International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.5, No.1, pp 254-263, Jan-Mar 2013

Single Versus Combined Atorvastatin And Lasuna: Investigating Changes In Laboratory Parameters And Hydrogen Sulfide Post Treatment

Forum S. Shah[1]*, Gaurang B. Shah[1]

Department of Pharmacology, K.B.I.P.E.R., Kadi Sarva Vishwavidyalaya, Gandhinagar, Gujarat, India.

Corres.Author: forumshah127@gmail.com

Abstract: The main challenge with herbal medicines is identifying which part of the plant is useful and again, which are the constituents beneficial in medical ailments. Animal studies conducted suggest a crucial role of hydrogen sulfide released from metabolism of active constituents of garlic. In the present study, we studied a well marketed over the counter formulation of Garlic, i.e., Lasuna capsules from Himalaya Herbal Healthcare, 250 mg Lasuna capsules were given twice a day with patients suffering from mild Hyperlipidemia against Atorvastatin 10 mg (Mankind Company) in patients suffering from moderate Hyperlipidemia and where the physician felt necessary to start Statin (i.e., Atorvastatin 10 mg) along with a combined treatment group including both the listed medicines. Three months data of patients was recorded at baseline and thereafter in each of the two follow up visits scheduled at 6 weeks (visit 2) after baseline and another 6 weeks (visit 3) interval from visit 2. Total Cholesterol, LDL, HDL, VLDL, Triglycerides and LDL/HDL ratio and hydrogen sulfide levels were measured at all three visits whereas Homocysteine, the independent risk factor and high sensitivity-C reactive protein were measured at baseline and later, only if the baseline visit levels where recorded as higher than normal. It was observed that there were no significant changes in any of the parameters with Lasuna treatment alone except for changes in Total Cholesterol, HDL and Triglycerides. However, the combined treatment showed significant changes before and after treatment. Also, there was an increase in the levels of plasma hydrogen sulfide levels on treatment with Lasuna. This may suggest the probable mechanism of Lasuna, a form of garlic powder through gaseous release which supports one of the many hypotheses postulated for cardio-protective effects of hydrogen sulfide. Our study shows that the use of Lasuna as an herbal mmay tend to act as a supportive therapy with Statins in mild to moderate cases and one may also be able to prevent use of higher doses of Statins, if combined therapy is continued. But, the latter should be preferably confirmed with a larger sample size.

Keywords: Lasuna, Atorvastatin, Hyperlipidemia, Hydrogen sulfide, Himalaya Herbal Healthcare, Homocysteine.

INTRODUCTION

Cardiovascular disease is a complex and multi-factorial disease and is characterized by multiple factors. Epidemiologic studies have identified these as elevated serum lipids (cholesterol and triglycerides), increased plasma fibrinogen and coagulation factors, increased platelet activation, alterations in glucose metabolism, and smoking (1). The oxidative modification of LDL by reactive oxygen species (ROS) is also now considered an important mechanism in the development of atherosclerosis, as is the pathogenesis of hypertension (2,3).

Statin therapy lowers the risk of cardiovascular events by reducing plasma cholesterol levels, and practice guidelines for patients with known cardiovascular disease emphasize the importance of reaching target goals for low-density lipoprotein (LDL) cholesterol (4). However, a study by a Researcher has shown that Statins therapy results in a greater clinical benefit when levels of the inflammatory biomarker C-reactive protein (CRP)

are elevated (5, 6) and that Statins lower CRP levels in a manner largely independent of LDL cholesterol levels (6, 7). A study conducted in 3745 patients with acute coronary syndromes concluded that patients who have low CRP levels after Statins therapy have better clinical outcomes than those with higher CRP levels, regardless of the resultant level of LDL cholesterol. Also, it concluded that strategies to lower cardiovascular risk with Statins should include monitoring CRP as well as cholesterol (8). Another study in 502 patients with angiographically documented coronary disease concluded that for patients with coronary artery disease, the reduced rate of progression of atherosclerosis associated with intensive Statin treatment, as compared with moderate Statin treatment, is significantly related to greater reductions in the levels of both atherogenic lipoproteins and CRP (9). Two recent trials demonstrated that intensive lipid-lowering therapy with statins improved clinical outcomes (10) and reduced the progression of atherosclerosis (11). In both recent comparisons, at the conclusion of the trials, CRP levels were 30 to 40 percent lower after intensive Statin therapy than after moderate treatment (12). Large observational studies have established a strong relationship between CRP levels and the morbidity and mortality associated with coronary disease (13, 14). Evidence of a dual mechanism of benefit for Statins — lipid lowering and a reduction in inflammation — has important implications for current and future treatment of atherosclerosis (9). Statin therapy seems to be effective in the primary prevention of coronary events among patients with elevated CRP levels, even when lipid levels are relatively low (15).

