International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 23-10-2018; Accepted: 29-11-2018
www.medicalsciencejournal.com
Volume 4; Issue 12; December 2018; Page No. 199-201

Study of comparative evaluation of Atorvastatin and Salacinol (*Salacia roxburghii*) on BMI, Lipid profile and adiponectin in patient of chronic kidney disease with hypertension

Dr. Manish Kumar Bhaskar[1], Dr. RG Singh[2*]
[1] Junior Resident, Department of General Medicine, Sir Sunderlal Hospital, BHU, Varanasi, Uttar Pardesh, India.
[2] Professor, Department of General Medicine, Sir Sunderlal Hospital, BHU, Varanasi, Uttar Pradesh, India
[*] Corresponding Author: Dr. RG Singh

Abstract
Hippocrates in 5th century B.C blamed malfunctioning kidney tor certain signs and symptoms. Progression of renal failure is an area of Nephrology where our understanding has improved appreciably in the last century but still our knowledge is like a drop in ocean. Progression of renal failure is an area of Nephrology where our understanding has improved appreciably in the last century but still our knowledge is like a drop in ocean. We have ample of evidence that progression of renal failure can be slowed down but we still need more definite information whether established renal failure can be reversed. Retarding the progression of renal failure is one of the most important task for the nephrologists as it not only improves the quality of life of the patient but also delays the development of end stage renal disease. This pilot clinical study was planned to explore the therapeutic potential of salacinol on BMI, Lipid profile and Adiponectin.

Objectives: To study of comparative evaluation of atorvastatin and salacinol (*Salacia roxburghii*) on BMI, Lipid profile and Adiponectin in patient of chronic kidney disease with hypertension

Methods: The present study was conducted in the Department of General medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi. Eighty patients of mild to moderate stable chronic renal failure with hypertension attending Nephrology OPD were admitted in Nephrology ward from May 2015 to June 2016 were included in the study. Initially patients were explained in detail about the experimental nature of the drugs and plan of study and only willing patient were included in the study after signing of the written consent. Before starting the drugs a through history was taken and clinical examination was done. The patients were then subjected to baseline urine, hematological, biochemical and immunological investigation.

Results: Overall 80 patients completed the six months follow-up and were finally included in the study. Atorvastatin and Salacinol group finally had 40 patients and there were 40 patients in Atorvastatin group. Age of patient ranged from 20 years onwards. Mean age of patient in various group were well matched & there was no significant statistical differences. Mean age of group-I was 53.9 yrs & Mean age of Group-II was 51.75 Yrs. There was male preponderance in our patient. Overall 65% patients were male & 35% were female. In Group-1 623% patient were male while in Group-II 67.5% were male. Mean body mass index in Group-I & Group-II at baseline were 25.9±2.3 & 26.7±1.7 & on subsequent follow up at three and six months were statistically significant. LDL/HDL ratio at baseline in Group-I & Group-II were 4.35±0.50 & 4.44±0.53 respectively changes were statistically significant on subsequent visit at three and six months on intergroup comparison changes were statistically significant at the end of three months & six months probably of hypolipidemic role of salacinol. Similarly serum cholesterol value comparison in intergroup, changes were statistically significant at three & six months. Mean Adiponectin level at baseline in group-I and Group-II were 5.29 and 4.25 respectively and changes were statistically significant at three and six months in group-I while at six months in Group-II. On intergroup comparison were statistically significant at three and six months. On intergroup changes baseline comparison, changes were also statistically significant.

Conclusion: The male patients dominated over the female patients with a male to female ratio of 2:1. Age of the patient ranged from 20yrs onward. Majority of the patient were above 40yrs of age. Commonest symptom was weakness in all the groups followed by anorexia, swelling over body, pallor & sleep disorders. In patient treated with Atorvastatin and Salacinol BMI (Body mass index) showed significant decrease (<0.05) on 3rd and six months. Patient treated with Atorvastatin and Salacinol, lipid profile including LDL/HDI, ratio, serum total cholesterol & triglyceride showed significant decrease (<0.05) at three months and at the end of study. In patient treated with Atorvastatin and salacinol, the changes in Adiponectin level were statistically significant (<().()()l) at three and six months.

Keywords: Atorvastatin, Salacinol (*Salacia roxburghii*), BMI

Introduction

Hippocrates in 5th century B.C blamed malfunctioning kidney tor certain signs and symptoms. He commented that suppression of urine was a sign and could be followed by smell of urine in the breath, coma and convulsions since then our understanding of nephrology has had revolutionary

changes. Progression of renal failure is an area of Nephrology where our understanding has improved appreciably in the last century but still our knowledge is like a drop in ocean.

We have ample of evidence that progression of renal failure can be slowed down but we still need more definite information whether established renal failure can be reversed. Retarding the progression of renal failure is one of the most important task for the Nephrologists as it not only improves the quality of life of the patient but also delays the development of end stage renal disease, This also forestalls the considerable financial burden of dialysis, transplantation and immunosuppressive drugs.

