International Journal Dental and Medical Sciences Research (IJDMSR)
ISSN: 2393-073X Volume 2, Issue 8 (Aug- 2018), PP 12-20
www.ijdmsr.com

Effect of Biotin on the Lipid Profile – Total Cholesterol, LDL, Triglyceride, VLDL and HDL of Dyslipidemic Patients

[1]Dr. N. Asvini,[MBBS.,DDVL.,MD], [2]Prof. Dr. G. Hemavathy,[MBBS.,MD],
[3]Prof. Dr. M. Kulandaiammal.,[MBBS.,DGO.,MD], [4]Dr. M. Rajakumar.,[BDS.,MDS.,
[1]*Assistant Professor, Department of Pharmacology, Government Stanley Medical College, Chennai, India*
[2]*Professor, Department of Pharmacology, Government Stanley Medical College, Chennai, India*
[3]*Professor &HOD, Department of Pharmacology, Government Stanley Medical College, Chennai, India*
[4]*Associate Professor, Department of Prosthodontics, The Tamil Nadu Government Dental College and Hospital, Chennai, India*
**Corresponding Author: Dr. N. Asvini*

ABSTRACT:- *Biotin supplementation has been found effective in reducing the plasma lipoproteins of Diabetic and non diabetic subjects[1]. This trial was performed to determine the efficacy of Biotin as an adjuvant hypolipidemic agent. .We conducted an open label, single centre, prospective comparative study among the outpatients attending the hypertension clinic of the medicine department from March 2013 to February 2014. Patients between 45 and 60 years of age with newly diagnosed secondary dyslipidemia, with mild to moderate elevations in lipid profile were recruited for the study. The patients were randomly allocated to the two groups consisting of 30 patients each. The study group received combination therapy of Atorvastatin with Biotin and the control group received monotherapy of Atorvastatin for 6 weeks. At the end of each week percentage reduction in the mean total Cholesterol, LDL, Triglycerides, HDL and VLDL of the two groups from the baseline levels was calculated and compared by using students t test. Combination therapy group showed a 34.66% reduction in total cholesterol at the end of the 2nd week and 41.33% reduction in the 4th week of treatment .The difference in the percentage reduction rates were statistically significant when compared to the monotherapy group. By the end of the second week, there was greater percentage reduction in triglyceride levels in the study group when compared to the control group, which was also statistically significant. There was also a greater reduction in VLDL when compared to monotherapy with Atorvastatin but the difference was less and not statistically significant. After the 2nd week of study both the groups had a rise in HDL levels but the difference was not statistically significant. Addition of Biotin along with Atorvastatin in the treatment of dyslipidemias has resulted in a statistically significant reduction in Total Cholesterol , LDL cholesterol , Triglyceride levels. Biotin can be considered as an adjuvant drug in treating dyslipidemias.*

Key words: *Lipoproteins, dyslipidemia, Biotin, LDL, HDL.*

I. INTRODUCTION

Dyslipidemia is a common metabolic disorder and an important modifiable risk factor for atherosclerosis and its complications. The prevalence of dyslipidemia has been increasing over years and is 8-9.6% in the urban population of India [2].The National health Survey conducted in US during 1999 to 2000 have shown that 25% of adults had raised total cholesterol (>239 mg per dl) and were on lipid lowering medication[3].

Statins have been the major class of drugs in the management of these dyslipidemias but their role has been disputed nowadays due to its association with Diabetes mellitus. There is a need for more drugs with better efficacy and less adverse effects for treating these patients. Biotin is one such agent which found to causes significant decrease in phospholipids in rats. Biotin supplements have shown to reduce the plasma cholesterol and triglyceride in patients with type II Diabetes Mellitus and non diabetic patients with triglyceridemia.

This study was designed to find out the effect of pharmacological doses of Biotin on plasma lipid profile of dyslipidemic patients .If Biotin is proved to be an efficacious lipid lowering agent it would emerge as a cheaper and better tolerated adjuvant drug in the management of dyslipidemia. As Biotin cannot be used as monotherapy for known ethical reasons, it was given as adjuvant drug along with Atorvastatin and the effect of this combination therapy on lipid profile was compared with monotherapy.

II. METHODOLOGY

The study was conducted from March 2013 to February 2014 in the department of medicine of Government Stanley Medical College. Insitutional ethics committee approval was obtained before the study was started.

Newly diagnosed cases of dyslipidemic patients with mild to moderate rise in plasma lipids were included in the study. The other inclusion criteria were age between 45-60 years, a plasma total cholesterol of 200 – 499 mg/dl , plasma LDL cholesterol level of 100-189 mg/dl, plasma triglyceride level of 150-500 mg/dl, plasma VLDL level of more than 30 mg/dl and plasma HDL level of less than 40 mg/dl. Patients with co existing Diabetes mellitus and /or hypertension were eligible to participate in the study.

Patients with high levels of LDL (more than 500mg/dl) alone or high level of triglyceride alone (more than 500 mg/dl) alone were not eligible to participate in the study. Patients with uncontrolled diabetes Mellitus (fasting blood glucose more than 140 mg/dl) and uncontrolled hypertension (BP> 160/100 mm hg) were also not eligible to participate in the study. We also excluded patients with ischaemic heart disease or cerebrovascular disease or peripheral arterial disease or neuromuscular disorders. Patients with laboratory evidence of liver dysfunction, renal dysfunction, thyroid dysfunction and patients who were smokers or alcoholics or those who took antiplatelet drugs were also excluded.