The lipid-lowering effects of garlic (*Allium sativum*) have been demonstrated in animal experiments (16), and garlic's efficacy in lowering cholesterol levels in humans has been the subject of randomized clinical trials. A meta-analysis of the effect of garlic on total serum cholesterol level (17) found a significant reduction in total cholesterol levels of 0.59 mmol/L (22.8 mg/dL), which was equivalent to a decrease of approximately 9% compared with placebo. This figure was based on four statistically homogeneous trials that included 324 participants. A subsequent meta-analysis (18) assessing 952 persons from 16 trials reached a similar conclusion, reporting a reduction of 0.77 mmol/L (29.7 mg/dL); this represented a 12% average decrease in total cholesterol level. When these authors later reanalyzed the data, including the results of their own trial of 115 persons (19), the overall reduction in total cholesterol level had diminished to 0.65 mmol/L (25.1 mg/dL); however, it remained significantly greater than that seen with placebo. Direct measurements of enzyme activity have indicated that garlic and various constituents inhibit human squalene monooxygenase and HMG-CoA reductase, enzymes involved in cholesterol biosynthesis (20, 22). This inhibition of HMG-CoA reductase by garlic has also been confirmed in a recent study (23). It has also been shown that the more water-soluble compounds like *S*-allylcysteine (SAC) present in aged garlic extract are less cytotoxic and more efficient in inhibiting cholesterol biosynthesis than the lipid-soluble sulfur compounds such as diallyl sulfide (DAS) (21). In-vitro studies strongly suggest that garlic has the ability to reduce parameters associated with cardiovascular disease. This has prompted a number of clinical studies, some of which give conflicting messages (24). However, most of these studies focused on alterations in lipid profile or CRP using placebo against garlic. There are rarely any studies to showcase the comparison of allopathy versus herbal therapy in mild to moderate Hyperlipidemia and that too, a well marketed garlic formulation from Himalaya Herbal Healthcare. The present study focused on whether Lasuna formulation against Atorvastatin 10 mg (the minimal dose of Statin) can produce a significant efficacy in lipid profile, hs-CRP, Homocysteine and hydrogen sulfide after three months of treatment. Also, most of the studies are carried out evaluating C-reactive protein. Recently high sensitivity C-reactive protein is considered a better inflammatory marker compared to CRP alone. Again, role of Statins (if any) in release of hydrogen sulfide lack any evidence. The present study aimed to evaluate whether there is any enhanced release of hydrogen sulfide post Lasuna and atorvastatin treatments, compared to basal levels, esp. when garlic's constituents have sufficient evidence of gas release in in-vitro and in-vivo studies i.e., shown production and release of hydrogen sulfide, the popular third gaseous transmitter with possible role in cardio protective mechanism after Nitric oxide and Carbon monoxide. Garlic apart from its role in retardation of lipid profiles and other markers, here may prove its worth through another novel mechanism via hydrogen sulfide, the rarely studied effect in a clinical setting.

MATERIALS AND METHODS

The present study was carried out in a screened population with pre-defined inclusion exclusion criteria and Independent Ethics Committee Approval from Jagruti Independent Ethics

Committee (JIEC, registered under U.S Department of Health and Human Services, USDHHS) to enroll hyperlipidemic patients. Additionally, as a part of the formal Hospital procedure, permission/approval was also obtained from Jivraj Mehta Hospital Executive Committee that sits annually to review and approve the Research Projects undertaken at Research & Development Department, Jivraj Mehta Hospital.

Patients with age between above or equal to 18 and less than or equal to 65 were included. Table 1 shows different groups involved in the study along with the baseline demography of patients. The completed Health Check up files in CHC department was scrutinized for higher than normal values of Total Cholesterol (more than 210 mg/dL) and/or Low Density Lipoprotein (LDL More than 130 mg/dL) along with age and other medical history. Those patients witnessing any of the lipid parameters (either Total Cholesterol or LDL) in higher than normal laboratory range (Normal range: ≥ 200 mg/dL Total Cholesterol and ≥ 130 mg/dL Low Density Lipoprotein, as per the Hospital Laboratory Reference Ranges) were considered eligible for enrollment. Patients showing history or presence of any clinically significant Respiratory system disorders, Central nervous system disorders, Reproductive system disorders, Gastro intestinal disorders having problems in swallowing or digesting or any other major diseases were considered in exclusion criteria. Informed consent were designed in English and local language (Gujarati) for patients interaction, reading and understanding. Patients were explained about all the aspects of the study as documented in ICF in a brief manner. Patients willing to sign informed consent form after thorough understanding and giving time to ask questions were included in the study. Complete Health Check up Department (CHC), Dr. Jivraj Mehta Smarak Health Foundation, Ahmedabad was the main center for screening and enrolling patients for study. Written Permission to conduct the study was taken from the Director, Research & Development Department, Jivraj Mehta Hospital. Clinics of private practitioners, Out Patient Departments of M.D, Physicians were also included as Centers to accelerate the patient recruitment rate. Ambulatory patients coming to collect reports in a reputed Clinical Laboratory of Ahmedabad were also screened for enrollment and following the study procedures after taking consent form the Laboratory Director.