This pilot clinical study was planned to know the beneficial effect of salacinol on BMI,Lipid profile and Adiponectin level. The antidiabetic property of salacia species has been recognized since ancient time. The Ayurvedic practitioners of south India particularly Tamil Nadu and Kerala are using this plant for the treatment of diabetic complications like peripheral neuritis, diabetic gangrene.

The scientific evaluation on salacia species was conducted at BHU by Dubey *et al* (1993) and reported its antidiabetic property and its role in diabetic complications (Dubey 1994, Wani 2006, Singh 2007, Sharma 2007, Rajesh 2009).

The findings were confirmed in collaborative studies in 2005. The antidiabetic and anti-inflammatory activity of salacia was studied by Syed Ismail and Elango (1997) at the Tamil Nadu University. Salacia depresses cardiac angiotensin Π signaling of AT-1 receptors

1. Supression of overexpression of cardiac PPAR-a in diabetic heart
2. Salacia as PPAR-y agonists in diabetes mellitus and insulin resistance.
3. Salacia as PPAR-a agonists in the management of dyslipidemia
4. Salacia inhibits a-glucosidase
5. Salacia decreases postprandial glycaemia
6. Salacia inhibits aldose reductase
7. Salacia inhibits pancreatic lipase

In view of the need for the drugs to retard or reverse the progression of renal failure and atherosclerosis scavenging property and also in view of the unchartered wealth of traditional medicines which is found in India, this study was planned to explore the therapeutic potentials of the traditional medicines in case of chronic renal failure especially with respect to its atherosclerosis scavenging properties.

Material and Methods

The present study was conducted in the Department of General medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi. Eighty patients of mild to moderate stable chronic renal failure with hypertension attending Nephrology OPD or admitted in Nephrology ward from May 2015 to June 2016 were included in the study. Patient with acute MI, congestive heart failure, unstable angina, myopathy. Non-compliant patient & those patient taking medicines for their disease which is known to improve lipid profile (lipid lowering agent other than atorvastatin) were excluded from the study.

Initially patients were explained in detail about the experimental nature of the drugs and plan of study and only willing patient were included in the study after signing of the written consent. Before starting the drugs a through history was taken and clinical examination was done. The patients were then subjected to baseline urine, hematological, biochemical and immunological investigation. All the patients were given strict dietary instruction and a diet chart was given for their reference. They were maintained on low protein 0.6mg/kg/day), low salt (s 5mg/day) as potassium restricted 40-60 meq/day) diet. A caloric intake of 30-35 kcal/kg body weight was planned. All of the patient were needed were given phosphate binders & none of the patient was taking ACE inhibitor. Subsequently patients were allocated randomly to one of the two groups, the first group consisted of patient treated with atorvastatin salacinol and second group was treated with atorvastatin only.

The allocated drug was started and after a period of one month they were assessed for dietary control by asking them to recal their diet in last 24hrs and for any symptomatic improvement or deterioration as compared to the last visit. They were also examined thoroughly and baseline investigations were repeated on three & six months.

The drug used were salacinol & Atorvastatin. Salacinol, is extract from *Salacia roxburghii* which is a climbing shrub or small tree found in evergreen forest of North Bengal, Assam, Sikkim & N.E.F.A. Ripe fruits are edible, common name satrangi saptachakra, swarnamala part used were root. This is antidiabetic drug used in the treatment of diabetes. It is also having anti-inflammatory and analgesic action. The stems have been used as anti-inflammatory cardiotonic, antidiabetic and anti-oxidant

Investigations

The following investigations were done at baseline, 3 months & 6 months.

1. Hematological investigation — These included estimation of hemoglobin by sahli's hemoglobin meter, TLC by Neubaurs chamber.
2. Biochemical Analysis
   - Blood sugar (fasting) (Varley, 1980)
   - Blood urea - diacetyl monoxine method (Varley, 1980)
   - Serum creatinine - Alkaline picrate method of Jaffe reaction (Varley, 1980)
   - Serum cholesterol — Timed end point method using cholesterol reagent.
   - Total serum protein — Biduret method (Varley, 1980)
   - Serum Albumin — dye binding capacity buffer method (Varley, 1980)
   - Serum calcium and phosphorous Direct calorimetry with complexing agents (Varley, 1980)
3. Urinalysis
   - Routine examination for urinary pH, albumin sugar and detailed microscopic study was done as described by (Varley, 1980).
   - Quantitative examination of 24hs urinary protein was done by Biduret method.
4. Radiological examination - Ultrasonography of abdomen for kidney size cortical thickness, cortico-medullary differentiation, pelvi-calyceal system Ureters urinary bladder and prostate was done in all patient.

5. Creatinine clearance were estimated by using cockroft-gault equation.
6. Adiponectin estitnation was done by ELISA method in department of pathology IM>, BIIU Varanasi.

Sample Collection

Blood were drawn by 20G needle from the median cubital vein of patient with disposable syringe. Patients were healthy at the time of sample collection, without recent illness, infection, inflammation, tissue injuries. 10ml of blood was drawn for these tests. Sample can be refrigerated up to lweek, frozen up to 3 months. Fasting sample should be drawn for best results. On follow up at three and six months, samples were taken using same methodology for routine investigations and other specific tests.

