

Final report of the study
“The efficacy of a Poly Herbal Formulation (Cholest Guard)
manufactured by Good Care Pharma (P) Ltd
on Hyperlipidemia”

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Place of Study



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Introduction

In the current century our life style has been totally distorted. Physical inactivity, unhealthy diet and the harmful use of alcohol and tobacco has resulted in many fatal outcomes for health. Hyperlipidemia is one such outcome. Hyperlipidemia or hyperlipoproteinemia involves abnormally elevated levels of any or all lipids and/or lipoproteins in the blood ^[1]. In other words hyperlipidemia can also be defined as raised serum levels of cholesterol or triglyceride or both of these. According to a US based survey hyperlipidemia came second followed by hypertension in a list of 10 most common chronic conditions that were encountered by primary health care providers ^[2]. It has been proved beyond doubt that hyperlipidemia is one of the major modifiable risk factors for cardiovascular diseases ^[3]. This is because raised blood cholesterol levels lead to atherosclerosis, a condition in which the arterial walls are thickened due to deposition of fatty materials. This was proved by Anitschkow and Chaltow way back in 1913 in their experimental study on rabbits ^[4]. Hyperlipidemia is estimated to cause 18% of global cerebrovascular disease (mostly nonfatal events) and 56% of global ischaemic heart disease which amounts to about 4.4 million deaths (7.9% of total) and 40.4 million disease adjusted life years or DALYs (2.8% of total) ^[5]. A landmark study that helped establish that therapeutic interventions to lower cholesterol levels result in reduced risk of cardiovascular morbidity or mortality was the Lipid Research Clinics Coronary Primary Prevention Trial which was published in two parts ^[6,7]. This is why doctors pay considerable focus in diagnosing and treating hyperlipidemia in order to prevent cardiovascular events. Statins are the preferred class of drugs to lower elevated low density lipoprotein cholesterol augmented by ezetimibe, fibrates, niacin and dietary supplements. But there are cases where lipid goals are not met in spite of maximal statin therapy. There are also situations where statins are contraindicated or not tolerated. So there is always a therapeutic scope for alternative remedies in hyperlipidemia. Many patients prefer herbal medicines to allopathic pharmaceutical products as they are less expensive to purchase, are effective and safe. However studies in this area are scanty.

There is no direct description of hyperlipidemia in ayurvedic texts. However ayurvedic researchers have described hyperlipidemia as "santarpanjanya vyadhi" or disease due to defective nutrition where there is increase of "asthaya medodhatu" ^[8].

Since there is not enough published research on this topic, we undertook the current study with an effort to evaluate the efficacy of a polyherbal formulation (Cholest Guard) in hyperlipidemia.

Materials and Method

Patients attending the OPD & IPD of PG Department of Kayachikitsa of Gopabandhu Ayurveda Mahavidyalaya, Puri, Odisha were screened for their lipid profile irrespective of their sex, religion, cast etc. Only those patients who fulfilled the inclusion criteria and were ready to give informed consent for the study were

registered for the trial. A specially designed research case sheet was used for collecting and maintaining different data. 30 patients were randomly allocated to the trial group (TG) and were treated with the trial drug (Cholest Guard Capsule) for a period of three months. 30 patients were also randomly allocated to the control group (CG) and were treated with the control Drug (Atorvastatin). Randomization was done by computerized Random number generator. The entire study was completed in a span of six months (September 2013 to February 2014).

Inclusion Criteria

Patients were diagnosed basing on their lipid profile reports with the following criteria.

- Age group : 20 -60 years.
- BMI < 40

Satisfying one or more of the following criteria

- Serum cholesterol 201 mg/dl or more
- Serum Triglycerides 151 mg/dl or more
- Serum LDL 131 mg/dl or more
- Serum VLDL 41 mg/dl or more

Exclusion Criteria

Patients with the following conditions were excluded from the study.

- Secondary hyperlipidemia
- Drug induced hyperlipidemia
- Chronic Alcoholics
- Patients with diabetes
- Patients with renal insufficiency
- Patients with serious cardiac disorders
- Pregnant women & lactating mothers

Concomitant Medication

Concomitant medications were monitored throughout the study and recorded in the research case sheet. Twenty one patients took no other drugs, 6 took antihistamines or anti-allergic preparations, 2 took laxatives, 3 took non-steroidal anti-inflammatory drugs (NSAID), 4 took antacids, and 1 took antibiotics. Most of these medications

were taken for very short periods. None of the patients took any known lipid lowering medication other than trial drug and control drug.