The patients were assigned to either Lasuna or Atorvastatin or combined treatment group (Lasuna 250 mg, twice a day and Lipikind 10 mg, once in a day) based on severity of Hyperlipidemia. Lasuna being an over the counter product, was started in patients with total cholesterol more than 210 mg/DL and/or LDL more than 140 mg/dL. However, Lipikind 10 mg was prescribed only and only at the clinical discretion of the Physician. As per the discussion with the physician, they looked for medical history of the patients along with significant presence of other cardiac disease risk factors like hypertension, diabetes etc. before starting Statins class of medication. Since a higher dose of Atorvastatin may mask the efficacy of Lasuna capsules (if any), minimal fixed dose of Atorvastatin i.e., 10 mg was prescribed to patients in mutual agreement with the practicing Physician taking care of patient. The different methods used to escalate patient recruitment rate included phone calls to patients, personal counseling to patients and their relatives (if present at that time) during their in-person visits, discussion with the Doctors and convincing them of the study aspects to play a supporting role in recruitment, distributing study cards to the practicing physicians and putting a study notice, both in English and locale Gujarati language in Pathology laboratory, Complete Health Check Up Premises and in Research & Development Department of the Hospital to create awareness about the study.

The measurement of Hydrogen Sulfide was carried out using Double beam UV Spectrophotometer, Shimadzu Model, 1700 at FRIGE Center, Ahmedabad using the method demonstrated in a study published by Utpal Sen et al. Standard curve of Hydrogen sulfide was measured in nanogram range and its reproducibility was checked inter-day as well as intra-day. The chemicals required for processing and analysis were procured from Purvi Chemicals, Ahmedabad. The blood samples were collected from subjects by the Hospital phlebotomist or by home visits of phlebotomist, stored and analyzed. The laboratory parameters were measured at baseline and later at follow-up visits to evaluate the clinical efficacy of investigational product. Total cholesterol, LDL, HDL, Triglycerides, VLDL, LDL/HDL ratio, and hs-CRP (only if required) were measured at each of the three visits using the facility of in-house Laboratory at Jivraj Mehta Hospital.

The demography details, height, weight, BMI and WHR were measured in each visit along with blood pressure using the digital B.P instrument. The systolic and diastolic BP measurement was undertaken thrice and an average of the three reading was taken as documented reading.

RESULTS AND DISCUSSION

Table 1: Demography data & Characteristics of study groups

Demography Characteristics	Group A (N = 45)	Group B (N = 33)	Group C (N = 26)	Statistical Significance
Male	20 (60.61 %)	13 (39.39 %)	7 (26.92 %)	-
Female	13 (39.39 %)	20 (60.61 %)	19 (73.08 %)	-
Age	49.33 ± 10.11	51.48 ± 8.06	51.65 ± 7.71	NS
Body Weight	70.05 ± 13.99	64.03 ± 9.04	64.68 ± 9.92	NS
Body Mass Index	27.24 ± 3.88	24.37 ± 3.70	24.94 ± 3.88	0.0079
Waist Hip Ratio	0.94 ± 0.04	0.95 ± 0.03	0.94 ± 0.03	NS
Systolic BP	122 ± 7.2	117.13 ± 8.34	117.88 ± 9.07	NS
Diastolic BP	82 ± 6.92	77.80 ± 6.55	76.04 ± 9.43	NS

Where, Group A = Lasuna, Group B = Atorvastatin, Group C = Atorvastatin + Lasuna, NS – Not Significant

TABLE 2: Visit wise Comparison of Test Parameters - Lasuna

Sr No.	Parameter	Treatment period	P value	Significant/Non-significant
1	Total Cholesterol	V1 - V2	0.1142	NS
		V1 – V3	**0.0144**	S
2	LDL	V1 - V2	0.4561	NS
		V1 – V3	0.5465	NS
3	HDL	V1 - V2	**0.0289**	S
		V1 – V3	**0.0018**	VS
4	Triglycerides	V1 - V2	**0.0390**	S
		V1 – V3	0.2018	NS
5	VLDL	V1 - V2	0.1699	NS
		V1 – V3	0.5885	NS
6	LDL/HDL	V1 - V2	0.1706	NS
		V1 – V3	0.1145	NS
7	Hydrogen sulfide	V1 – V2	0.4550	NS
		V1 – V3	0.6779	NS
8	Homocysteine	V1 – V3	0.5055	NS
9	hs-CRP (n-26,12)	V1 – V2	0.9605	NS