Observations

Ninety five patients of mild to moderate chronic renal failure with abnormal lipid profile were included in the study. Each was randomized to two groups. Group-I was treated with Atorvastatin & Salacinol, Group-Il with Atorvastatin. Overall 80 patients completed the six months follow-up and were finally included in the study. Atorvastatin and Salacinol group finally had 40 patients and there were 40 patients in Atorvastatin group.

Table 1: Sex wise distribution in group 1 and group 2

Sex	Group 1		Group 2	
	No.		No.	
Male	25	62.5	27	67.5
Female	15	37.5	13	32.2
Total	40	100	40	100

$X^2 = 0.220$; p = 0.639

There was male preponderance in our patients. Overall 65% of patient were male & 35% were female. In Atorvastatin+Salacinol group 62.5% were male & in Atorvastatin group 67.5% were male.

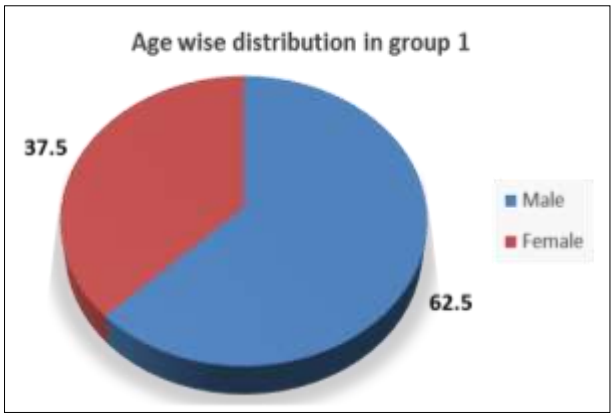

Fig 1

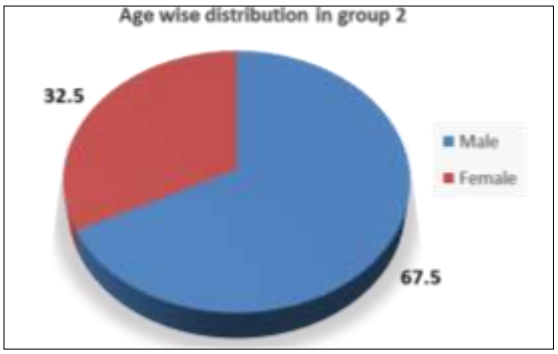

Fig 2

Table 2: Age wise distribution in group 1 and group 2

Age group (years)	Group 1		Group 2	
	No.		No.	
20-30	1	2.5	3	7.5
31-40	4	10	0	
41-50	12	30	17	42.5
51-60	13	32.5	13	32.5
> 60	10	25	7	17.5

Age of patient ranged from 20 years onwarads. Mean age of patient in group-I was 53.9yrs ranging from 23yrs to 80yrs while mean age of pt. in group[I was 51.7yrs ranging from 23 yrs to 68 yrs. Mean age of patients in various groups were well matched and there was no significant statistical difference.

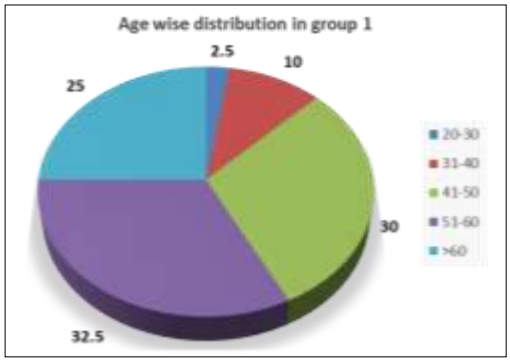

Fig 2

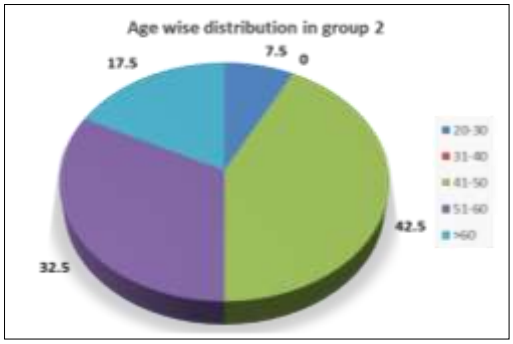

Fig 3

Most common presenting features was the subjective feeling of weakness present in all the patient of Group-I & II. Other common symptoms were anorexia, oedema, pallor, in Group-I anorexia was present in 82.5% of cases, oedema in 72.5% of cases, pallor in 65%. In Group-Il, anorexia was present in 85 0/0, pedal oedema in 52.5% and pallor in 80%.