Investigations

All patients were investigated for their Lipid profile, Routine haematological tests, Fasting Blood Sugar (FBS), Postprandial Blood Sugar (PPBS), Serum Urea, Serum Creatinine & Liver Function Test before starting and after the completion of the trial. All the tests were performed in NABL accredited laboratory.

Study Design

The current study was a randomized, standard controlled, comparative clinical trial. The study was started after obtaining the approval of the Institutional Ethical Committee (IEC). Informed written consent was obtained from every patient before registering them in to the trial.

Drugs and Posology

Trial Drug : Cholest Guard Capsule (composition given below) was orally administered to the patients in the trial group in a dose of 2 capsules twice in a day after food with lukewarm water for a period of 3 months.

Control Drug : Atorvastatin Tablet of strength 10 mg each was orally administered to the patients of control group once daily with plain water for a period of 3 months.

Composition of Cholest Guard

Each Capsule contains

Guggulu Purified (<i>Commiphora mukul</i>)	: 125 mg
Ghanasatwa of Arjun Chhal (<i>Terminalia arjuna</i>)	: 100 mg
Lashun (<i>Allium sativum</i>)	: 125 mg
Sunth (<i>Zingiber officinale</i>)	: 50 mg
Chai (<i>Camellia sinensis</i>)	: 100 mg
Excipients(Talc)	: q.s

Pathyapathya (Dietary & Exercise Advice)

All the patients were advised to follow a specific diet plan in order to maintain a fairly uniform dietary pattern and the compliance was assured by routine interview by the investigators during the fortnightly follow up visits. They were advised to stop

smoking and avoid certain foods containing high saturated fat. They were instructed to do brisk walking for 30 minutes at least 5 days a week during the therapy period.

Assessment of the Study

Criteria of Assessment

Since hyperlipidemia is mostly asymptomatic, the study was assessed using objective criteria alone. The following objective criteria were fixed for assessment of the study.

Complete lipid profile including Total serum Cholesterol, High Density Lipoproteins (HDL), Low Density Lipoprotein (LDL), Very Low Density Lipoproteins (VLDL) and Triglyceride (TG) was done for every patient included in the trial before starting and after completion of the study. Change in these parameters were analysed to get the outcome of the study by using suitable statistical method. The normal reference range for different components of lipid profile was fixed as per the guideline of Medline Plus Medical Encyclopedia (An online service provided by the U.S. National Library of Medicine & National Institutes of Health ^[9]).

Statistical Analysis

The values of different components of lipid profile before and after treatment were compared using Student's Paired t-test. If the p – value was found to be < .05 the result was interpreted as insignificant. If the p – value was found to be < .01 the result was interpreted as significant. If the p – value was found to be < .001 the result was interpreted as extremely significant. All the calculations were done by using Graphpad statistical software.

The overall benefit of the therapy was assessed by a specially designed scoring system. A percentage change in before treatment (BT) & after treatment (AT) was calculated for each of the components of Lipid Profile i.e. total Cholesterol, HDL, LDL, VLDL & TG for every patient. A corresponding score equal to the percentage change was assigned for each observation. These individual scores were added to get a total score. The total score was interpreted as per the following.