Where, ES = Extremely Significant, VS = Very Significant, S = Significant, NS = Significant
V1 - Visit 1, V2 - Visit 2, V3 - Visit 3

Total of sixteen subjects (twelve from Lasuna group, four from Statins group) did not complete the study because of personal reasons (n = 11) or due to adverse events (n = 5). Five of these subjects did contribute to statistical analysis as they provided the data till 1-mo assessment. Demography and other characteristics of study population are listed in Table 1. Mainly, no significant differences were observed between populations of the three study groups with respect to demographic characteristics. The male and female subjects in Lasuna group accounted for 20 and 13 respectively (excluding those who left the study for personal reasons), reversely so in Atorvastatin group whereas the combined treatment group had 7 male and 19 female subjects. The average age in years of the subjects was 49.33 yrs, 51.48 yrs and 51.65 yrs which was statistically not significant. Also, the average body weight of the population was 70.05 kg, 64.03 kg and 64.68 kg respectively in Lasuna, atorvastatin and Lasuna with atorvastatin treatment groups. The Mean body mass index was 27.24, 24.37 and 24.94 while the Waist to Hip ratio was 0.94, 0.95 and 0.94 respectively for Lasuna, atorvastatin and Lasuna with atorvastatin treatment groups. The difference between means of three groups was found to be not significant (NS) for average body weight and WHR but found very significant (p value - 0.0079) for BMI. The systolic and diastolic blood pressure was also statistically insignificant and hence, the sample size is considered to belong to the same population. The adverse events observed were mainly acidity. There were no any complaints of foul smell due to the Lasuna capsules.

The data was collected and analyzed using Graph pad Instat software, Version 3.10. The p value less than or equal to 0.05 was considered significant and the confidence interval was taken as 95%.

Table 2, 3 and 4 shows visit-wise paired t test comparison for Lasuna, Statin & Statin + Lasuna treatments respectively. All of the tables show significant p values in bold. Here, we refer to treatment with Atorvastatin (10 mg) wherever Statins is mentioned. Baseline data (visit 1) of each of the groups was compared with visit 2 (1.5 months) and visit 3 (3 months) respectively, as indicated in treatment period column of Tables 2, 3 and 4. As shown in Table 2, most of the p values are not significant except visit 1 versus visit 3 for total cholesterol (p value – 0.0144) and both visit 1 versus visit 2 (p value – 0.0289) and visit 3 (p value – 0.0018) respectively for HDL. Similarly, the triglycerides also show a statistically significant difference between visit 1 and visit 2 (p value – 0.0390). The hs-CRP data was not considered for paired t test comparison between visit 1 and visit 3 of lasuna group owing to very few values in visit 3 (n = 2). A single-blind, placebo controlled study, lipid profiles of 150 hyperlipidemic patients in cardiology outpatient department showed similar supporting results for garlic enteric-coated tablet concluding that garlic tablet has a significant favorable effect on cholesterol, LDL cholesterol and HDL cholesterol and that garlic may play an important role in therapy of hypercholesterolemia.(25). Our study also has reported a favorable effect for total cholesterol and HDL. Similarly, in animal experiments, garlic extracts have been shown to lower plasma lipid and cholesterol in rats (26, 27), and (28), rabbits (29), chickens (30), and swine (31). Moreover, a number of intervention studies have similarly shown that garlic significantly reduced plasma lipids, especially total cholesterol and Low Density Lipoprotein (LDL) cholesterol in humans (32, 33), and (34).

As show in Table 3, the two visit wise comparisons for Atorvastatin (10 mg) shows significant p values for each of the test parameters i.e., Total Cholesterol, LDL, HDL, Triglycerides, VLDL, LDL/HDL ratio and hs-CRP. Hydrogen sulfide comparison resulted in a significant difference (p value – 0.0121) between visit 1 and visit 3. This once again confirms the efficacy of Statins not only in altering the lipid profile but also in affecting hs-CRP levels. However, the production of hydrogen sulfide after treatment with Statins was on a lower side and hence the role of Statins owing to hydrogen sulfide is probably very nil. A study on Statins reported a linear relationship between the levels of LDL cholesterol achieved after Statin therapy and the risk of recurrent myocardial infarction or death from coronary causes (8). Also, Statins being a well marketed drug, there is no doubt on its efficacy. Table 3 shows a substantial effect on hs-CRP, which is evolved to show a significant pathophysiology in progression of atherosclerosis. An analysis supporting our study results for hs-CRP show that the reduction in CRP levels play an independent role in the beneficial effects of Statins on the progression of coronary atherosclerosis Thus evidence of a dual mechanism of benefit for statins — lipid lowering and a reduction in inflammation — has important implications for current and future treatment of atherosclerosis (9). However, our study measured high sensitive – CRP compared to CRP and also, the dose of Statins used in former study was a little higher.

