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COMPARATIVE STUDY OF HYPOLIPIDEMIC EFFECTS OF ATORVASTATIN WITH EMBLICA OFFICINALIS (AMLA) IN PATIENTS OF TYPE II HYPERLIPIDEMIA

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ABSTRACT

Aims and objectives: The present study was undertaken for an evaluation of the effect of *E. Officinalis* powder on the serum lipids level & comparing standard hypolipidemic drug Atorvastatin in the patients of hyperlipidemia type II at NIMS Medical College & Hospital, Jaipur. **Methods:** A prospective randomized open label study was done in medicine O.P.D. NIMS Hospital Jaipur from November 2011 to April 2013 after taking ethical clearance and written informed consent. Out of 93 patients, 45 patients (Group-A) were given two tablet of *Amla* (500 mg) daily, while the other 48 patients (Group-B) received one tablet of Atorvastatin (10 mg) daily for 16 weeks.All routine biochemical investigations including lipid profile were performed before starting the intervention as well as after completion of each treatment round i.e at the end of 4 weeks, 8 weeks, 12 weeks & 16 weeks. **Results:** Amla showed significant increase in HDL and decrease in triglyceride level ($P < 0.05$) at the end of 16 wks while atorvastatin has shown better effect on TC, LDL and VLDL ($P < 0.05$). There was no adverse drug event in either group. **Conclusion:** In our study on amla when compared with

atorvastatin, amla has been shown better effect on TG and HDL while atorvastatin has shown better effect on TC, LDL and VLDL.

Keywords: Hyperlipidemia, Atorvastatin, Amla(*Emblica officinalis).*

INTRODUCTION

Claude Bernard stated that-"*The work of science is to substitute* demonstrations *for* impressions *and* facts *for* beliefs*".* Hyperlipidemia indicates high level of fats (or lipids) in the blood. These fats include cholesterol and triglycerides. They are important for our body function but when they are too high, they can put people at risk for heart disease and stroke. [1] Hyperlipidemia is one of the major culprits for various cardiovascular and central nervous system disorders. Both genetic disorders and diet enriched with saturated fats and cholesterol, contribute to the elevated lipid levels in our population as well as in many other developed countries around the world .[2]

Hyperlipidemia is also known as one of the most frequently implicated risk factor for development of atherosclerosis.[3]

A strong association exists between hyperlipidemia and coronary artery disease (CAD), cerebro-vascular stroke and peripheral vascular disease. [4] The hypolipidemic drugs have attracted considerable attention because of their potential to prevent cardiovascular disease by retarding the accelerated atherosclerosis in hyperlipidemic individuals .[5]

All parts of *E. Officinalis* are used in clinical practice: e.g., Root bark in stomach ulcer; bark in gonorrhea, jaundice and diarrhea . [6] Leaves in conjunctivitis and inflammation.[7] Fruits as digestive, laxative and antipyretic .[8] In addition, it has been shown to reduce cholesterol level in experimental animals .[9] and in clinical studies . [10]

Keeping in view of the above ideas, the present study was undertaken for an evaluation of the effect of *E. Officinalis* powder on the serum lipids level & comparing standard hypolipidemic drug Atorvastatin in the patients of hyperlipidemia type II at NIMS Medical College & Hospital, Jaipur.

OBJECTIVES OF THE STUDY

1. To study the hypolipidemic effect of atorvastastin in type II hyperlipidemia patients.
2. To study the hypolipidemic effect of Amla in type II hyperlipidemia patients.
3. To evaluate the difference of outcome and analyze it, if any.

ETHICAL CLEARANCE

The protocol was approved by the Institutional Ethics Committee of NIMS Medical College & Hospital, Jaipur.NIMS University.

INCLUSION CRITERIA

Those consenting to participate in the study were enrolled if there was

1. Presence of type II hypercholesterolemia (i.e., serum Total Cholesterol (TC)>240 mg/dl and serum Low Density Lipoprotein-cholesterol (LDL)>130 mg/dl).
2. Presence of at least two of the following risk factors of Coronary Heart Disease (CHD):

a. Family history of CHD,

b. Male >45 years or female >55 years (but not on estrogen replacement therapy),

c. Smoking,

d. Hypertension,

e. Serum high density lipoprotein (HDL) <35 mg/dl,

f. Obesity (Body Mass Index >27).