Scores > 100 – Excellent Result

Scores between 61 to 100 – Good Result

Scores between 21 to 60 – Satisfactory Result

Scores ≤ 20 – Unsatisfactory Result

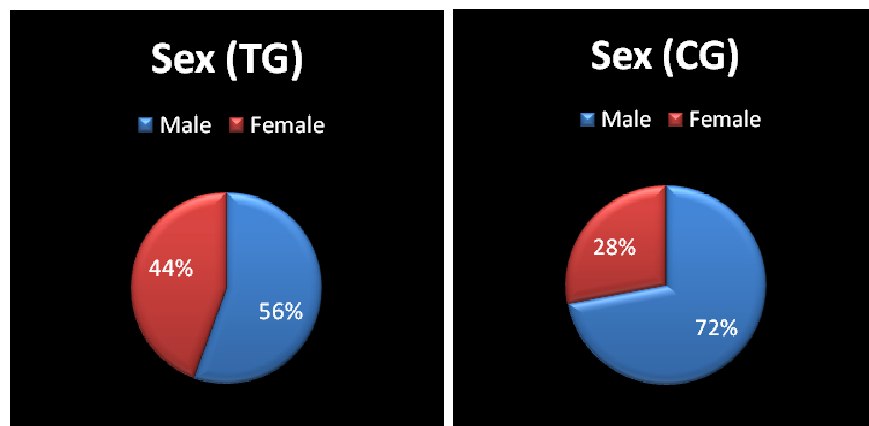
Observation & Result

Initially we registered 30 patients in each Trial Group (TG) & Control Group (CG). But there was a drop out of 3 and 5 patients from TG and CG respectively due to

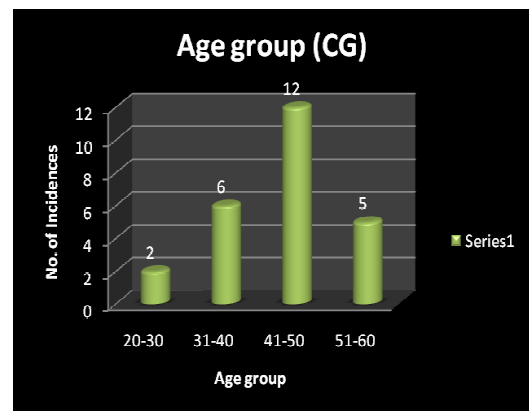
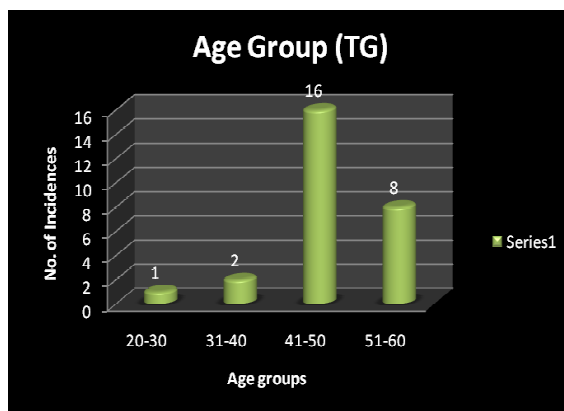
different reasons. Therefore 27 patients from TG and 25 patients from CG completed the trial.

Demographic Data

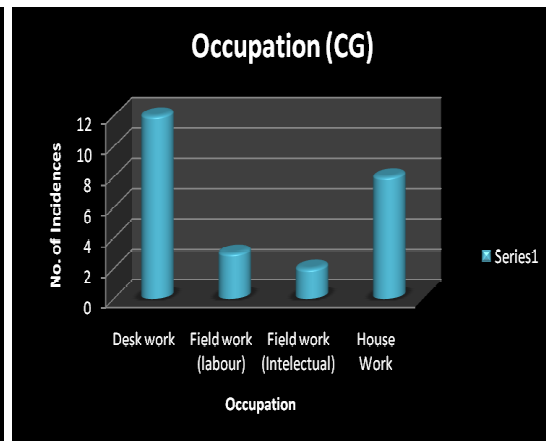
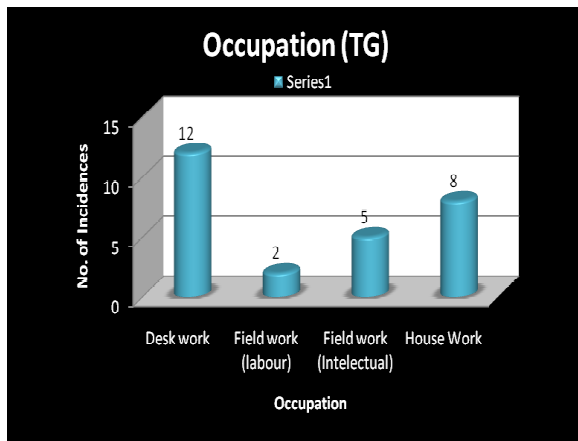
1. Sex wise distribution				
Sex	Trial (N=27)		Control(N=25)	
	No.	%	No.	%
Male	15	55.56	18	72.00
Female	12	44.44	7	28.00