Again, Table 4 shows that the means of differences between visits is significant for all parameters and all visits except for hydrogen sulfide comparison between visit 1 and visit 2 which is not significant (p value – 0.3701). However, the percentage effect of lasuna may be very less as alone atorvastatin (10 mg) also shows equally significant results as in Table 3 except a few parameters. Alternatively, this may also mean that lasuna when given with statins, may act as a supportive agent in reducing lipid profile, keeping a check over Homocysteine and hs-CRP.

Unpaired t test results are described in Table 5, where comparison between differences in means was carried out between parameters of each of the groups. The visit wise difference between data was carried out i.e., the values of baseline data were subtracted from final visit 3 and the difference was compared using unpaired t test in Graph pad Instat.

Only Total cholesterol and LDL show significant p values for all the three groups comparison whereas in HDL and LDL/HDL ratio, Lasuna versus Statins and Lasuna versus combined treatment indicates significant difference. The hydrogen sulfide values do now show any major differences between groups. However, if we see the column chart for hydrogen sulfide across all visits (figure 1), it shows an increase in hydrogen sulfide levels in each of the subsequent visits for Lasuna group as well as the combined treatment group while, the Statin group alone shows a decreasing trend with each consecutive visit. Thus, one may say that there is a rise in the levels of hydrogen sulfide after treatment with Lasuna since Statins alone does not show any significant increase, the enhanced levels of gaseous transmitter in the combined treatment group is attributed more or

less to intake of Lasuna by patients. Also, it is beneficial to use an herbal medicine with Statins as latter even though have proven to be highly effective in treating hypercholesteremia; it has also shown to have adverse effects such as impotence (35).

TABLE 3: Visit wise Comparison of Test Parameters - Atorvastatin

Sr No.	Test Parameters	Treatment period	P value	Significant/Non-significant
1	Total Cholesterol	V1 - V2	**< 0.0001**	ES
		V1 – V3	**< 0.0001**	ES
2	LDL	V1 - V2	**< 0.0001**	ES
		V1 – V3	**< 0.0001**	ES
3	HDL	V1 - V2	**0.0004**	ES
		V1 – V3	**0.0013**	VS
4	Triglycerides	V1 - V2	**< 0.0001**	ES
		V1 – V3	**< 0.0001**	ES
5	VLDL	V1 - V2	**< 0.0001**	ES
		V1 – V3	**0.0104**	S
6	LDL/HDL	V1 - V2	**<0.0001**	ES
		V1 – V3	**<0.0001**	ES
7	H2S	V1 - V2	0.0590	NS
		V1 – V3	**0.0121**	S
8	Homocysteine	V1 – V3	0.3570	VS
9	Hs-CRP	V1 - V2	**<0.0001**	ES
	Hs-CRP	V1 – V3	**0.0001**	ES

Where, ES = Extremely Significant, VS = Very Significant, S = Significant, NS = Significant
V1 - Visit 1, V2 - Visit 2, V3 - Visit 3

TABLE 4: Visit wise Comparison of Test Parameters – Statins + Lasuna

Sr No.	Parameter	Treatment period	P value	Significant/Non-significant
1	Total Cholesterol	V1 - V2	**< 0.0001**	ES
		V1 – V3	**< 0.0001**	ES
2	LDL	V1 - V2	**< 0.0001**	ES
		V1 – V3	**< 0.0001**	ES
3	HDL	V1 - V2	**0.0055**	ES
		V1 – V3	**0.2034**	NS
4	Triglycerides	V1 - V2	**0.0016**	VS
		V1 – V3	**0.0016**	VS
5	VLDL	V1 - V2	**0.0016**	VS
		V1 – V3	**0.0016**	VS
6	LDL/HDL	V1 - V2	**< 0.0001**	ES
		V1 – V3	**0.0160**	S
7	H2S	V1 - V2	0.3701	NS
		V1 – V3	**0.0034**	ES
8	Homocysteine	V1 – V3	**0.0056**	VS
9	hs-CRP	V1 - V2	**<0.0001**	ES
	hs-CRP	V1 – V3	**0.0040**	VS