Table 3: Comparison of BMI between groups and within group on successive follow up

Group	BMI (Mean+-SD)			Within the group comparison paired 't' test	
	0 month	3 month	6 month	0 vs 3	0 vs 6
Group 1	25.9+2.3	23.7±5.8	24.0±5.4	2.419 P<0.020	2.179 P<0.035
Group 2	26.7+1.7	26.4±1.8	26.0±1.8	3.263 P<0.001	7.910P<0.001
t-value	-1.642	-2.812	-2.161	-	-
p-value	0.105	0.006	0.034		

Mean BMI in Group-I at baseline was 25.95±2.39 ranging from 20.1 to 29.8 & there was sigmficant changes on subsequent visit. In Group-Il BMI at baseline was 26.71±1.70 ranging from 22.1 t029.4, and on subsequent visit, sigmficant changes were observed.()n intergroup comparison statistically significant changes were observed at three and six month visit.

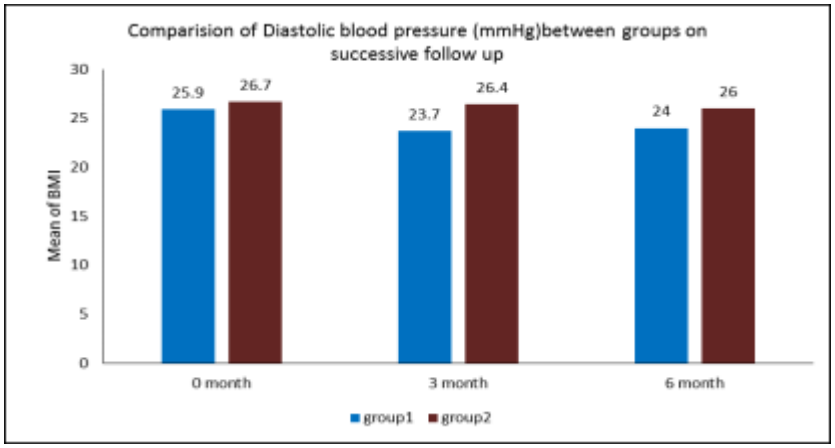

Fig 4

Table 4: Comparison of LDL/HDL ratio between groups and within group on successive follow up

Group	LDL/HDL ratio (Mean+-SD)			Within the group comparison paired 't' test	
	0 month	3 month	6 month	0 vs 3	0 vs 6
Group 1	4.35±0.50	3.26±0.30	2.46±0.27	13.966P<0.001	21.427P<0.001
xGroup 2	4.44±0.53	3.51±0.47	2.68±0.51	17.036P<0.001	-23.526P<0.001
t-value	-0.796	-2.850	-2.340	-	-
p-value	0.428	0.006	0.022		

LDL/HDL ratio at baseline was 4.35±0.50 in Group-I ranging from 4 to 6 & 4.44±0.53 in Group-Il ranging from3 to 6& was statistically significant on subsequent visit, while comparing between two groups, reduction in ratio were statistically significant at three and six months.

Table 5: Comparison of Cholesterol between groups and within group on successive follow up

Group	Cholesterol (Mean+-SD)			Within the group comparison paired 't' test	
	0 month	3 month	6 month	0 vs 3	0 vs 6
Group 1	287.2±24.8	226.6±12.8	177.1±12.5	15.149P<0.001	22.780P<0.001
Group 2	288.6±36.7	244.0±36.5	195.3±37.1	12.559P<0.001	23.601P<0.001
t-value	-0.193	-2.828	-2.936	-	-
p-value	0.848	0.006	0.004		

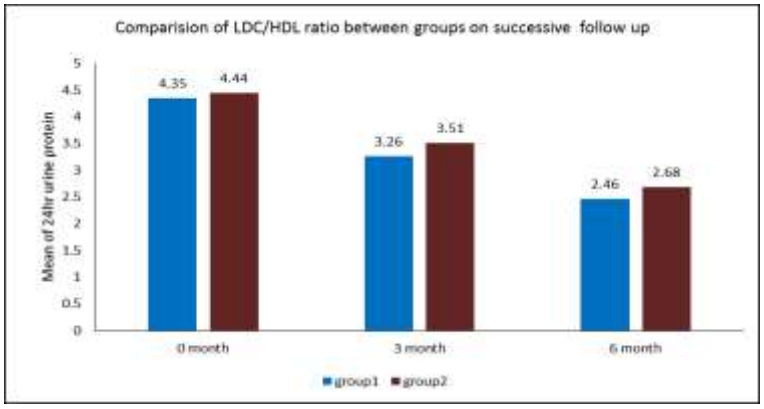

Fig 5

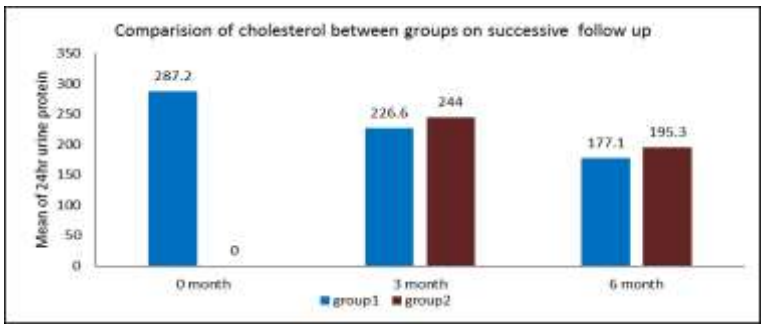

Fig 6

Mean Serum cholesterol at the time of start of study in Group-I was 287.2±24.8 ranging from 254 to 364, while in Group-Il was 288.6±36.7 ranging from 254 to 368 & was statistically significant on subsequent visit. while comparing the reduction between two groups at three and six months, they were statistically significant.