Outpatients attending the hypertension clinic and diabetology clinic were screened for dyslipidemia by a fasting lipid profile. Among them patients with elevated lipid levels and who were willing to give a written informed consent were selected and included in the study. A written informed consent was obtained from these patients. Each patient was registered and a case record form was maintained. A detailed medical and drug history was taken and a complete clinical examination and laboratory investigations which included complete hemogram, liver function tests, renal function tests, thyroid function tests and serum creatinine phosphokinase were done. 60 patients were selected based on the selection criteria and inducted into the study. These patients were randomly allocated by computer generated allocation sequence into two groups A and B.

Study groups and interventions:

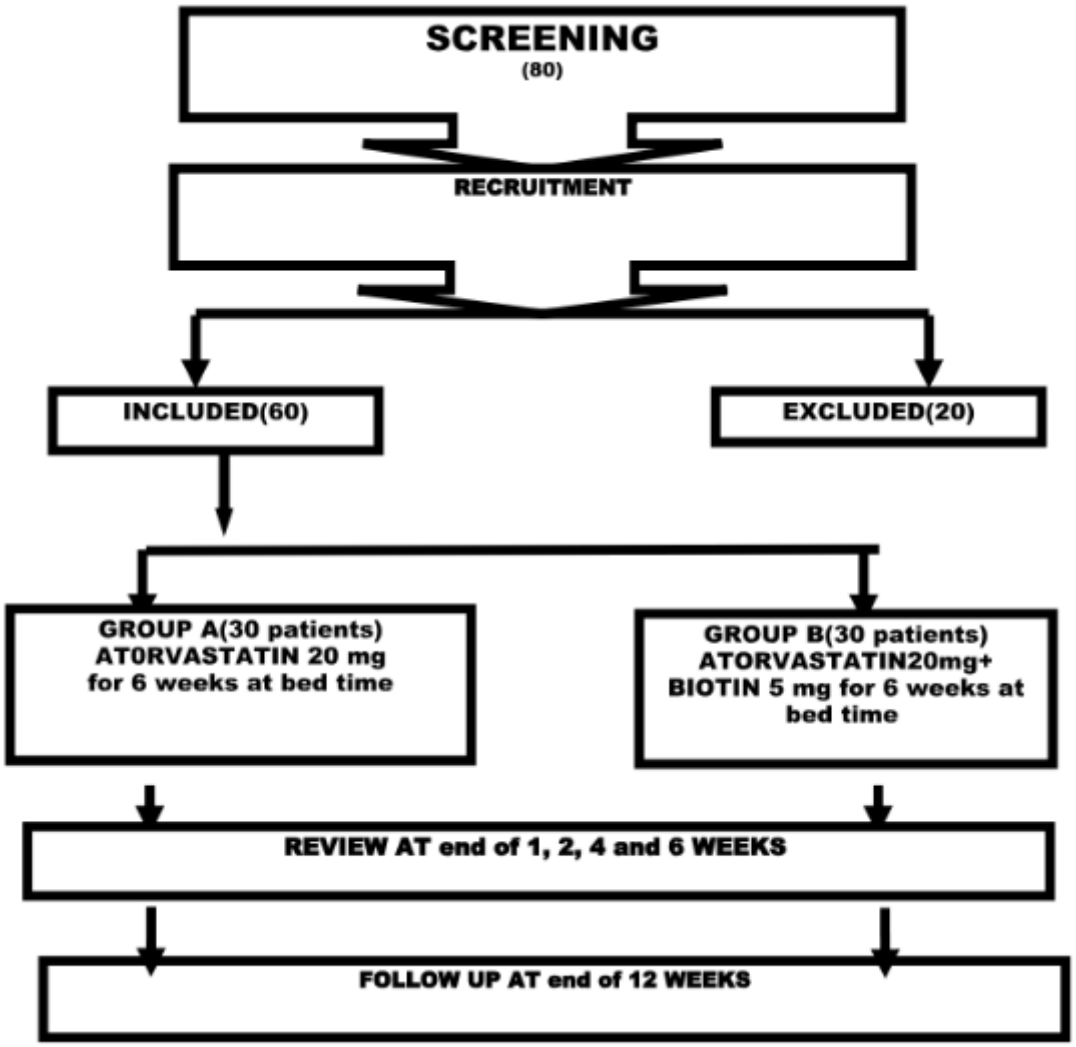
The group A was the control group and it received Tablet Atorvastatin 20 mg once daily at bed time for 6 weeks. The group B was the study group which received T.Biotin 5 mg along with Tablet Atorvastatin 20 mg once daily at bed time for 6 weeks. The patients received the study drugs in the op weekly and were reviewed every week. The participants were advised to continue their other medications and to come in between if any myalgia or muscle weakness or any other adverse event occurred. Fasting lipid profile was done at the end of 1^{st} ,2^{nd} ,4^{th} and 6^{th} week.