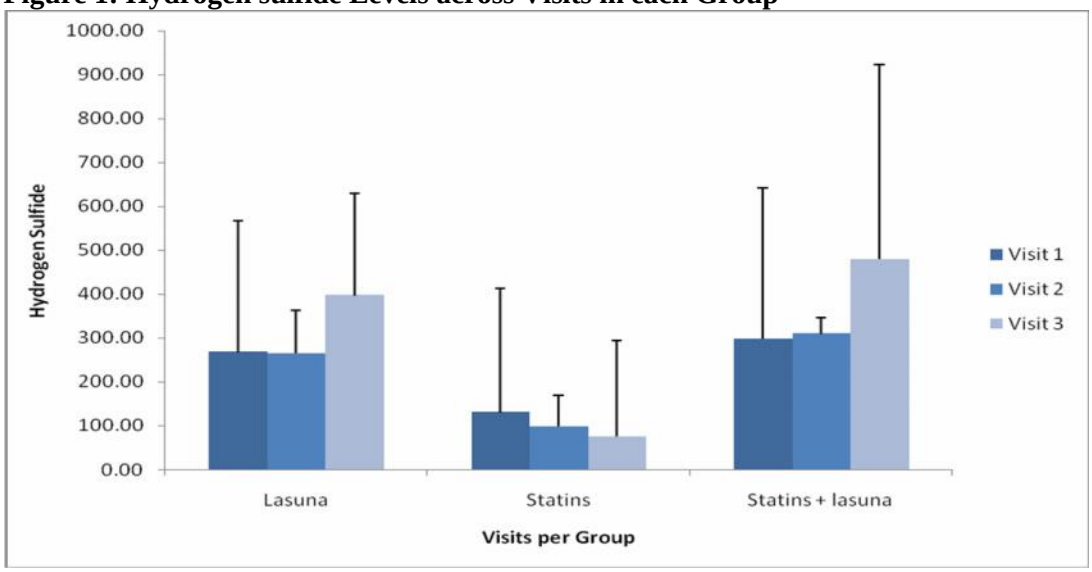
Where, ES = Extremely Significant, VS = Very Significant, S = Significant, NS = Significant
V1 - Visit 1, V2 - Visit 2, V3 - Visit 3

TABLE 5: Group wise Comparison of Test Parameters – Unpaired t test

Sr No.	Parameter	Treatment period	P value	Significant/Non -significant
1	Group A & B	Total Cholesterol	< **0.0001**	ES
	Group A & C		< **0.0001**	ES
	Group B & C		**0.0348**	S
2	Group A & B	LDL	< **0.0001**	ES
	Group A & C		< **0.0001**	VS
	Group B & C		**0.0016**	VS
3	Group A & B	HDL	**0.0015**	VS
	Group A & C		**0.0065**	VS
	Group B & C		0.6549	NS
4	Group A & B	Triglycerides	0.4260	NS
	Group A & C		0.8337	NS
	Group B & C		0.1330	NS
5	Group A & B	VLDL	0.5666	NS
	Group A & C		0.1566	NS
	Group B & C		0.1374	NS
6	Group A & B	LDL/HDL	<**0.0001**	ES
	Group A & C		**0.0024**	VS
	Group B & C		0.3897	NS
7	Group A & B	H_2S	0.7777	NS
	Group A & C		0.2627	NS
	Group B & C		0.1738	NS
8	Group A & B	Homocysteine	0.6315	NS
	Group A & C		0.9264	NS
	Group B & C		0.1688	NS
9	Group A & B	hs-CRP	-	NS
	Group A & C		-	NS
	Group B & C		0.0976	NS

Where, Group A – Lasuna, Group B – Atorvastatin, Group C – Lasuna + Atorvastatin, Where, ES = Extremely Significant, VS = Very Significant, S = Significant, NS = Significant

Figure 1: Hydrogen sulfide Levels across Visits in each Group



CONCLUSIONS:

The clinical study, very rare of its kind to establish the role of hydrogen sulfide release after garlic formulation administration here, affirms the role of Lasuna to enhance the basal levels of hydrogen sulfide post treatment to a remarkable extent (Figure 1). The evaluation now remains of third known gaseous transmitter's role in the proposed cardio-protective effect or reduction in lipid levels or both. Also, though there are few studies showing the role of garlic by comparison against Statins, this clinical study investigated the role of Lasuna formulation (Courtesy: Himalaya Herbal Healthcare, Dr. Patki) against a fixed dose of Atorvastatin (10 mg) and derived that Lasuna may evolve as a sole agent in patients with borderline Hyperlipidemia and further so, patients advised diet control and exercise to prevent subsequent progression are likely to benefit in the starting scenario of emergence of disease. But, diet control and exercise along with use of Lasuna needs to be investigated as a separate study. However, further studies in larger diseased population probably with escalation in Lasuna dose should be carried out to confirm these findings. Escalation of dose may be studied without much of the adverse effects, as at the prescribed dose of Lasuna i.e., 250 mg capsules, twice day, no any severe adverse events have been reported that resulted in discontinuation of Lasuna in patients. Again, based on the results we conclude that Lasuna certainly may be given as a supportive therapy with atorvastatin as there were no any significant herbal-drug interactions reported (on verbal questioning of any discomfort to patients) during treatment of three months, as evident from the follow up of the patients and verbal confirmation from them. Moreover, use of Lasuna may prevent further increase in dose of atorvastatin in patients with mild to moderate Hyperlipidemia and thus patients can be saved of the typical adverse effects of Statins, i.e., muscle fatigue, myalgia etc on prescription of a very high dose of 40 mg or 80 mg of the medicine. Though not much effect is seen on homocysteine, theoretically a decrease in levels should be reported as it is a precursor to hydrogen sulfide levels in the body so an increase in levels of the latter suggest a decrease in homocysteine, except for if Lasuna itself is the cause of gas release due to metabolism of its sulfur compounds which is the case reported in several in-vitro and animal studies. But, since fewer samples were analyzed for homocysteine to save cost, another study to confirm homocysteine levels against hydrogen sulfide shall be carried out in future.