Table 12: Comparison of Adiponectin between groups and within group on successive follow up.

Group	Adiponectin (Mean+-SD)			Within the group comparison paired 't' test	
	0 month	3 month	6 month	0 vs 3	0 vs 6
Group 1	5.29±1.49	5.73±1.35	6.89±1.16	7.359P<0.001	10.072P<0.001
Group 2	4.25±1.69	4.14±1.51	4.00±1.44	1.428P=0.161	2.137P=0.039
t-value	2.933	4.953	9.848	-	-
p-value	0.004	<0.001	<0.001		

The mean adiponectin value in group 1 and group 2 at baseline were 5.29±1.49 and 4.25±1.69 and on successive follow up changes were statistically significant at 3 and 6 months in group 1 and at 6 months in group 2. On intergroup comparison changes were statistically significant at 3 and 6 months. However, changes were statistically significant even at baseline.

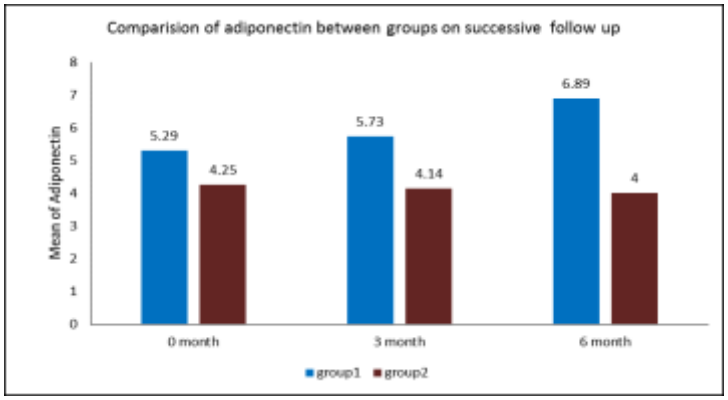

Fig 7

Table 15: Comparison of Triglyceride between groups and within group on successive follow up

Group	Triglyceride (Mean+-SD)			Within the group comparison paired 't' test	
	0 month	3 month	6 month	0 vs 3	0 vs 6
Group 1	171.2±27.2	125.1±10.4	107.7±8.2	13.012P<0.001	16.055P<0.001
Group 2	170.5±22.6	136.2±22.3	115.7±20.8	15.148P=0.161	19.113P=0.001
t-value	0.120	-2.854	-2.274	-	-
p-value	0.904	0.006	0.026		

Mean Triglyceride level at baseline in group-1 in 171.2+27.2 ranging from 130 to 279, while in group-2 170.5+22.6 ranging from 140 to 279. Changes in triglyceride level within groups are statistically significant on subsequent visit in both group. While, in between comparison, mean triglyceride level are statistically significant on 3 month and 6 month visit.

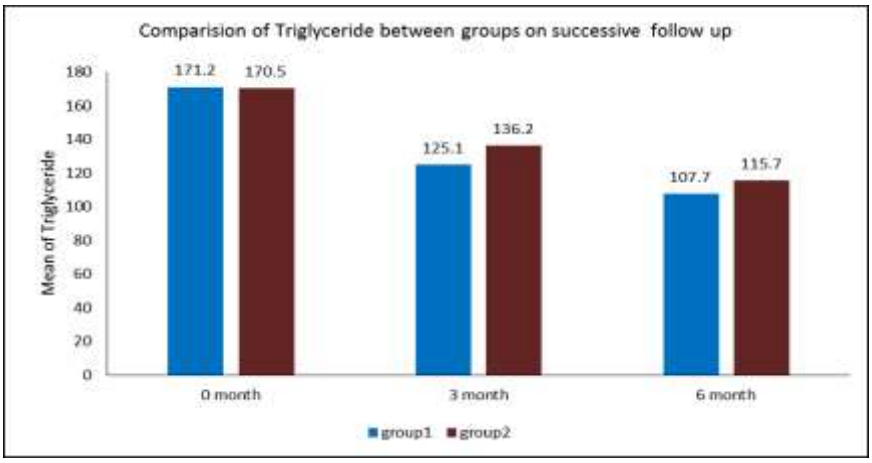

Fig 7

Discussion

Due to rapid urbanization and industrialization, the incidence of diseases particularly Diabetes mellitus, Hypertension and CHD are increasing worldwide at an alarming rate. Due to remarkable risk profile of modern synthetic agents there is an urgent need to develop eco-friendly and bio-friendly plant-based products to replace synthetic chemicals since chronic disease is a lifelong process. India has a rich national heritage in the form of plant based remedies. These plants have shown pharmacological therapeutic potentials in the prevention and managements of various mental and physical diseases. It is pertinent to mention here that we have extensive experience based knowledge but we are lacking with evidence based scientific documentation required for global acceptance of these natural products. Recently World Health Organization has provided guidelines for validation of these plant origin products for its global acceptance.