Follow up:

The patients of both the groups were followed up for 6 more weeks during which they received Tablet Atorvastatin 20 mg once daily at bed time. At the end of the follow up period another fasting lipid profile was done and results noted. Complete hemogram, liver function tests, renal function tests and serum creatinine phosphokinase was done .During the period of 12 weeks the patients monitored for adverse events .

III. STATISTICAL ANALYSIS

The baseline characteristics of the two groups which included the mean age, sex distribution, co-existing diseases like Diabetes Mellitus , Hypertension and base line lipid profile were compares and found to be similiar. The demographic data was expressed as mean +/- standard deviation. The fasting lipid profile of the patients was were obtained at the beginning of the study, end of 1^{st} week, 2^{nd} week, 4^{th} week ,6^{th} week and 12^{th} week. The percentage change from base line lipid levels was calculated and tabulated for each patient. The mean percentage change in the plasma lipids was compared between the two groups was compared by using students independent t test. ** $p \leq 0.010$ it implies Highly Significant, * $p \leq 0.050$ it implies Significant, $p > 0.050$ it implies Not Significant. The comparative statistics was expressed in the form of graphs and bar diagrams.



IV. RESULTS

A total of 80 patients who were attending the medicine outpatient department for either diabetes mellitus or hypertension were willing to participate in the study. After a preliminary screening 20 patients were excluded and 60 newly diagnosed patients of dyslipidaemia were selected and treated according to the trial protocol. All the patients completed the treatment and were included in the statistical analysis.

At baseline the mean age of the patients in the study group was **50.13 yrs** and the mean age of patients in the control group was **50.70 yrs**. Diabetes mellitus was present in **23.3%** of the subjects in the control group *vs.* **26.6%** of the subjects in the study group. Hypertension was present in **93.3%** of the subjects in the control group *vs*. **90%** of the subjects in the study group. At the beginning of the study, the mean total cholesterol of the control group - **263.76mg/dl *vs.* 286.73 mg/dl** in study group.

The mean LDL of the control group - **158.06 mg/dl *vs.* 173.76 mg/dl** in study group.

The mean triglycerides of the control group - **170 mg/dl *vs.* 210 mg/dl** in the study group. The mean VLDL of the control group - **36.33 mg/dl *vs.*41 mg/dl** in the study group. Mean HDL of the control group - **46.44 mg/dl *vs.*47.33 mg/dl** in the study group.

EFFECT ON TOTAL CHOLESTEROL LEVELS

By the first week of study there was16.7% reduction in total cholesterol in control group vs 16.06% in study group, but this difference was not statistically significant p=0.623. By second week of study there was **26.32%** reduction in total cholesterol in the control group vs **34.66%** reduction in the study group. At fourth week of study there was **28.33%** reduction in total cholesterol in the control group vs **41.33%** reduction in the total cholesterol in the study group. At six weeks, there was **28.68%** reduction in total cholesterol in the control group vs.**40.37%** reduction in the study group. On follow up 12^{th} week, there was **27.56%** reduction in total cholesterol in the control group vs **26.96%** reduction in total cholesterol in the study group. The mean

percentage reduction in total cholesterol and the standard deviation is given in Table no 1. Fig no 1 shows the mean percentage reduction in Total cholesterol of the two groups during the study.

Table 1: Comparison of % reduction from Baseline in Total Cholesterol between two groups

	Control(% redn)		Study(% redn)		'p' value
	Mean	**SD**	**Mean**	**SD**	
Baseline	-	-	-	-	
1st week	16.7%	5.6	16.06%	4.37	0.623
2nd week	**26.32%**	4.4	**34.66%**	8.52	**0.000****
4th week	**28.33%**	5.05	**41.33%**	7.74	**0.000****
6th week	**28.68%**	5.56	**40.37%**	9.91	**0.000****
12th week	27.56%	5.7	26.96%	5.02	0.671

** $p \leq 0.010$ it implies (Highly Significant), * $p \leq 0.050$ it implies (Significant) , $p > 0.050$ it implies Not Significant