The safety of Himalaya's Lasuna formulation is evident as no patients of those who enrolled and completed the study reported intolerable, severe side effects during the treatment. Neither was any case reported for Lipikind at the prescribed dose in the study. Mainly, Acidity in few cases and one ulceration case was reported. Ulcers were a rare occurrence (observed in 1 patient of Lasuna group) and thus whether a result of any side effect or deficiency needs to be reported further with treatment in larger population.

ACKNOWLEDGEMENTS

We are thankful to Complete Health Check Up Department, Research & Development Department & Pathology Laboratory, Jivraj Mehta Hospital, Dr. Patki, Director, Research & Development, Himalaya Herbal Health Care for providing free samples of Lasuna capsules, FRIGE (Foundation for Research In Human Genetics & Endocrinology) Center, APL Institute of Clinical Laboratory & Research Pvt. Ltd., Mugdha Joshi, Jayesh Pipariya and all the Clinicians who provided thorough support with their infrastructure, resources and enrollment of patients for the study.

REFERENCES

1. Wood D., Established and emerging cardiovascular risk factors, Am Heart J. 2001., 141, S49–57.
2. Keaney J.F., Jr. Atherosclerosis: from lesion formation to plaque activation and endothelial dysfunction, Mol Aspects Med., 2000, 21:99–166.
3. Dhawan V. and Jain S., Effect of garlic supplementation on oxidized low density lipoproteins and lipid peroxidation in patients of essential hypertension. Mol Cell Biochem., 2004, 266, 109–15.
4. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA, 2001, 285, 2486-97.
5. Ridker P. M., Rifai N., Pfeffer M.A., et al., Inflammation, pravastatin, and the risk of coronary events after myocardial infarction in patients with average cholesterol levels, Circulation, 1998, 98, 839-44.