There is an urgent need to focus new concepts and targets for the managements of chronic diseases. As in the present investigation, we are concentrating on the treatment modalities for chronic kidney disease with hypertension with abnormal lipid profile.

Among 95 patients of chronic renal failure taken for study, Eighty patient of chronic renal failure with hypertension completed the six months follow-up and were finally included in the study. Group-I consisted of forty patients treated with Salacinol and Atorvastatin, Group-II consisted of forty patients treated with Atorvastatin only.

Age of patient ranged from 20 years onwards. Mean age of patient in various group were well matched & there was no significant statistical differences. Mean age of group-I was 53.9 yrs & Mean age of Group-II was 51.75 Yrs.

There was male preponderance in our patient. Overall 65% patients were male & 35% were female. In Group-1 623% patient were male while in Group-II 67.5% were male. The male predominance in our patient is probably a reflection of male dominance in the social structure of our society. We have a society where male children are more cared for and adult male is the bread earner of the family. So. probably male patient are brought for the treatment to the hospital more frequently.

Most common presenting features was the subjective feeling of weakness in 100% of patients in all groups Other common symptoms were anorexia, edema. nausea & vomiting sleep disorder Systolic blood pressure & Diastolic blood pressure in Group-I at baseline were & 99.4±10.8 while in Group-II were 156.5±12.1 & 94.5±6.8 respectively. On Subsequent follow up SBP & DBP were statistically significant. probably because of tight control of blood pressure by using anti hypertensive therapy along With.

Mean body mass index in Group-I & Group-II at baseline were 25.9±2.3 & 26.7±1.7 & on subsequent follow up at three and six months were statistically significant. On intergroup comparison at 6 months BMI decrement were statistically significant probably because of role of Salacinol (Wong and Schotz 2002,Goldberg and Merkel 2001) found that LPL is one of the most important target responsible for development of obesity. ati obesity role of salacinol might be due to LPL inhibitory role of salacinol.

LDL/HDL ratio at baseline in Group-I & Group-II were

4.35±0.50 & 4.44±0.53 respectively changes were statistically significant on subsequent visit at three and six months on intergroup comparison changes were statistically significant at the end of three months & six months probably of hypolipidemic role of salacinol. Similarly serum cholesterol value comparison in intergroup, changes were statistically significant at three & six months, strongly supporting the above hypothesis.

Mean Adiponectin level at baseline in group-I and Group-II were 5.29 and 4.25 respectively and changes were statistically significant at three and six months in group-I while at six months in groupll. on intergroup comparison were statistically significant at three and six months. On intergroup changes baseline comparison, changes were also statistically significant.

As above mentioned, triglyceride changes in Group-I & Group-II were statistically significant on subsequent visit at three and six months. On intergroup comparison, changes were statistically significant at three and six months, suggesting probably the role of salacinol as triglyceride lowering agent (Huang *et al*, 2006a) [20] demonstrated that extract from salacia root decreases plasma triglyceride and non-esterified fatty acid in the liver of Zucker diabetic fatty rat (ZDF). Mangiferin, a component of salacia oblonga root extract (1.4%) lowers blood lipids in type-2 diabetic animals (Li *et al* 2004; Miura *et al*, 2001). This compound specifically activates PPAR-« luciferase activity in HEK293 cells and enhances PPAR-a dependant lipoprotein lipase expression and activity in the THP-I derived macrophage cell line (Huang *et al*, 2006a) [20].

Mean triglyceride level in diabetic & non-diabetic at baseline were 167.6±18.6 & 167.6±14.8 and on comparison with each other changes were statistically significant at six months.

Thus the beneficial effect of salacinol was observed and for further substantiating the finding by prospective study is recommended.

Summary and conclusion

Present study entitled "Study of Comparative evaluation of atorvastatin and salacinol (*Salacia roxburghii*) on GFR and carotid intima media thickness in patient of chronic kidney disease with hypertension" was conducted at the Department of Nephrology, Institute of Medical Sciences, Banaras Hindu University, Varanasi between the period of May 2015 to June 2016.

Eighty patient of mild to moderate chronic renal failure were included in the study. Forty patient, each were randomized to two groups. Group-I were on Atorvastatin & Salacinol while Group-Il were kept on Atorvastatin only. The salient features of this study are.