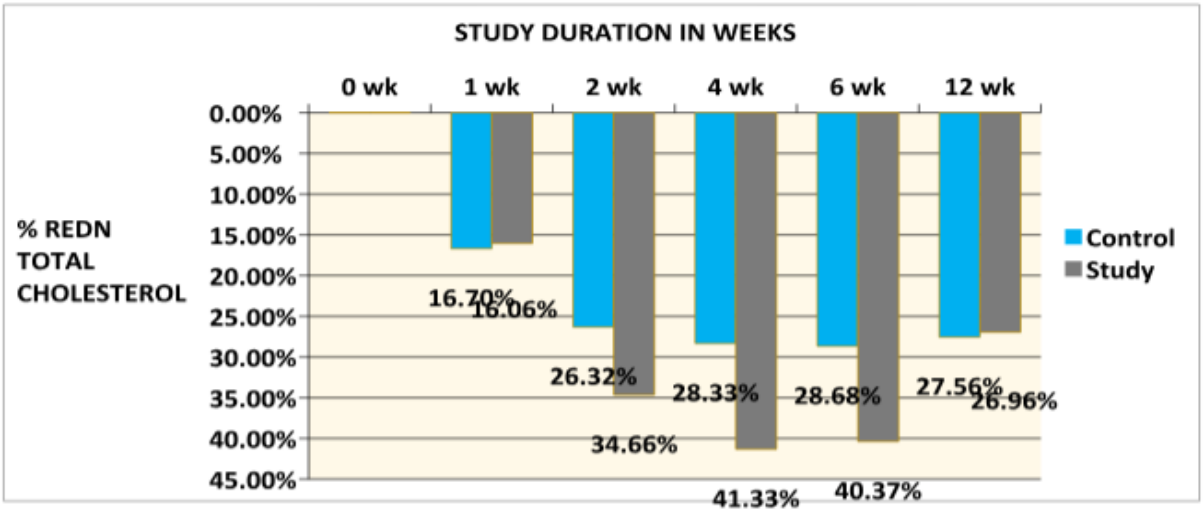


Figure 1: Comparison of % change in Total Cholesterol between two groups

EFFECT ON LDL CHOLESTEROL LEVELS

By the first week, there was a 19.08% reduction in LDL cholesterol levels from baseline in the control group vs. 16.90 % reduction from baseline in the study group. At the second week, there was a 39.89% reduction in LDL cholesterol levels from baseline in the study group vs. 34.35% reduction in LDL cholesterol levels from baseline in the control group. .At the fourth week, the study group showed a 42.62% reduction in LDL cholesterol levels from baseline vs. 35.89% reduction from baseline in the control group. At the sixth week, the study group showed a 43.28% reduction in LDL cholesterol vs. 36.95% reduction in control group . At the twelfth week there was no statistically significant difference in the percentage reduction in LDL cholesterol levels.

The mean and standard deviation of the percentage reduction in LDL levels is shown in table no 2. Figure 2 is a column chart representing the percentage reduction from baseline in LDL levels in the control and study groups at 0,1st, 2nd, 4th, 6th&12th week.

Table 2: Comparison of % reduction from Baseline in LDL levels between two groups

	Control(% redn)		Study(% redn)		'p' value
	Mean	**SD**	**Mean**	**SD**	
Baseline	-	-	-	-	
1st week	**19.087%**	4.14	**16.90%**	4.04	**0.044***
2nd week	**34.35%**	1.77	**39.89%**	6.24	**0.000****
4th week	**35.89%**	6.65	**42.62%**	5.65	**0.000****
6th week	**36.95%**	3.92	**43.28%**	5.007	**0.000****
12th week	35.12%	4.37	36.57%	4.51	0.544**

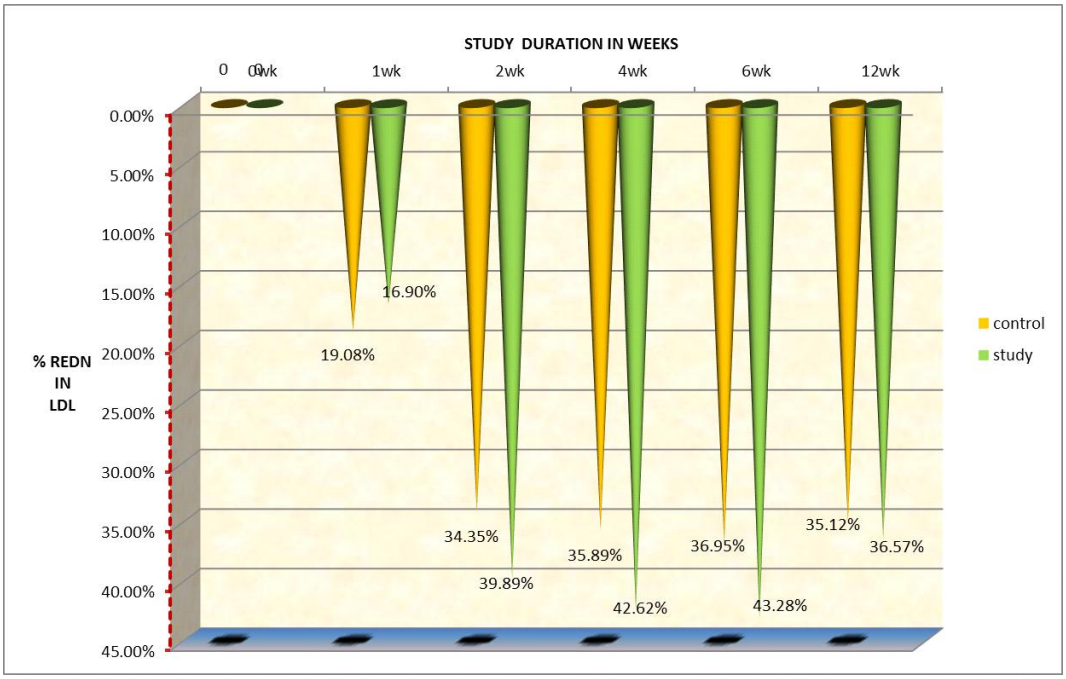


Figure 2: Comparison of % reduction from Baseline in LDL Cholesterol between two groups

EFFECT ON TRIGLYCERIDE LEVELS

By the end of the first week, the control group had **5.66%** reduction in triglycerides vs **13.96%** reduction in the study group. By the end of the second week, there was greater percentage reduction in triglyceride levels in the study group when compared to the control group. The percentage reduction in study group was **25.92%** when compared to the control group which had **18.34%** reduction. At the end of the fourth week the control group had **19.88% reduction vs 25.65%** reduction in the study group.At the sixth week the control group had **20.66% reduction vs 28.45%** reduction in the study group.At the end of the twelfth week, there was no significant difference in percentage reduction in triglyceride levels between the two groups (p=0.422). The percentage reduction in triglyceride levels was **19.36%** in the control group **vs 20.69%** in the study group.