6. Ridker P. M., Rifai N., Clearfield M., et al., Measurement of C-reactive protein for the targeting of statin therapy in the primary prevention of acute coronary events, N Engl J Med, 2001, 344, 1959-65.
7. Ridker P.M., Rifai N., Lowenthal S.P., Rapid reduction in C-reactive protein with cerivastatin among 785 patients with primary hypercholesterolemia, Circulation, 2001, 103, 1191-3.
8. Ridker P. M., Cannon C. P., Morrow D., Rifai N., Rose L. M., McCabe C. H., Pfeffer M. A. and Braunwald E., C-Reactive Protein Levels and Outcomes after Statin therapy, N Engl J Med, 2005, 352, 20-8.
9. Nissen S. E., Tuzcu E. M., Schoenhagen P., Crowe T., Sasiela W. J., Tsai J., Orazem J., Magorien R. D., Shaughnessy C. O., and Ganz P., Statin Therapy, LDL Cholesterol, C-Reactive Protein, and Coronary Artery Disease, N Engl J Med, 2005, 352, 29-38.
10. Cannon C.P., Braunwald E., McCabe C.H., et al., Intensive versus moderate lipid lowering with statins after acute coronary syndromes, N Engl J Med, 2004, 350, 1495-504.
11. Nissen S.E., Tuzcu E.M., Schoenhagen P., et al., Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial, JAMA, 2004, 291, 1071-80.
12. Topol E.J., Intensive statin therapy — a sea change in cardiovascular prevention, N Engl J Med, 2004, 350, 1562-4. (ref no 4 statin CRP pdf)
13. Ridker P.M., Rifai N., Rose L., Buring J.E. and Cook N.R., Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events, N Engl J Med, 2002, 347, 1557-65.
14. Ridker P.M., Hennekens C.H., Buring J.E. and Rifai N., C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women, N Engl J Med, 2000, 342, 836-43.
15. Ridker P.M., Rifai N., Clearfield M., et al., Measurement of C-reactive protein for the targeting of statin therapy in the primary prevention of acute coronary events, N Engl J Med, 2001, 344, 1959–1965.
16. Schulz V., H騬el R. and Tyler V.E**.,** Rational Phytotherapy: A Physician's Guide to Herbal Medicine, New York, Springer-Verlag, 1998.
17. Warshafsky S., Kamer R.S. and Sivak S.L**.,** Effect of garlic on total serum cholesterol. A meta-analysis, Ann Intern Med, 1993, 119, 599-605.
18. Silagy C. and Neil A., Garlic as a lipid lowering agenta meta-analysis, J R Coll Physicians Lond, 1994, 28, 39-45.
19. Neil H.A., Silagy C.A., Lancaster T., Hodgeman J., Vos K., Moore J.W., et al. Garlic powder in the treatment of moderate hyperlipidaemia: a controlled trial and meta-analysis, J R Coll Physicians Lond, 1996, 30, 329-34.
20. Gebhardt R., Multiple inhibitory effects of garlic extracts on cholesterol biosynthesis in hepatocytes, Lipids, 1993, 28, 613–9.
21. Yeh Y.Y. and Liu L., Cholesterol-lowering effects of garlic extracts and organosulfur compounds: human and animal studies, J Nutr., 2001, 131, 989S–93S.
22. Gupta N., and Porter T.D., Garlic and garlic derived compounds inhibit human squalene monooxygenase, J Nutr, 2001, 131, 1662–7.
23. Augusti K.T., Chackery J., Jacob J., Kuriakose S., George S. and Nair S.S., Beneficial effects of a polar fraction of garlic (Allium sativum Linn) oil in rats fed with two different high fat diets, Indian J Exp Biol, 2005, 43, 76–83.
24. Rahman K., and Lowe G. M., Garlic and cardiovascular disease: a critical review, J Nutr, 2006, 136, 3, 736S-740S.
25. Kojuri J., Vosoughi A. R. and Akrami M., Effects of anethum graveolens and garlic on lipid profile in hyperlipidemic patients, Lipids in Health and Disease, BioMed Central, 2007, 6, 1-5. (ref IJPTR folder – 1476-511).
26. Gorinstein S., Leontowicz H., Leontowicz M., Drzewiecki J., Najman K., Katrich E., Barasch D., Yamamoto K. and Trakhtenberg S., Raw and boiled garlic enhances plasma antioxidant activity and improves plasma lipid metabolism in cholesterol-fed rats, Life Sci., 2006, 78, 655-663. (ref IJPTR folder – 1476-511-ref 8).
27. Chi M.S., Effects of garlic products on lipid metabolism in cholesterol-fed rats, Proc Soc Exp Biol Med., 1982, 171, 174-178. (ref IJPTR folder – 1476-511- ref 9).
28. Saravanan G. and Prakash J., Effect of garlic (Allium sativum) on lipid peroxidation in experimental myocardial infarction in rats, J Ethnopharmacol., 2004, 94, 155-158. (ref IJPTR folder – 1476-511- ref 10).
29. Bordia A. and Verma S.K., Effect of garlic feeding on regression of experimental atherosclerosis in rabbits, Artery, 1980, 7, 428-437. (ref IJPTR folder – 1476-511- ref 11).
30. Qureshi A.A., Abuirmeileh N., Din Z.Z., Elson C.E. and Burger W.C., Inhibition of

cholesterol and fatty acid biosynthesis in liver enzymes and chicken hepatocytes by polar fractions of garlic, Lipids, 1983, 18, 343-348. (ref IJPTR folder – 1476-511-ref 12).
31. Qureshi A.A., Crenshaw T.D., Abuirmeileh N., Peterson D.M. and Elson C.E., Influence of minor plant constituents on porcine hepatic lipid metabolism: impact on serum lipid, Atherosclerosis, 1987, 64, 109-115. (ref IJPTR folder – 1476-511- ref 13).
32. Arora R.C. and Arora S., Comparative effect of clofibrate, garlic and onion on alimentary hyperlipemia, Atherosclerosis, 1981, 39, 447-452. (ref IJPTR folder – 1476-511 ref 14).
33. Jain A.K., Vargas R., Gotzkowsky S., McMahon F.G., Can garlic reduce levels of serum lipids? A controlled clinical study. Am J Med., 1993, 94, 632-635. (ref IJPTR folder – 1476-511 – ref 15).
34. Yeh Y.Y., Lin R.I., Yeh S.M. and Evens S., Garlic reduces plasma cholesterol in hypercholesterolemic men maintaining habitual diets**.** In *Food Factors for Cancer Prevention* Edited by: Ohigashi H., Osawa T. T,. Watanabe J., Toshikawa S. and Springer T., Tokyo, Japan, 1997, 226-230. (ref IJPTR folder – 1476-511 – ref 16).
35. Venkataramaiah, H. and Kulkarni K. S., Double-blind comparative clinical trial of Abana and Simvastatin in Hyperlipidaemia, Stroke, 2002. (ref – IJPTR folder – abana study).

*****