2. Age group wise distribution				
Age group in yrs	Trial (N=27)		Control(N=25)	
	No.	%age	No.	%age
20-30	1	3.70	2	8.00
31-40	2	7.41	6	24.00
41-50	16	59.26	12	48.00
51-60	8	29.63	5	20.00

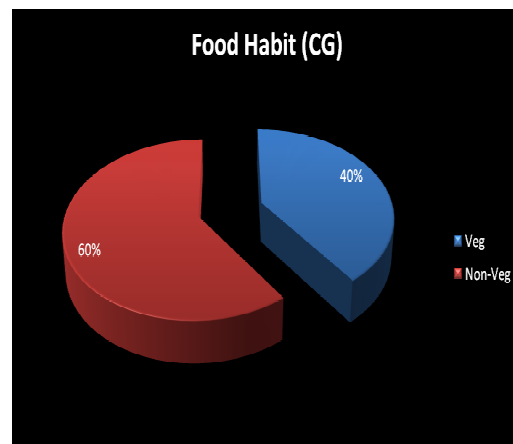
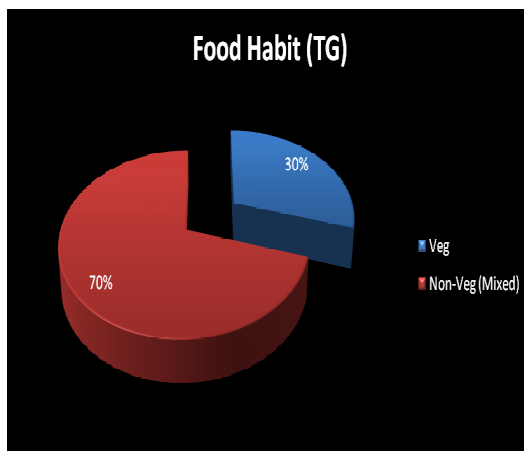


3. Occupation wise distribution				
Occupation	Trial (N=27)		Control(N=25)	
	No.	%	No.	%
Desk work	12	44.44	12	48.00
Field work (labour)	2	7.41	3	12.00
Field work (Intellectual)	5	18.52	2	8.00
House Work	8	29.63	8	32.00

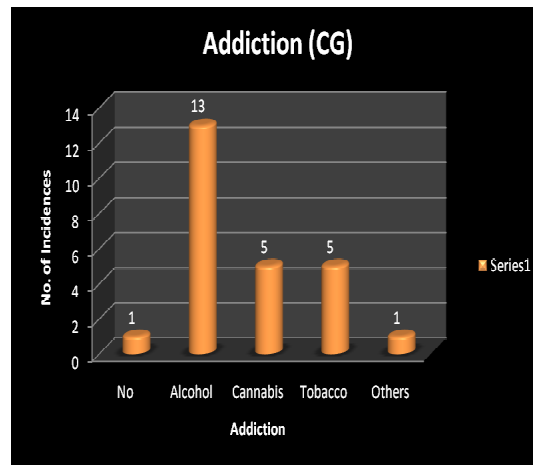
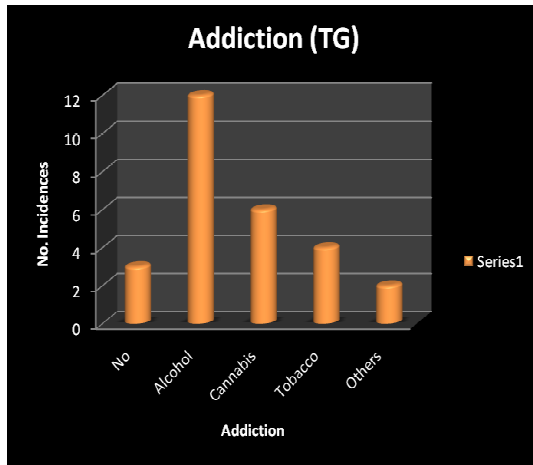


