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The efficacy and safety of Rosuvastatin versus Atorvastatin, a double blind, randomized control study and comparison in patients with dyslipidemia

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Abstract:*The Present study was a double blind randomized comparative study of Rosuvastatin versus Atorvastatin in patients with dyslipidemia at Rangaraya Medical College,Government General Hospital, Kakinada, A.P India. The total 50 patients aged 35 – 70, were enrolled into the study group and 50 age, sex matched healthy individuals were enrolled as control group and they were analysed for the lipid profiles. The study group was randomly allocated into 2 groups as group A (n=25) and group B (n=25). GroupA received the drug Rosuvastatin 10mg and the groupB received the drug Atorvastatin 10mg. The patients were followed for 12 weeks. . There were no drop outs in both the study groups in the present study. Comparison was made regarding the reduction in the LDL-C, Total cholesterol, VLDL-C and Triglycerides, and improvement of of HDL-C,and side effects. Statistical analysis was done using the paired student 't' test for comparing the lipid profiles of the two groups before and after treatment. The results of the study showed that Rosuvastatin is better than Atorvastatin to treat dyslipidemias in terms of efficacy in lowering the lipid profiles and more safer for side effects.*

Key words*: Rosuvastatin, Atrovastatin, dyslipidemia*

I. Introduction:

Dyslipidemias are disorders of lipoprotein metabolism including lipoprotein overproduction and deficiency. They may manifest as one or more of the following: elevated levels of total cholesterol, low density lipoprotein cholesterol(LDL), and triglyceride levels or as decreased levels of high density lipoprotein cholesterol (HDL)[1]. Dyslipidemias are closely associated with atherosclerosis and is the major causal factor in the development of ischemic diseases. Ischemic cardiovascular and crebrovascular events are the leading causes of morbidity and mortality[2]. Dyslipidemias are classified into primary (familial hypercholesterolemia) and secondary dyslipidemias (disease states: hypothyroidism, nephritic syndrome, obesity, diabetes, alcoholism and drugs: thiazides, beta blockers, prednisone, progestins, oestrogens and anabolicsteroids)[3]**.** The benefits of treating hyperlipidemia are that we can reduce the chances of mortality, coronary events like myocardial infarction and stroke[2,4]. Over the past decade, the use of statins or HMG-COA reductase inhibitors for the treatment of hypercholesterolemia has revolutionized physician's ability to slow the progression of CHD[5].The broad range of significant clinical benefits of statin therapy include a decrease in major coronary events, coronary revascularization, stroke& TIA, death due to CHD, & total mortality[4].

II. Review of Literature:

Elevated levels of Total cholesterol and triglycerides showed the decrease in HDL-C[5].According to Lawrence et al, 2007, there is a strong relation between decrease of LDL-C causes a decreased risk of CHD.[6].The main Lipids and Lipoproteins are cholesterol, triglyceride and phosphholipid.Endogenous synthesis of cholesterol in the liver is controlled by the rate limiting step involving the microsomal enzyme 3-hydroxy-3-

methylglutaryl-COA(HMG-CoA) reductase. Lipids are transported in plasma as lipoproteins, which play an important role in the regulation of lipid transport and lipoprotein metabolism. They are classified on the basis of their densities as chylomicrons, VLDL, IDL,LDL,HDL.

III. Materials and methods:

Subjects participating in the research study were informed for consent as per the Helsinki declaration1977, and clinical history was collected through a structured questionare. Fasting blood samples were collected from Control and study group subjects and suitable anticoagulant was added and plasma was separated and used for further analysis. Total cholesterol was estimated by CHOD-PAP method. Triglycerides were measured by GPO method. HDL-C was measured by Phosphotungstic acid method. Results were obtained from ERBA CHEM 7 Semiautoanalyzer. VLDL was calculated by Friedewald's calculation. Results were expressed as mean ± SD, before and after treatment the parameters were again measured by paired student 't' test. T and p value are calculated and 0.05 are considered as statistically significant. SGOT & SGPT were measured by kinetic mode by semi auto analyser.