The mean and standard deviation of the percentage reduction in triglycerides is shown in table 3. **Figure no 3** is a column chart representing the percentage reduction in triglyceride levels from baseline at 1st, 2nd, 4th, 6th &12th week of the study.

Table 3: Comparison of % reduction from Baseline in Triglyceride levels between two groups

	Control(% redn)		**Study(% redn)**		**'p' value**
	Mean	**SD**	**Mean**	**SD**	
Baseline	-	-	-	-	
1st week	**5.66%**	2.79	**13.96%**	5.74	**0.000****
2nd week	**18.34%**	1.26	**25.92%**	9.60	**0.000****
4th week	**19.88%**	3.61	**25.65%**	8.55	**0.002****
6th week	**20.66%**	9.26	**28.45%**	8.93	**0.002***
12th week	19.36%	9.41	20.69%	8.86	0.577

** $p \leq 0.010$ it implies (Highly Significant), * $p \leq 0.050$ it implies Significant at 5 level (Significant) , $p > 0.050$ it implies Not Significant

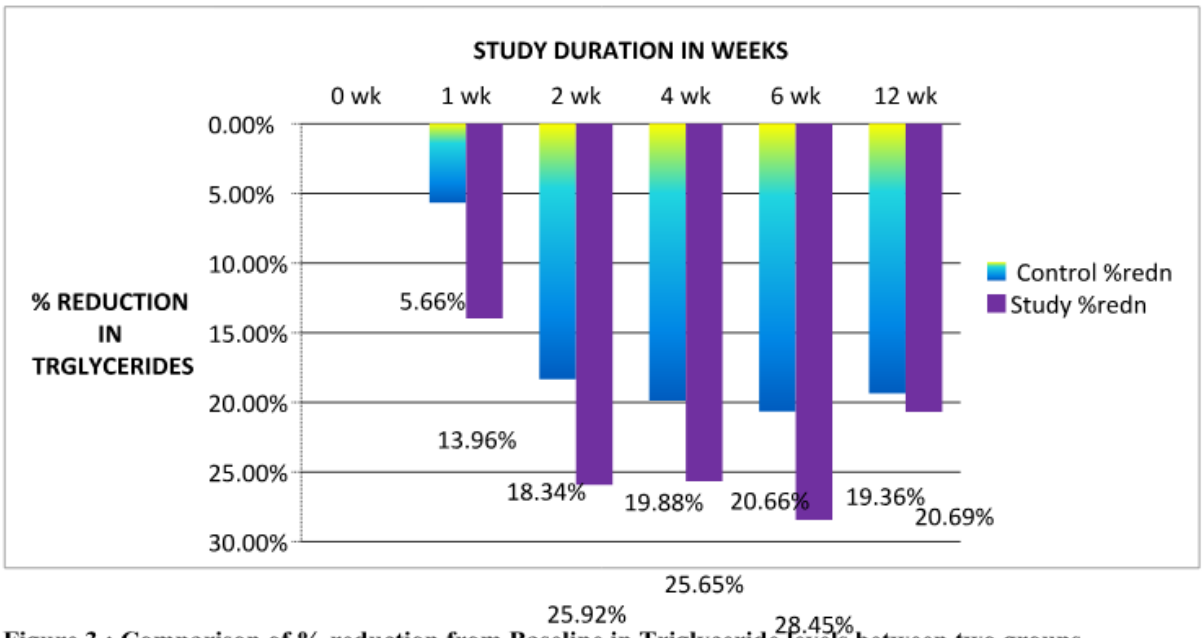


Figure 3 : Comparison of % reduction from Baseline in Triglyceride levels between two groups

EFFECT ON VLDL

At the end of the first week, the study group had **6.2%** reduction in VLDL levels vs **4.75%** reduction in control group. At the end of the second week, the study group had **30.3%** reduction in VLDL levels vs **23.05%** in control group. At the end of the fourth week, the study group had **33%** reduction in VLDL levels vs **32.03% in** the control group. At the end of the sixth week, the study group **had 35.4%** reduction percentage in VLDL level vs **36.16%** in control group. At the end of the twelfth week, there was **35.46%** reduction in VLDL levels vs **27.8%** reduction in the study group.

The mean and standard deviation of the percentage reduction in VLDL in both groups is shown in table 4. **Figure 4** is a column chart showing the percentage reduction in VLDL levels of the study and control groups at 0,1st ,2nd ,4th ,6th &12th week of the study.