Data related to Risk Factors

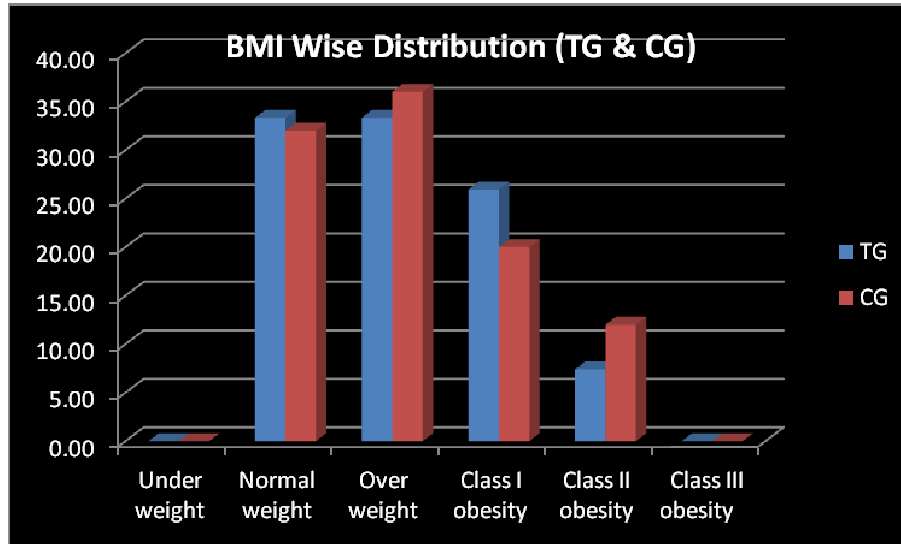
4. Food Habit wise distribution				
Food Habit	Trial (N=27)		Control(N=25)	
	No.	%age	No.	%
Veg	8	29.63	10	40.00
Non-Veg (Mixed)	19	70.37	15	60.00



5. Addiction wise distribution				
Addiction	Trial (N=27)		Control(N=25)	
	No.	%	No.	%
No	3	11.11	1	4.00
Alcohol	12	44.44	13	52.00
Cannabis	6	22.22	5	20.00
Tobacco	4	14.81	5	20.00
Others	2	7.41	1	4.00



6. BMI wise distribution				
BMI	Trial (N=27)		Control(N=25)	
	No.	%	No.	%
Under weight	0	0.00	0	0.00
Normal weight	9	33.33	8	32.00
Over weight	9	33.33	9	36.00
Class I obesity	7	25.93	5	20.00
Class II obesity	2	7.41	3	12.00
Class III obesity	0	0.00	0	0.00