1. The male patients dominated over the female patients with a male to female ratio of 2:1.
2. Age of the patient ranged from 20yrs onward. Majority of the patient were above 40yrs of age.
3. Commonest symptom was weakness in all the groups followed by anorexia, swelling over body, pallor & sleep disorders.
4. In patient treated with Atorvastatin and Salacinol BMI (Body mass index) showed significant decrease (<0.05) on 3rd and six months.
5. Patient treated with Atorvastatin and Salacinol lipid profile including LDL/HDI, ratio. serum total cholesterol & triglyceride showed significant decrease (<0.05) at three months and at the end of study.
6. In patient treated with Atorvastatin and salacinol,the changes in Adiponectin level were statistically significant(<().()()l) at three and six months.

Thus on overall favorable effect of salacinol was seen with respect to decrease in lipid profile parameter and BMI &. However in this study the follow-up period was only six months which is relatively a short period to assess the effect of salacinol, which has a natural course running into years, A large prospective study is recommended to further establish the findings of this study.

References

1. Agarwal R. Effects of statins on renal function. Mayo Clin Proc. 2007; 82:1381-90.
2. Alexander RW. Inflammation and coronary artery disease N Engl J Med. 1994; 331:468-469.
3. Anderson RJ, O'Brien M, MaWhinney S, *et al*. Mild renal failure is associated with adverse outcome after cardiac valve surgery. Am J Kidney Dis. 2000; 35:1127-1134.
4. Barzilai N, She L, Liu BQ, Vuguin P, Cohen P, Wang J, Rossetti L. Surgical removal of visceral fat reverses hepatic insulin resistance. Diabetes. 1999; 48:94-98**.**
5. Bello AK, de Zeeuw D, El Nahas M, *et al*. Impact of weight change on albuminuria in the general population. Nephrol Dial Transplant. 2007; 22:1619-1627.
6. Beers RF, Sizer IW. Journal of Biological Chemistry. 1952; 195:133-140.
7. Callister TQ, Raggi P, Cooil B, *et al*. Effect of HMG-CoA reductase inhibitors on coronary artery disease as assessed by electron-beam computed tomography. N Engl J Med.
8. Carey DG, Jenkins AB, Campbell LV, Freund J, Chisholm DJ. Abdominal fat and insulin resistance in normal and overweight women: direct measurements reveal a strong relationship in subjects at both low and high risk of NIDDM. Diabetes. 1996; 45:633-638.
9. Chakravarti R, *et al*. Antidiabetic and hypolipidemic potential of DRF-2519 a dual activator of PPARa and PPARg.Eur.j.pharmacol. 2004; 491:195206.
10. Dunn MJ, Hood VL. Prostaglandins and the kidney, The American Journal of Physioloev. 1977; 233(3):169-184.
11. Duncan BB, Schmidt Ml, Pankow IS, Bang H, Couper D, Ballantyne CM, Hoogeveen RC, Heiss G: Adiponectin and the development of type 2 diabetes: the Atherosclerosis Risk in Communities Study. Diabetes, 2004.
12. Saad E, Charra B, Raj DSC. Hypertension controlwith daily dialysis, Seminars in Dialysis. 2004; 17(4):295-298.
13. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998; 352:854-865.
14. Finck BN, Lehman JJ, Leone TC, Welch MJ, Bennett MJ, Kovacs A, *et al*. The cardiac phenotype induced by PPAR-a overexpression mimics that caused by diabetes