Exclusion criteria:

Patients with serious hypersensitivity to statins, severe CHF, Malignancy,hypothyroidism, history with chronic alcoholism, systemic illness, women in breast feeding were excluded from the study.

Inclusion criteria:

Age groups between 35 – 70, willing for research trial, were enrolled in the present study .

IV. Results and Discussion:

The mean baseline TC in group A and group B are 220.20±9.4(SD)mg/dl , where P>0.05(i.e P=0.0524) in the mean baseline TC values between the two groups and they are comparable. At the end of study, the mean TC at 12 weeks in group A and group B are 193.39±9(SD)mg/dl and 203.21±7.9(SD)mg/dl respectively. So there is a statistically significant difference at the end of the study where P<0.05(i.e. P=0.001) between two groups. Overall the mean drop in TC in group A and group B are 26.81 mg/dl and 21.76mg/dl. The percentage drop in mean TC in group A and B are 12.17% and 9.6% respectively. The mean baseline TG in group A and group B were 315.52±18.06(SD)mg/dl respectively. There is no significant difference where P>0.05(i.e. P=0.676) in the mean baseline values between the two groups and they are comparable. At the end of the study, the mean TG at 12 wks in group A and group B are 281.64±25.02(S.D)mg/dl and 295.72 ±17.05(S.D)mg/dl respectively. So there is statistically significant difference at the end of the study where P<0.05(i.e. P+0.0136) between the two groups. Overall the mean drop in TG in group A and group B are 31. 23mg/dl and 19.8 mg/dl. The percentage drop in mean TG in group A and B are 9.98% and 6.6% respectively. The mean baseline HDL-C in group A and group B are 28.87±7.492(SD)mg/dl . There wass no significant difference where P> 0.05(i.e. P=0.385) in the mean baseline HDL –C values between the two groups and they are comparable. At the end of the study the mean HDL-C at 12weeks in group A and group B are 33.8±7.874(SD)mg/dl and 29.43±6.669(SD) mg/dl respectively. So there is statistically significant difference at the end of the study where P<0.05(i.e. P=0.0241) between the two groups. Overall the mean increase in HDL-C in group A and group B are 4.93mg/dl and 2.10mg/dl. The percentage drop in mean TC in group A and B are 4% and 2% respectively. The mean baseline LDL-C levels in group A and group B were 134.373±4.828(SD)mg/dl respectively. There is no significant difference where P>0.05(i.e. P=0.2123) in the mean baseline LDL-C values between the two groups and they are comparable. At the end of the study, the mean LDL-C at 12 weeks in group A and group B are 112.05±4.543(SD)mg/dl and 116.49±4.507(SD) mg/dl respectively. So there is statistically significant difference at the end of the study where P<0.05(i.e. P=0.0003) between the two groups. Overall the mean drop in LDL –C in group A and group B are 20. 44 mg/dl and 17.88mg/dl. The percentage drop in mean LDL-C in group A and B are 15.42% and 13.3% respectively.There was no significant difference in the SGOT, group A and B 31 ± 9.2 , 30.9± 9.2,31.91±9.1 respectively and SGPT levels in group A and B before26.3± 9.1after treatment 26.5± 9.0, 26 ± 9.0 respectively with Resuvastatin and Atrovastatin. Both the drugs are equally safe (Tables-1, 2 &3).

There was a strong relation between CHD and dyslipidemias [5,6]. Hyperlipoproteinemias are the underlying cause of lipidemias[7,8]. ATP III recognized that LDL lowering is the primary surrogate end point toward reducting in the CVD events and mortality[9,10]. Statins are having anti inflammatory roles[11,12]. Statins has a role in vasodilation functions[13], also has a role in chemotaxis for plaques,[14]and enhances vasoreactivity of unstable statins reduce effects in plaques formation,[15,16]. Statins effects the leucocyte migration, [17,18] and role in endothelium function[19]. Also inhibit growth and proliferation of macrophages [20].Statins induce apoptosis and retard hyperplasia and re-stenosis, provide plaque stability[21,22], statins decrease T-cell proliferation[23].Statins