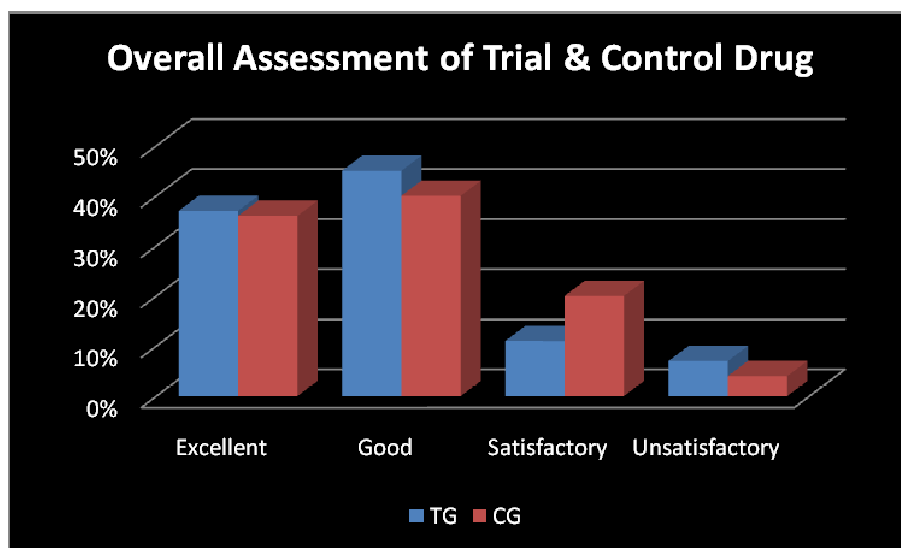


Data Related to Effectiveness of Trial Drug and Control Drug

7. Effectiveness of Trial Drug & Control Drug								
Parameter	Group		Mean ± S.D.	↑↓	d.f. (n-1)	t-Value	p-Value	Remarks
Total Cholesterol	TG	BT	210.09 ± 28.45	↓	26	4.94	< 0.0001	Extremely Significant
		AT	187.31 ± 21.28		26			
	CG	BT	234.18 ± 29.46	↓	24	4.99	< 0.0001	Extremely Significant
		AT	196.37 ± 19.92		24			
HDL	TG	BT	43.53 ± 7.19	↑	26	4.68	< 0.0001	Extremely Significant
		AT	50.75 ± 6.54		26			
	CG	BT	45.23 ± 7.84	↑	24	1.11	0.2691	Not Significant
		AT	47.32 ± 5.64		24			
LDL	TG	BT	137.65 ± 25.62	↓	26	3.19	0.0036	Very Significant
		AT	108.72 ± 19.83		26			
	CG	BT	144.32 ± 18.89	↓	24	5.35	< 0.0001	Extremely Significant
		AT	116.55 ± 13.71		24			
VLDL	TG	BT	45.09 ± 9.91	↓	26	4.31	< 0.0001	Extremely Significant
		AT	27.84 ± 5.44		26			
	CG	BT	44.16 ± 17.26	↓	24	2.64	0.0142	Significant
		AT	32.48 ± 11.38		24			
Triglyceride	TG	BT	175.44 ± 49.54	↓	26	4.29	< 0.0001	Extremely Significant
		AT	139.57 ± 28.01		26			
	CG	BT	222.11 ± 82.38	↓	24	2.84	0.0089	Very Significant
		AT	162.43 ± 56.93		24			

Overall Assessment of Effectiveness of Trial Drug & Control Drug

8. Overall Assessment of results after treatment				
Overall Assessment	Trial Group		Control Group	
	No. of Patients	Percentage	No. of Patients	Percentage
Excellent	10	37%	9	36%
Good	12	45%	10	40%
Satisfactory	3	11%	5	20%
Unsatisfactory	2	7%	1	4%



Assessment of Adverse Effects of Trial Drug & Control Drug

9. Adverse effect		
Type of Complain	No. of Patients showing Complain after treatment	
	TG	CG
Altered LFT Results	0	7
Muscle pain	0	3
Headache	0	4
Nausea	0	2
Sleep disturbances	0	5
Gastric Upset	1	7

Observation Highlights

- The study included both male and female patients. But males dominated female patients.
- The Study included patients in the age limit of 20 to 60 years (both inclusive). Patients in the age group of 41 – 50 years were maximum and in the age group of 20 – 30 years were minimum both in TG & CG.
- Hyperlipidemia was found to be well distributed among different occupation. However patients with Desk work or intellectual field work were found to be maximum both in TG & CG.
- The study included both Vegetarians and Non – vegetarians. But Non – Vegetarians clearly outnumbered the Vegetarians in both TG & CG.
- It was alarming that 89 % patients in the TG and 96 % patients in the CG were having some or the other addiction. However alcoholics were maximum followed by Cannabis and Tobacco users.
- Hyperlipidemia was found to be well distributed in different BMI groups. But we did not come across any underweight patient. The saliency of overweight patients was maximum followed in order by normal weight, Class – 1 obesity & Class – 2 obesity. But we did not register any Class – 3 obese patient (MBI > 40) as an exclusion criteria of the study.
- Both Cholest Guard (Trial Drug) & Atorvastatin (Control Drug) were found effective in reducing Total Cholesterol level. The Total Cholesterol reduced from 210.09 ± 28.45 mg/dl to 187.31 ± 21.28 mg/dl in the TG taking Cholest Guard. Reduction in Total Cholesterol from 234.18 ± 29.46 mg/dl to 196.37 ± 19.92 mg/dl occurred in CG taking Atorvastatin. Both the results were found to be extremely statistically significant ($p < 0.0001$).
- HDL Cholesterol was found to increase after treatment in both the groups. In the TG, Cholest Guard increased HDL from 43.53 ± 7.19 mg/dl to 50.75 ± 6.54 mg/dl and the result was extremely statistically significant ($p < 0.0001$). In the CG, Atorvastatin also increased HDL from 45.23 ± 7.84 mg/dl to 47.32 ± 5.64 mg/dl. However this marginal increase of HDL in the CG was not found statistically significant ($p = 0.2691$).
- Both Cholest Guard & Atorvastatin reduced the LDL level in TG & CG respectively. It was reduced from 137.65 ± 25.62 mg/dl to 108.72 ± 19.83 mg/dl in TG & it was also reduced from 144.32 ± 18.89 mg/dl to 116.55 ± 13.71 mg/dl in CG. Statistically the results were very significant in TG ($p = 0.0036$) & extremely significant in CG ($p < 0.0001$)