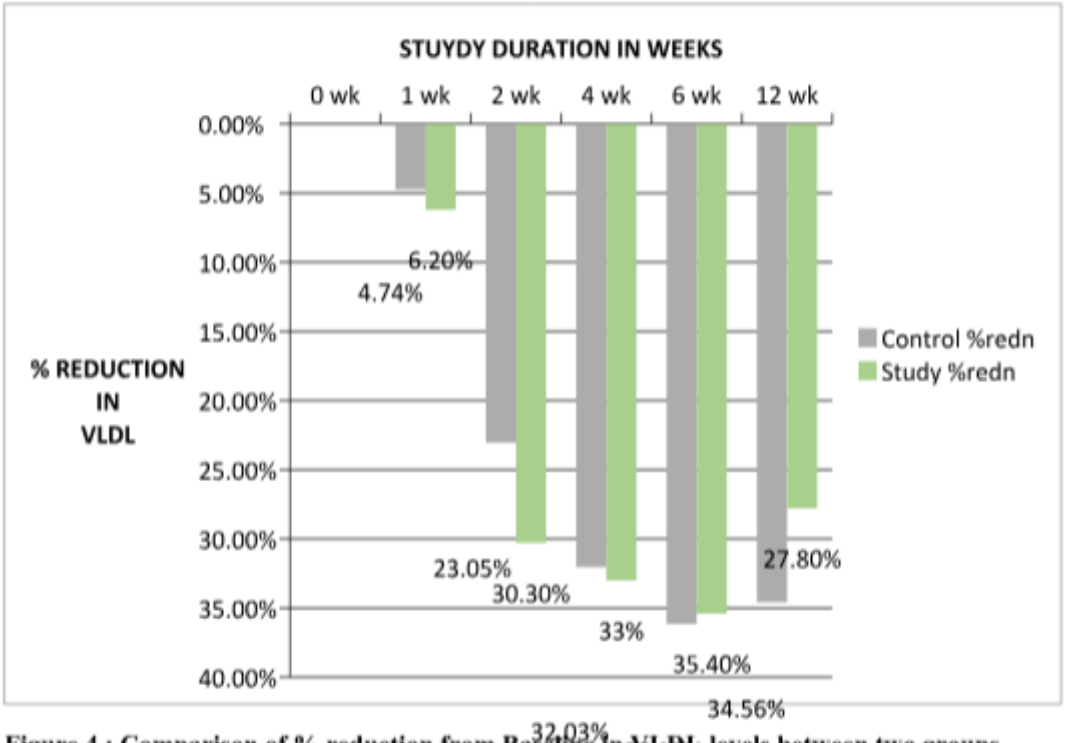


Figure 4 : Comparison of % reduction from Baseline in VLDL levels between two groups

EFFECT ON HDL

By the end of the first week, there was a 1.26% reduction in HDL levels in control group vs 2.2% reduction in study group. By the end of the second week. the control group had a 0.25% fall in HDL levels vs 0.35% fall in study group. At the end of the fourth week, the control group had a 0.11% reduction in HDL levels vs2.32% rise in study group. At the end of the sixth week, the control group had 2.83% rise in HDL level vs 4.17% rise in the study group. At the end of the twelfth week, the control group had 6.11% rise in HDL levels vs 3.47% rise in the study group. The mean percentage change from base line at 0, 1st , 2nd , 4th , 6th & 12th week in both the groups is shown in table no 5.The comparison of percentage change from baseline in HDL in both groups, statistical analysis was done by using students . Figure no 5 is a column chart showing the percentage change in HDL levels from base line at 0,1st, 2nd, 4th, 6th &12th week of both the groups.

Table 4: Comparison of % change from Baseline in HDL levels between two groups

	Control(% change)		Study(% change)		'p' value
	Mean	**SD**	**Mean**	**SD**	
Baseline	-	-	-	-	
1st week	-1.26%	6.54	-2.29%	2.95	0.09
2nd week	-0.25%	8.01	-0.35%	7.36	0.620
4th week	-0.11%	5.60	2.32%	7.23	0.150
6th week	2.83%	6.84	4.17%	9.01	0.518
12th week	6.113%	8.80	3.47%	4.09	0.142

** p ≤ 0.010 it implies (Highly Significant), * p ≤ 0. 050 it implies (Significant) , p > 0.050 it implies Not Significant