improve endothelial dysfunction by increasing nitric oxide bioavailability and reducing LDL oxidation and vascular inflammatory response. Statins increase the concentration of nitric oxide which has vasodilator, antithrombotic and antiproliferative properties[24]. Suppress superoxide formation and enhances NO generation by vascular endothelial cells via inhibition of Rac and Rho[25]. Rosuvastatin has been shown to increase vascular endothelial NO production and attenuate myocardial necrosis following ischemia and reperfusion in mice[26]. Statins decrease the LDL oxidation by increasing NO which can scavange superoxide free radical anions responsible for LDL oxidation[27].Antioxidant actions of No antagonizes the vasoconstrictive properties of the Reactive oxygen species(ROS). Reduces lipid peroxidation and ROS production[28].Plaque stability of statins stabilize plaque by inhibiting metalloproteinases, which play a potential role in atheromatous plaque disruption[29,30].Statins has coagulation function and inhibit extrinsic coagulation pathway, inhibit platelet adhesion and maintain a balance between prothrombotic and fibrinolytic mechanisms [31]. NO by its sympathoinhibitory action reduce angiotensin II and AT1 receptor expression[32,33]in Glomerulonephritis: reduce monocyte infiltration & expression of vascular cell adhesion molecule(VCAM-1). Reducess proteinuria [34],and has antiproliferative effects in cancers[35]

V. Tables:

Table.1Levels of Lipid profile in Control group and Study group

Parameters	Control (n=50)	Study group (n=50)
Total cholesterol (mg%)	155.0 ± 11.0	220 ± 9.4
HDL-C(mg%)	35.0± 6.1	28.0 ± 7.4
LDL-C(mg%)	83.0 ± 12.0	134.0 ± 6.0
Triglycerides(mg%)	71.0 ± 19.0	315.0 ± 29.0
VLDL(mg%)	23.0 ± 7.0	55.0 ± 12.0
SGOT(IU/L)	22 ± 6.1	31 ± 9.2
SGPT(IU/L)	24 ± 5.1	26.3 ± 9.1

Table.2 Lipid profiles of group A, before and after treatment of Rosuvastatins.

Parameters	Before treatment	After treatment	't' value	'p' value
Total cholesterol (mg%)	220 ± 9.4	193.3 9.0	1.9	0.05
HDL-C (mg%)	28± 7.4	33± 7.8	2.3	0.02
LDL-C (mg%)	134 ± 6.0	112 ± 4.5	3.8	0.0003
Triglycerides(mg%)	315 ± 29.0	281 ± 25.0	2.5	0.01
VLDL-C (mg%)	55 ± 12.0	46 ± 8.0	2.6	0.01
SGOT(IU/L)	31 ± 9.2	30- ± 9.1	0.001	0.12, NS
SGPT(IU/L)	26.3 ± 9.1	26.5 ± 9.0	0.02	0.12, NS

Levels are expressed as Mean ± SD, p-value <0.05 were considered as statistically significant

Table. 3Lipid profiles in group B, before and after treatment of Atrovastatin.

Parameters	Before treatment	After treament	't' value	'p' value
Totalcholesterol mg%)	220 ± 9.4	203 ± 7.9	0.4	0.6 , NS
HDL-C (mg%)	28.0 ± 7.4	29 ± 6.0	0.8	0.3 , NS
LDL- C (mg%)	134 ± 6.0	116 ± 4.5	1.2	0.2 , NS
Triglycerides (mg%)	315 ± 29.0	295 ± 17.0	0.4	0.67, NS
VLDL (mg%)	55 ± 12.0	50 ± 5.0	0.5	0.59, NS
SGOT (IU/L)	31 ± 9.2	31 ± 9.1	0.3	0.2, NS
SGPT (IU/L)	26.3 ± 9.1	26 ± 9.0	0.31	0.21, NS

Levels are expressed as Mean ± SD, p-value >0.05 were considered as statistically significant

VI. Conclusion:

The results of this study showed that Rosuvastatin is better than atorvastatin in terms of efficacy. Both drugs are equally tolerated and equally safe.

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