- VLDL was reduced after treatment in both the groups. Cholest Guard reduced VLDL from 45.09 ± 9.91 mg/dl to 27.84 ± 5.44 mg/dl in TG where as Atorvastatin reduced it from 44.16 ± 17.26 mg/dl to 32.48 ± 11.38 mg/dl in CG. The changes were found to be extremely statistically significant in TG ($p < 0.0001$) and statistically significant in CG ($p = 0.0142$) respectively.
- Serum Triglyceride was found to be reduced from 175.44 ± 49.54 mg/dl to 139.57 ± 28.01 mg/dl in TG who were taking Cholest Guard and it was also found to be reduced from 222.11 ± 82.38 mg/dl to 162.43 ± 56.93 mg/dl in CG who were taking Atorvastatin. Statistically, the changes were extremely significant in TG ($p < 0.0001$) & very significant in CG ($p = 0.0089$).
- On overall assessment of the effectiveness of Cholest Guard & Atorvastatin in hyperlipidemia we got the following results. Cholest Guard gave Excellent results in 37 % cases, Good result in 45 % cases, Satisfactory results in 11 % cases and Unsatisfactory results in 7 % cases where as Atorvastatin gave Excellent results in 36 % cases, Good result in 40 % cases, Satisfactory results in 20 % cases and Unsatisfactory results in 4 % cases.
- On analysing the incidence of adverse effects we got that Cholest Guard did not produce any unwanted or adverse effect except only one incidence of Gastric upset for very short period. Cholest Guard also did not alter the Liver Function & Renal Function Profile proving that it has no deleterious effect on vital organs. On the other hand Atorvastatin caused various adverse effects like muscle pain in 3 cases, headache in 4 cases, Nausea in 2 cases, sleep disturbance in 5 cases & Gastric upset in 7 cases. The LFT profile was altered in 7 cases showing that atorvastatin has deleterious effect on the liver. However it did not altered the Renal function.

Discussion

The male patients dominated the female patients in the study. This may be due to the reasons that males are more addicted to tobacco & alcohol and their food habit is more conducive for hyperlipidemia. Since in the state like Odisha males get better medical facility than females, their footfall might have been more during the trial period.

Patients in the age group of 41 – 50 were maximum in the trial indicating that hyperlipidemia is more prevalent in this age group. This may be due to the fact that these years in life are more stressful years. So there is every chance of altered dietary habits and getting addicted to alcohol or tobacco which might have facilitated the process of hyperlipidemia.

The Desk work professionals and people with intellectual field work were more in number in this trial. Their sedentary life style may be held responsible for accelerating hyperlipidemia.

Non – vegetarian food contains more saturated fats in comparison to Vegetarian foods. This may be the reason why the incidence of Non – Vegetarians was more than Vegetarians in this study.

Most of the patients were having some addiction or the other. High incidence of alcohol & tobacco users proves that these are potential risk factors for hyperlipidemia.

Contrary to the common belief that only obese patients are more likely to have hyperlipidemia, we found that non obese (over weight) & even normal weight patients also suffer from hyperlipidemia. Therefore hypercholesterolemia necessarily do not depend on body fat.

Both Cholest Guard and Atorvastatin were found effective in reducing Total Cholesterol, LDL, VLDL & Triglyceride and the results were comparable. However the raise in HDL was found much better in TG taking Cholest Guard. Pharmacologically Atorvastatin can also raise serum HDL level. In this study the raise in HDL in CG taking Atorvastatin was not statistically significant. This may be explained on the fact that the HDL elevating property of Atorvastatin is dose dependant. In this study we used only 10 mg of Atorvastatin once in a day. The result would have been better with higher doses.

