , D. Rekha kumari[1]

1 Associate Professor of Pharmacology, GSL Medical College, Rajahmundry,A.P

1 Professor of Biochemistry KIMS&RF, Amalapuram,A.P

1 Assistant Professor of Biochemistry, KIMS&RF, Amalapuram,A.P

1 Assistant Professor of Biochemistry, KIMS&RF, Amalapuram,A.P

Corresponding Author: Dr. K.Sivaji , Associate Professor of Pharmacology, GSL Medical College, Rajahmundry,A.P

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 by6 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 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) In this present study 106 patients who were hyperlipidiemic between thiry 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 ifference 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 Fenifibrate and with a male: female ratio of 1:3 in Atorvastatin and Ezetimible.

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 by6 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.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

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 paients 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.
- Patient must be willing to observe the Step I Died recommended by the NCEP throughout the study.

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 infraction, 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.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

- 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 herediatary 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 orogan 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.s

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 collecoted from healthy controls after informed consent.

1. Cholesterol Estimation**:** Allain CC, et al, 1974; Richmond W, 1973; Tarbuttor PN, et al, 1974

2.Triglycerides estimation: Rossati P. et al,1982,Eggstein M,et al,1974

3.HDL estimation: Lopes,1977, Allain CA,1974,Richmond W,1973,

Castelli WP et al,1977,Miller NE,et al,1977 ,Friedewald WT et al,1972

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 thiry 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

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

and 43 were females with a male: female ratio of 1:0.99 in Atorvastatin plus Fenifibrate and with a male: female ratio of 1:3 in Atorvastatin and Ezetimible.

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):

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

The mean total cholesterol in Group A (A+F) at initial, 3months, and 6monhs 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 repectively, ($p<0.05$).

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±5.45 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, ($p<0.05$).

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

The mean LDL in Group B (A+E) at initial, 3 months, and 6months 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 6months 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 6months 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, triglcerides, LDL, VLDL shows significant decrase 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:

1. Beamont JL, *et al*, Calassification of hyperlipidaemias and
2. hyprlipoproteinaemias Bull WHO 1970; 43: 891-915.
3. Corsini A, Pazzucconi F, Arnaboldi L, Pfister P, Fumagalli R, Paoletti R, *et al*. Direct effects of statins on the vascular wall. J CardiovascPharmacol 1998; 31:773-8.
4. Hersberger M, Von Eckardstein A, Low High density lipoprotein cholesterol; Physiological background, clinical importance and drug treatment. Drugs 2003;63:1907-45.
5. Jones SP, Gibson MF, Rimmer III DM, Gibson TM, Sharp BR, Lefer DJ, Direct vascular and cardioprotective effects of rosuvastatin a new HMG-CoA reductase inhibitor. KA, Coll Cardiol 2002;40:1172-8.
6. Lennernas H, Lennernas H. Clinical pharmacokinetics of Atorvastatin. Clin Pharmacokinet 2003; 42:1141-60.
7. Liao JK. Isorenoids as mediators of the biological effects of statins. J Clin invest 2002;110:285-8.
8. Liao JK. Statins and ischemic stroke. Atheroscler Suppl 2002;3:21-5
9. Pasternak RC, et al ACC/AHA/NHLBI Clinical advisory on the use and safety of statins. Circulation 2002; 106: 1024-8.
10. Pfeiffer CM, et al. Toxic epidermal necrolysis from Atorvastatin. JAMA 1998; 279: 1613-14.
11. Rosenson RS. Non-lipid lowering effects of statins on atherosclerosis. Curr Cardil Rep 1999;1:225-32.
12. Sattar N. et al, The end of triglycerides in cardiovascular risk assessment? BMJ 1998;317:553-4.
13. Stenestrand U, Wallentin L. Early statin treatment following acute myocardial infarction and 1-year survival. JAMA 2001;285:430-6.
14. Wilson SH, Simari RD, Best PJ, Peterson TE, Lerman