EXCLUSION CRITERIA

Patients with history of recent (within past 6 months)

1. Serious cardiovascular diseases (including stroke) or
2. Any endocrine disorder (esp thyroid) or
3. Concomitant serious disorder of the liver, kidney, heart, lung, muscle etc
4. Receiving any drug treatment
5. Patients with secondary hyperlipidemia (except diabetes mellitus)
6. Pregnant and lactating women.
7. Porphyria or allergic disorder

SCHEDULE OF INVESTIGATIONS

The patients were evaluated for physical and cardiovascular parameters. All routine biochemical investigations including lipid profile were performed before starting the intervention as well as after completion of each treatment round i.e at the end of 4 weeks, 8 weeks, 12 weeks & 16 weeks. All signs and symptoms previously identified or present and new signs and symptoms or adverse effects, if any, were assessed during as well as after completion of the treatment. Blood pressure and Body Mass Index (BMI)were monitored only for safety purpose and to assess any deterioration of patient condition (Baral et al, 2006).

LIPID PROFILE MEASUREMENT

For lipid profile, venous blood samples of 05 ml were collected in sterilized bulbs after at least 12 hours of overnight fasting. The samples were centrifuged at 3,000 rpm for 10 minutes and serum was separated from formed cellular elements. Samples were analyzed and values of TC and triglycerides were estimated, while HDL was calculated using the HDL kit and LDL and Very Low Density Lipoprotein (VLDL) were calculated by using Friedewald's formula.

STUDY DESIGN

Study type :This was prospective randomized open label study.

Study site : Medicine O.P.D. NIMS Hospital Jaipur.

Study period : November 2011 to April 2013.

DRUGS/ REGIMENS

GROUP A :- *Amla Tablet* of (500 mg) (dried *Amla* fruit juice powder) was procured from Nirogam India Pvt.Ltd. Faribad.

Group B :- Atorvastatin of 10 mg: brand name Azerva (10 mg) was procured from Intas pharma, East sikkam.

A coded envelope containing either 56 tablet of Amla (500 mg) to be administered 2 tablet once daily at night for 4 weeks or 28 tablet of Atorvastatin (10 mg) to be administered once daily at night for 4 weeks. Patients after screening **,**those enrolled in the study were explained in detail study pattern in their own language & written informed consent was filled by each patient.

Baseline level of lipid and baseline investigation like CBC, LFT, RFT & LUNG PFT were recorded and repeated at the end of 4 weeks, 8 weeks,12 weeks and 16 weeks. Fourth visit i,e at the end of 16 weeks, lipid profile will be repeated i.e total cholesterol (TC), triglycerides (TG), HDL, LDL and VLDL were measured along with BP, BMI, RBS to asses general health. Final outcomes were evaluated.

ADVERSE EFFECTS

Adverse effects were monitored throughout the study and assessments followed up to two weeks post treatment. At every visit patient was asked for any adverse effect Like muscle pain,etc & if any it was recorded .

STATISTICAL ANALYSIS

For statistical analysis, other than arithmetic mean based curve for the four week of follow up for all the five parameters (total cholesterol, triglycerides, HDL, LDL and VLDL). ANOVA assumes normality of the data distribution as well as equality of means of distribution which is not seen in our case. Based on Normquant, and PPCC (probability plot correlation co-efficient), the data has not been proven normal in its distribution.

As Dunnet's multiple comparison test or stepdown test requires equal sample size (our samples are unequal) and Bonferronin test is weak due to over-conservative α – Tukey's test (studentized version, $p<0.05$) was preferred for analysis in this study. In biological samples we have kurtosis in the plotted distribution curve with a heavy tail on the either side. That's why the most commonly used t-test/ ANOVA/ F test were not opted for this study (An Introduction to Medical statistics, 2000).