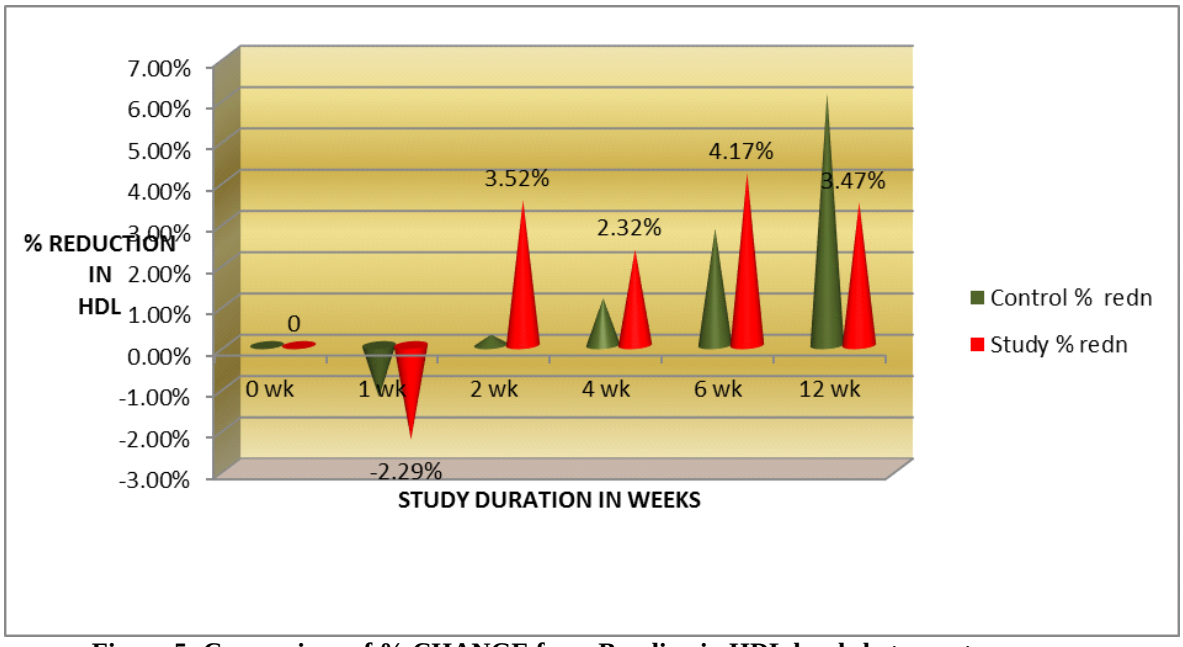


Figure 5: Comparison of % CHANGE from Baseline in HDL levels between two groups

There was no significant difference in the laboratory parameters before and after the study in both the groups. There was no significant difference in the mean SGOT and SGPT levels and CPK levels before and after the study in both the groups. Out of 30 patients 10 patients in the control group vs 8 patients in the study group experienced minor self limiting side effects. In the study group which received biotin one male patient reported reduced hair fall by the end of the fourth week of the study.

V. DISCUSSION

In this clinical study the therapeutic effect and side effect profile of combination of Biotin 5mg with Atorvastatin 20 mg was compared with the monotherapy of Atorvastatin 20 mg for 6 weeks.

Patients with primary dyslipidemias will be symptomatic at an early stage and have associated cardiovascular complication. By excluding patients less than 45 yrs of age at the screening, the possibility of inducting primary dyslipidemias is low. Moreover age more than 45 in males and 55 in females is considered as a serious risk factor for atherosclerosis. Thus, we have included only newly diagnosed cases with secondary dyslipidemias at high risk of atherosclerosis in the study.

Statistical analysis of the baseline characteristics has showed both the groups to be comparable in terms of mean age, age distribution, sex distribution, associated co-morbid diseases. Patients compliance was good in both the groups with all patients coming for regular visits. In the study group patient follow up was good and there were no dropouts and all the patients completed the study.

Effects on LDL cholesterol:

Monotherapy with atorvastatin 20 mg resulted in greater 16.7% reduction in total cholesterol at the end of 1st week when compared to the 16.06% reduction in the combination therapy group, but this was not statistically significant, which implies that there are no early effects of biotin in the study group. Therafter monotherapy resulted **in 26.32% reduction in total cholesterol at the end of 2nd week, 28.33% reduction at the end of 4th week and 28.68% reduction at the end of 6th week**. These reduction rates are similar to those observed in other studies by Wilinski et al [4] . Combination therapy group showed a **34.66% reduction in total cholesterol at the end of the 2nd week, 41.33% reduction in total cholesterol at the end of the 4th week and 40.37% reduction in total cholesterol at the end of the 6th week respectively** (vide Table 1,Fig 1). Thus the combination of biotin 5 mg with atorvastatin 20 mg resulted in a greater reduction in total cholesterol from the 2nd week onwards which was well maintained till the 6th week, this difference was also **statistically significant.** At the follow up visit the percentage reduction came down to 29.96% in the study group which was similar to the 27.56% reduction in control group implying that Biotin has no delayed effects on plasma lipoproteins.

Effects on LDL cholesterol:

There was a 19.08% reduction in the mean LDL levels from baseline in the group which received Atorvastatin alone at the first week, later the percentage reduction plateaued at around **34.35%, 35.89% and 36.95% at 2nd, 4th and 6th week** respectively. These reduction rates are similar to previous studies showing a 25-40% reduction after treatment with Atorvastatin 20 mg for 12 weeks[5] . The study group which received 5 mg biotin along with Atorvastatin had a 16.90% reduction in mean LDL levels at 1st week followed by a **39.89% reduction in LDL levels at the end of 2nd week, 42.62% reduction at the end of the 4th week and 43.28% reduction at the end of the 6th week.** On statistical analysis the difference in percentage reduction in LDL levels between the study group and the control group was statistically significant at 2nd, 4th, and 6th week (vide Table 2, Fig 2). At the follow up visit both the groups had similar reduction percentages 35.12% in control vs. 36.57% in study group implying the absence of delayed effects of biotin on LDL levels.

Effect on triglycerides:

The combination therapy resulted in a significantly greater reduction in triglyceride level from the first week onwards. The mean triglycerides were reduced by **13.96% at the end of 1st week, 25.92% at the end of 2nd week, 25.65 at the end of 4th week and 28.45% at the end of 6th week in the study group** when compared to the control group which resulted in **a 5.66% reduction at the end of 1st week, 18.34% reduction at the end of 2nd week, 19.88% at the end of 4th week and 20.66% at the end of 6th week** . On statistical analysis the difference in reduction perecntages were statistically significant from the first week till the sixth week(vide Table 3, Fig3). At 12 weeks after Biotin was discontinued the percentage reduction of the study group was similar to the control group, it was 20.69% in the study group as against 19.36% in the control group.