The overall effectiveness of Cholest Guard and Atorvastatin is also comparable.

But these two drugs differ greatly in terms of their adverse effects. Cholest Guard did not produce any adverse effect except gastric upset in only one patient for a very short period in the beginning of the therapy. This may be due to the reason that the particular patient usually does not take onion and garlic in his food. Garlic which is an ingredient of Cholest Guard might have caused some problem in the beginning and after few days the problem automatically subsided. On the other hand Atorvastatin produced many adverse effects like muscle pain, nausea, headache, sleep disturbance & gastric upsets in considerable number of cases.

Liver Function Profile and Renal function profile were not at all altered in the TG taking Cholest Guard proving that the drug do not produce harmful effects on vital organs where as Atorvastatin altered the LFT in 7 cases showing its hepatotoxicity. However it does not produce any harmful effect on the Renal function.

Considering the effectiveness & adverse effects of both Cholest Guard & Atorvastatin in managing hyperlipidemia, we can say that the former has many advantages over the later. Cholest Guard has unique ability to manage hyperlipidemia without causing any adverse effect or deleterious effect on the vital organs.

Possible Mode of Action of Cholest Guard

Cholest Guard is an unique formulation containing Guggulu Purified (*Commiphora mukul*) - 125 mg, Ghanasatwa of Arjun Chhal (*Terminalia arjuna*) - 100 mg, Lashun (*Allium sativum*) - 125 mg, Sunthi (*Zingiber officinale*) - 50 mg & Chai (*Camellia sinensis*) - 100 mg. Each of these drugs has been proved to have antihyperlipidemic effect in several experimental & human trials.

Different mechanisms has been proposed to explain the antihyperlipidemic effect of Guggulu. It may decrease hepatic steroid production and increase the catabolism of LDL cholesterol^[10]. Another mechanism is that the proposed guggulsterones E and Z (active components of Guggul), may increase hepatic binding sites for LDL cholesterol thereby increasing LDL clearance^[11]. One more mechanism is prevention of cholesterol synthesis in the liver by ketonic steroids^[12]. Guggulsterones E and Z act as antagonists at the farnesoid X receptor which causes more cholesterol catabolism and excretion from the body. This receptor mediates the conversion of cholesterol to bile acids. When this receptor is antagonized, 7 α -hydroxylase is released and cholesterol catabolism is stimulated^[12, 13].

Garlic acts as an antihyperlipidemic agent by depressing the hepatic activities of cholesterogenic enzymes such as malic enzyme, fatty acid synthase, glucose-6 phosphate dehydrogenase (G-6 PD) and 3-hydroxy-3-methyl-glutaryl-CoA (HMG CoA) reductase^[14]. Garlic also increases the excretion of Cholesterol^[15]. Water-soluble organosulfur compounds present in garlic, especially S-allyl cysteine (SAC) & Diallyl di-sulfide (DADS) are also potent inhibitors of cholesterol synthesis^[14].

Terminalia arjuna acts as a lipid lowering agent by inhibition of hepatic cholesterol biosynthesis, increased faecal bile acid excretion, and stimulation of receptor-mediated catabolism of LDL cholesterol^[16, 17, 18].

Constituents within ginger inhibit the process of cholesterol biosynthesis^[19]. Ginger also enhances the activity of hepatic cholesterol 7 α -hydroxylase, the rate limiting enzyme in bile acids biosynthesis, thereby stimulating cholesterol conversion to bile acids and thus cholesterol is eliminated from human body^[20].

Active principles in tea increase the expression of hepatic LDL-C receptor –A cell surface protein which controls the plasma cholesterol and increase the faecal excretion of bile acids and Cholesterol^[21].

Conclusion

As per the results of this study, both Cholest Guard & Atorvastatin significantly reduced Total Cholesterol, LDL, VLDL & Triglyceride with comparable results. Since Atorvastatin produced considerable incidence of adverse effects and altered the Liver function in many cases, therefore Cholest Guard would definitely be a better and safer choice in managing hyperlipidemia.

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