RESULTS

A total of 250 patients were screened out and finally 93 patients were selected for the study as per inclusion and exclusion criteria. Of these, 45 patients (Group-A) were given two tablet of *Amla* (500 mg) daily at night for 16 weeks, while the other 48 patients (Group-B) received one tablet of Atorvastatin (10 mg) daily at night for 16 weeks. All data of all 93 patients of group A & B were compiled separately at end of study & result were as follows.

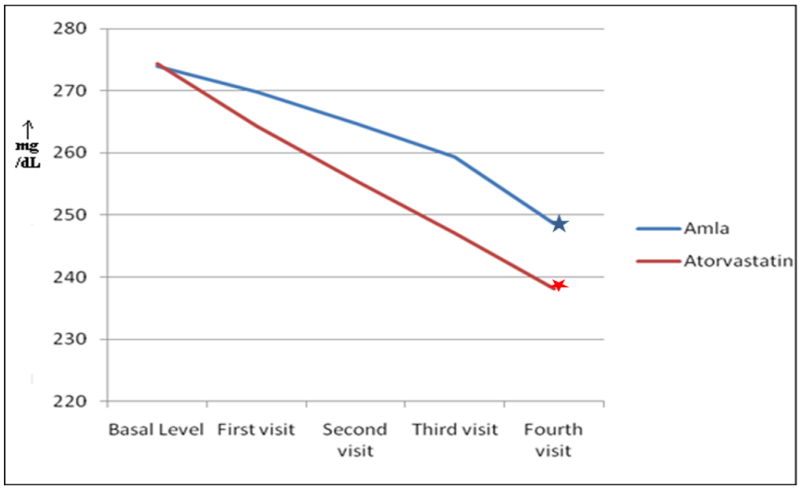

Figure 1 Variation of total cholesterol level (mg/ dL) * $P < 0.05$

THE EFFECT OF AMLA & ATORVASTATIN ON TOTAL CHOLESTEROL

Atorvastatin provides sustained improvement by lowering cholesterol level. Amla & Atorvastatin showed significant decrease in TC at the end of 16 weeks as shown in Figure 1.

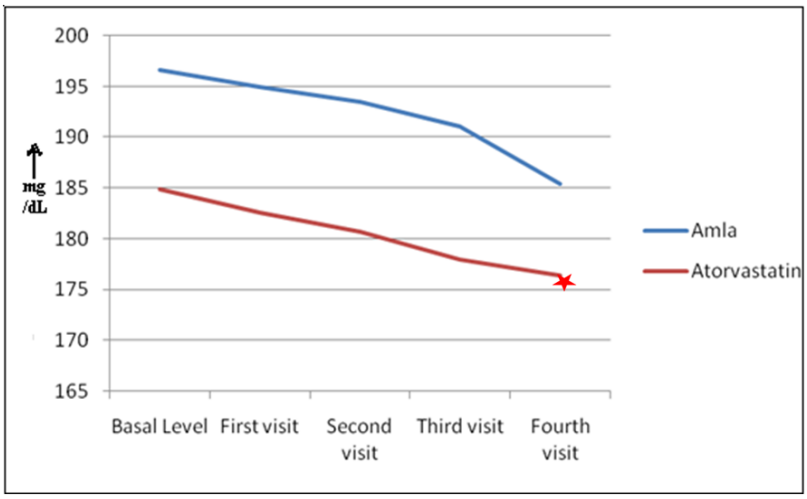

Figure 2 Variation of total triglyceride level (mg/ dL) * P < 0.05

THE EFFECT OF AMLA & ATORVASTATIN ON TRIGLYCERIDES: The decrease in triglyceride level is less rapid (graph sloping slower) even with atorvastatin but amla maintains the same dual phase in decrease i.e. intensive betterment on continued therapy and lesser effect than atorvastatin. But the difference of basal level in amla group can be also a reason, adjusting which, amla might have been more beneficial than atorvastatin. This fact requires separate study by adjusting the effects at different basal levels. Atorvastatin showed significant decrease in TC at the end of 16 wks. as shown in Figure 2.