Effect on VLDL:

The combination therapy of biotin and atorvastatin resulted in a greater reduction in VLDL when compared to monotherapy with atorvastatin but the difference was less and not statistically significant.

Effect on HDL:

After the 2nd week of study both the groups had a rise in HDL levels . Though there was a greater rise in HDL percentage in the combination group it was not statistically significant.

There was no significant difference in the incidence of adverse effects between the two groups. The occurrence of adverse effects was similar to those seen in previous studies with atorvastatin 20 mg[6] . The common adverse events were myalgia and general body weakness. The occurrence of gastrointestinal distress was similar in both the groups. There was a better hair growth in few patients who received Biotin , this

observation correlated with previous studies showing the effects of Biotin in androgenic alopecia by Fameneni et al[7] .

Biotin is a very safe vitamin and levels upto 300 times the normal have shown to be non toxic. Thus the addition of Biotin had resulted in fewer side effects and some additional observed effects also. None of the patients had any significant abnormality in the laboratory investigations performed. Studies investigating the effect of Biotin administration in small groups of patients have concluded that pharmacological doses of biotin decrease hypertriglyceridimia[9]

From these results we can infer that addition of biotin has produced significantly more reduction in total cholesterol, LDL and triglyceride level . This lipid lowering effect of biotin can be attributed to the role of Biotin in the regulation of genes associated with intermediary metabolism and in the maintanence of glucose and lipid hemostasis [10] .

Biotin can thus be considered an effective and safe add on drug with Atorvastatin. It can be a valuable adjuvant drug in patients with secondary dyslipidemias. Further trials to find the effect of Biotin on the lipid profile can be done by giving only biotin alone in mild cases.

VI. CONCLUSION

From these results it can be concluded that addition of Biotin along with Atorvastatin in dyslipidemias will result in a better control of cholesterol levels and that Biotin can be a better adjuvant drug in treating dyslipidemias.

REFERENCES

[1]. Revilla- Monsalve C, Zendejas-Ruiz l, Hernandez-quiroz PM et al. Biotin supplementation reduces plasma triglycerol and VLDL in type 2 diabetic patients and in non diabetic subjects with hypertriglyceridemia. Biomedicine & pharmacotherapy.May 2006; vol.60 (4): p 182-185.

[2]. Shashank R. Joshi, Ranjit Mohan anjana, Mohan Deepa, Rajensra Pradeepa et al, Prevalence of Dyslipidemia in urbn and Rural India: The ICMR-INDIAB Collaborative study group. May 09 2014.

[3]. Joshi SR, Anjana RM Deepa M, Pradeepa R, Bhansali A, Dhandania VK, et al. (2014) Prevalence of Dyslipidemia in Urban and Rural India: The ICMR – INDIAB study. PLOS ONE 9(5): e96808. doi: 10.1371/ journal.pone.0096808.

[4]. Enas A Enas et al. The Metabolic syndrome- Prevalence of lipid abnormalities in the United States: the National Health and nutrition Examination Survey 2003 – 2006. Journal of Clinical Epidemiology, July-Aug 2008, issue 4: p 325-330.

[5]. Sharon F Suchy and Barry Wolf. Effect of Biotin deficiency and supplementation on metabolism in rats: Cholesterol and Lipoproteins 1-3. The American Journal of Clinical Nutrition. May 1986; vol 43: p831-838.

[6]. Bernini F, Poi A, Paoletti R. Safety of HMG – Co A reductase inhibitors: Focus on Atorvastatin. Cardiovascular drug therapy 2001 ; 15(3): 211-8.

[7]. Upendra Kaul, Jagmohan Varma, Dhiman K Ahali, MS Hiremath et al. Postmarketing study of experience of Atorvastatin 80 mg vs 40 mg in randomized , multi – centre study (CURE-ACS). JAPI; February 2013; vol 61: p 97-101.

[8]. Famenini S, `Gosh C. Evidence of supplemental trements in androgenetic alopecia. Journal of drugs dermatology 2014 July ; 13(7): 809-912.

[9]. Eng W K, Giraud D, Schiegel VL, Wang D, Lee B H, Zempleni J. Identification and assessment of markers of markers of biotin status in healthy adults. Journal of nutrition 2001 july.

[10]. Larrieta E, Velasco F,Vital P, Rojas A et al. Pharmacological concentrations of Biotin reuces serum Triglycerides and the expression of Lipogenic genes, uropean journal of Pharmacology, vol 6444(1-3): p 263 -268

[11]. Armida Boez-Saldana, Ivan Zendejas – Ruiz, Cristina Revilla – Monsalve et al, Effects of Bioitn on Pyruvate carboxylase and markers for glucose and lipid homeostasis in type 2 Diabetic patients and non diabetic subjects. American Journal of Clinical Nutrition 2004; vol 79: p – 238-243.

Corresponding Author: Dr. N. Asvini
[1]Assistant Professor, Department of Pharmacology, Government Stanley Medical College, Chennai, India