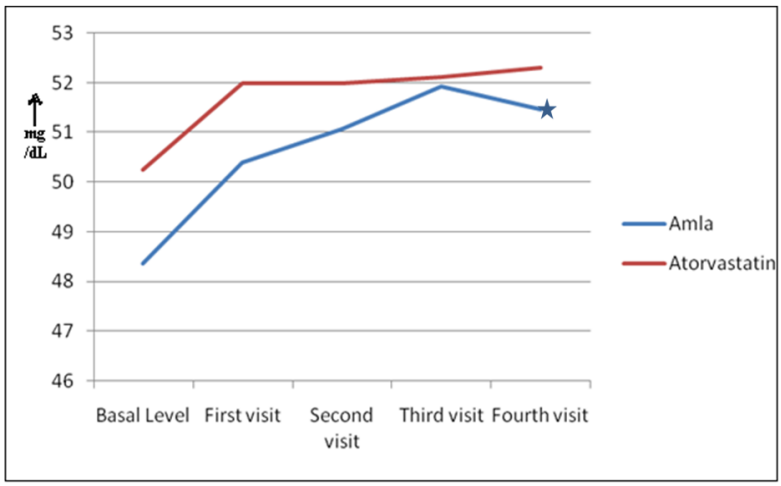

Figure 3 Variation of total HDL level (mg/ dL) * P < 0.05

THE EFFECT OF AMLA & ATORVASTATIN ON HDL LEVEL

Despite difference in basal levels, improvement in HDL level with amla is as good as atorvastatin though the height of achievement might not be sustained as shown with the terminal portion of the graph showing amla effect. Amla showed significant increase in HDL at the end of 16 wks. as shown in figure 3.

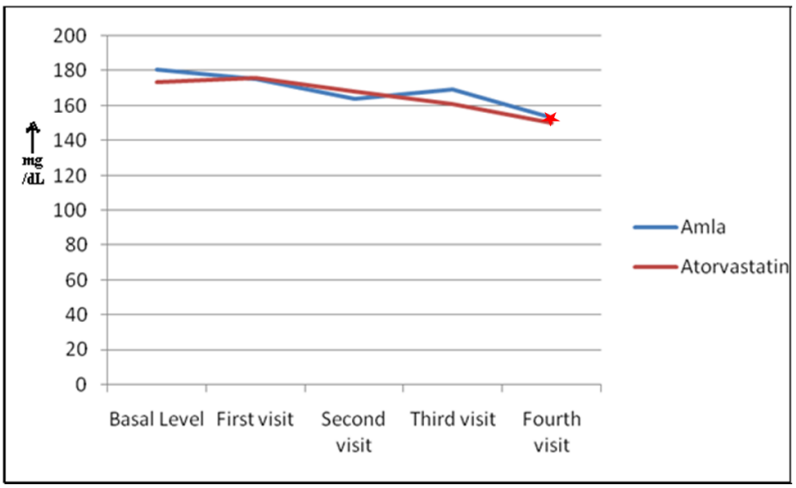

Figure 4 Variation of LDL level (mg/ dL) * P < 0.05

THE EFFECT OF AMLA & ATORVASTATIN ON LDL: Amla has no significant effect on L.D.L levels. Atorvastatin showed significant decrease in LDL at the end of 16 wks. as shown in Figure 4.

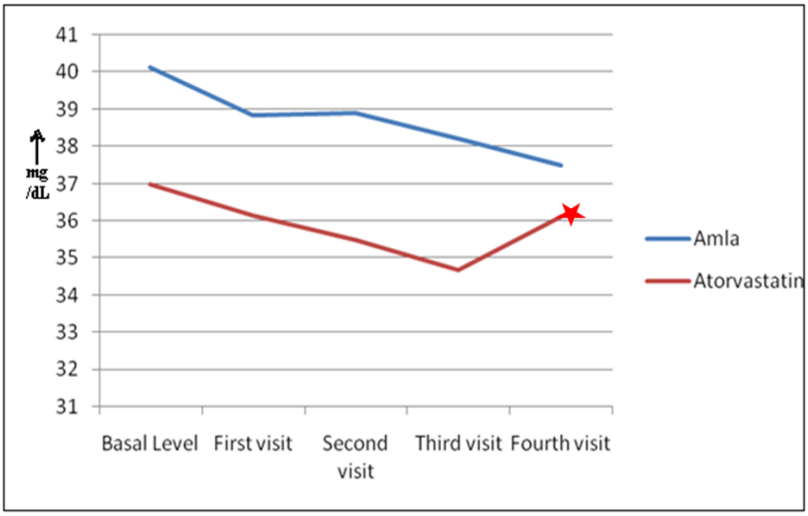

Figure 5 Variation of VLDL level (mg/ dL) * P < 0.05

THE EFFECT OF AMLA & ATORVASTATIN ON VLDL LEVEL

The effect of amla on VLDL level decrease is sustained and not reserved at any stage of treatment. But the benefit is not that sustained with Atorvastatin as shown in the terminal portion of atorastatin action graph Atorvastatin showed significant decrease in VLDL at the end of 16 wks. as shown in figure 5.

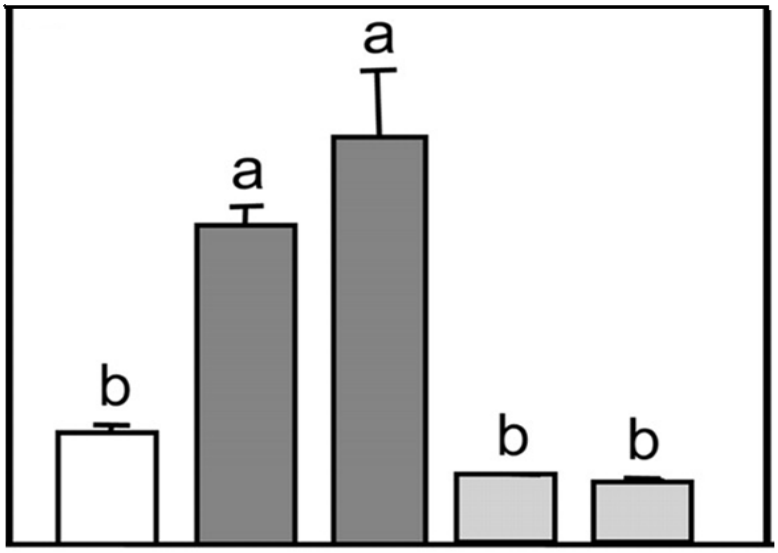

Figure 6 Better response elicited on Tukey's test (bar 1= total cholesterol; bar 2 = triglycerides; bar 3 = HDL; bar 4 = LDL; bar 5 = VLDL)

THE EFFECT OF AMLA & ATORVASTATIN ON:- COMPARATIVE BETEERMENT ON ALL LIPID LEVELS

Results of comparative betterment are shown in figure 6 given below (here "a" indicates better response by Amla and "b" is better response by Atorvastatin). Thus (bar 1= total cholesterol; bar 2 = triglycerides; bar 3 = HDL; bar 4 = LDL; bar 5 = VLDL in figure 6) we see that on the two counts of reduction of triglycerides and increase in HDL, amla is much better while on remaining three counts of total cholesterol lowering, LDL lowering and VLDL lowering atorvastatin is slightly better.

But here the rebound rise in VLDL level after atorvastatin (figure 6, bar 5) has been automatically excluded as accidental outlier effect on the mean value – otherwise atorvastatin effect was speedier than amla which resulted in better grading of atorvastatin in Tukey's test.

The tabulated form of the mean values of the two groups (amla and atorvastatin) on various parameters are given in table 1-2.

Table 1 **: Effect of amla on various hepatic parameters (mg/ dL)**

Amla (Group A)	TC	TG	HDL	LDL	VLDL
Basal level	273.9333	196.6	48.36	180.9067	39.32
Week 1	269.8667	194.9333	50.4	175.64	38.98666
Week 2	264.6667	193.4667	51.06667	164	38.69334
Week 3	259.4	191.0667	51.93333	169.4267	38.21334
Week 4	248.6	185.4667	51.46667	153.0733	37.09334

Table 2 **: Effect of atorvastatin on various hepatic parameters (mg/ dL)**

Atorvastatin (Group B)	TC	TG	HDL	LDL	VLDL
Basal level	274.3125	184.9375	50.25	173.1563	36.9875
Week 1	264.3125	182.625	52	175.7625	36.525
Week 2	255.4375	180.75	52	168.3	36.15
Week 3	247.0625	178	52.125	160.9438	35.6
Week 4	238.125	174.375	52.3125	150.3063	34.875

In our study, *Amla* showed a reduction of TC, LDL and TG and an increase in HDL. It is also interesting to note that both *Amla* and Atorvastatin produced similar changes in the lipid profile but to a varying degree.

There was no significant change noted in blood pressure and body mass index during the therapy, neither there was any problem of attrition for any reason whatsoever.

Adverse effects :- No significant adverse event was observed in both the groups that necessitated any change in regimen. Even after 2 weeks of stopping the drug treatment in both the group no any adverse effect was reported by the patients. From group B i.e those who were taking Atorvastatin 10 mg daily, 4 (four) patients reported mild muscle pain. Liver function tests were repeated at the end of study i.e at the end of 16 weeks.

From Group B, 8 patients showed mild raised Aspatate aminotransferase & Alanine Aminotransferase levels at the end of 16 weeks.

DISCUSSION

Hyperlipidemia, an abnormal elevation of plasma lipids, is associated with a higher rate of cardiovascular, cerebrovascular, and peripheral vessel involvement, and hence increased morbidity and mortality. The Multiple Risk Intervention Trial (MRFIT) reported that there is a curvilinear relationship between TC and CAD. The study showed that the CAD-related mortality rate escalated more dramatically with cholesterol levels exceeding 280 mg/ml .[11] In the primary prevention trials, decrements in total cholesterol regardless of the therapeutic modality were associated with significantly decreased CAD events .[12] In the Framingham study, it was reported that low level of HDL cholesterol is an independent risk factor for CAD .[13]

In the secondary prevention trials it has been reported that in patients with CAD having TC 250 mg/ml, therapy with Atorvastatin produced reduction of TC Mean percent reductions for TC, LDL-C and TG were significant 18.5% , 22% & 19 % respectively. No significant changes were observed in HDL-C .[14] Numerous other studies like Dwivedi et al, 2009[14], Yokozawa et al, 2007[15], amla has favorable effect on each parameter of lipid profile and matter is just debated over how and how much.

Careful monitoring of LFTs to avoid atorvastatin-associated hepatotoxicity.[17]In our study only 8 paients out of 48 who where taking atorvastatin (Group B) showed mild increase in Liver enzymes at the end of 16 wks;where symptomless & no any treatment was given.While patients on Amla (Group A) do not reported any any adverse effect. Gopa et al, 2012 showed that amla is better effective on TC and LDL while simvastatin was shown better on HDL, TG and VLDL.[18] However, the discrepancy in the lipid lowering capacity of statin in our study and that reported in the literature could be attributed to the shorter duration of treatment as well as smaller sample size employed by us.

CONCLUSION

In our study of amla compared with atorvastatin, amla has been shown better on TG and HDL while atorvastatin has shown better effect on TC, LDL and VLDL. There was no adverse drug event in either group, which could force a change or stoppage of regime or attrition of sampled population. Secondary parameters of physical well being like blood pressure or body mass index showed no alarming change .

LIST OF ABBREVIATIONS

- BMI – Body Mass Index
- BP – Blood Pressure
- HDL – High Density Lipoprotein
- IDL – Intermediate Density Lipoprotein,
- LDL – Low Density Lipoprotein,
- PUFA – Polyunsaturated Fatty Acid
- RBS – Random Blood Sugar
- TC – Total Cholesterol
- TG – Triglycerides

VLDL – Very Low Density Lipoprotein

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Conflicts of Interest: The authors declare that they have no competing interests.

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