mellitus. J Clin Invest. 2002; 1 09:121-30.
15. Finn AV, Kolodgie FD, Virmani R. Correlation Between Carotid Intimal/Medial Thickness and Atherosclerosis. A Point of View From Pathology [published online ahead of print August 13, 2009]. Arterioscler Thromb.
16. Flamming, *et al*. Genotoxicity testing of salacia oblonga extract. Food and chemical toxicology. 2006; 44:1868-1874.
17. Opelz G, Dohler B. Improved long-term outcomes after renal transplantation associated with blood pressure control, American Journal of Transplantation. 20005; 5(11):2725- 2731..
18. Unal Al G, Duman S, Ozkahya M, *et al*. Strict volume control normalizes hypertension in peritoneal dialysis patients, American Journal of Kidney Diseases. 2001; 37(3):588-593.
19. Howard G, Burke GT, Szklo M, *et al*. Active and passive smoking are associated With increased carotid wall thickness. The Atherosclerosis Risk in Communities study. Arch Intern Med.
20. Huang *et al*., Salacia oblonga root improves cardiac lipid metabolism in Zucker diabetic fatty rats: modulation of cardiac PPAR- ct mediated transcription Of fatty acid and metabolic genes. Toxciology and applied pharmacology\. 2006; 210:78-85.
21. Isbel NM, Haluska B, Johnson DW, *et al*. Increased targeting of cardiovascular risk factors in patients with chronic kidney disease does not improve atheroma burden or cardiovascular function. Am Heart J. 2006; 151:745-753.
22. Ishani A, Xue JL, Himmelfarb J, *et al*. Acute kidney injury increases risk of ESRD among elderly. J Am Soc Nephrol. 2009; 20:223-228.
23. Jinnouchi Y, Yamagishi S, Takeuchi M, Ishida S, Jinnouchi Y, Jinnouchi J, *et al*. At0rvastatin decreases serum levels of advanced glycation end products (AGES) in patients with type 2 diabetes. Clin Exp Med. 2006; 6:191-3.
24. Johnson RJ, Riviighn SD, Kim YG, *et al*. Reappraisal of the pathogenesis and consequence of hyperuricemia in hypertension, cardiovascular disease and renal disease. Am J Kidney Dis. 1999; 33:225-234.
25. Kakkar P, Das B, Viswanathan PN. A modified spectrophotometric assay of superoxide dismutase. Ind. J of Biochem. Biophys. 1984(21): 130-32.
26. Kakkar P, Das B and Viswanathan PN.: A modified spectrophotometric assay of superoxide dismutase. Ind. J of Biochem. Biophys. (21): 130-32, 1984.
27. Lott JA, Lu CJ. Lipase isoforms and amylase isoenzymes assays and application in the diagnosis ofacute pancreatitis. Clin. Chem. 1991, 37:361.
28. Israelian-Konaraki Z, Reaven PD. peroxisome proliferator-activated receptor aalpha and atherosclerosis: from basic mechanisms to clinical implications. Cardiol Rev; 13:240-6; 2005.
29. Manjunath G, Tighiouart H, Coresh J, *et al*. Level of kidney function as a risk factor for cardiovascular outcomes in the elderly. Kidney Int. 2003;63:1121—1129.
30. Manjunath G, Tighiouart H, Ibrahim H, *et al*. Level of kidney function as a risk factor for atherosclerotic cardiovascular disease in the community. J Am coil Cardiol.
31. National Kidney Foundation. K/DOQI kidney disease outcome quality initiative. Am J Kidney Dis.
32. Neely JR, Rovetto MJ, Oram JF. Myocardial utilization of carbohydrate and lipids. Prog Cardiovasc Dis; 15:289-329; 1972.
33. O'Brien MM, Gonzales R, Shroyer AL, *et al*. Modest serum creatinine elevation affects adverse outcome after general surgery. Kidney Int. 2002;62:585— 592.
34. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Annals of Biochemistry 1979 (95): 351-58.
35. Preston E, Ellis MR. Kulinskaya E, Davies AH, Brown EA. Association between carotid artery intima-media thickness and cardiovascular risk factors in CKD. Am J Kidney Dis.
36. Prieto, P., Pineda, M.. & Aguilar, M. Spectrophotometric quantitation of antioxidant capacity through the formation of phosphomolybdenum complex: specific application to determination of vitamin E. Analytical Biochemistry, 269: 337-341; 1999.
37. R. Agarwal and R. R. Lewis, "Prediction of hypertension in chronic hemodialysis patients," Kidney International, vol. 60, no. 5, pp. 1982-1989, 2001.
38. R. Cocchi, E. D. Esposti, A. Fabbri *et al*., "Prevalence of hypertension in patients on peritoneal dialysis: results of an Italian multicentre study," Nephrology Dialysis Transplantation, vol. 14, no. 6, pp. 1536-1540, 1999.
39. strippoli GF, Navaneethan SD, Johnson DW, *et al*. Effects of statins in patients with chronic kidney disease: metaanalysis and meta-regression of randomised controlled trials. BMJ. 2008;336:645-651.
40. studer M, Briel M, Leimenstoll B, *et al*. Effect of different antilipidemic agents and diets on mortality: a systematic review. Arch Intern Med. 2005;165:725730.
41. Taal MW, Brenner BM. Renal risk scores: Progress and prospects. Kidney Int.
42. Tanaka T, Yamamoto J, Iwasaki S, Asaba H, Hamura H, Ikeda Y, Watanabe M,
43. U S Renal Data System, USRDS 2010 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Bethesda, Md, USA, 2010.
44. U.S. Renal Data System. USRDS 2007 Annual Data Report: Atlas of End Stage Renal Disease in the United States. Bethesda, Md: National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases; 2007. Available at: www.usrds.org.
45. Vaziri ND, Moradi H. Mechanisms of dyslipidemia of chronic renal failure. Hemodial Int. 2006; 10:1-7.
46. Vaziri ND, Sato T, Liang K. Molecular mechanisms of altered cholesterol metabolism in rats with spontaneous focal glomerulosclerosis. Kidney Int.
47. wolf BW, Weisbrode SE. Safety evaluation of an extract from Salacia oblonga. Food and chemical Toxicology 41, 867-874. (Flammang, A.M., Erexson, G.L., Mecchi,

M.S., Murli, H., 2006. Genotoxicity testing of a Salacia oblonga extract. Food and Chemical Toxicology. 2003; 44:1868-1874.
48. Wright RS, Reeder GS, Herzog CA, *et al*. Acute myocardial infarction and renal dysfunction: a high-risk combination. Ann Intern Med. 2002; 137:563-570.
49. Yamagishi S, Matsui T, Nakamura K. Atorvastatin and diabetic vascular complications. Curr Pharm Des. 2006; 12:1549-54.
50. Yamagishi S, Matsui T. Advanced glycation end products (AGEs), oxidative stress and diabetic nephropathy. Oxid Med Cell Longev. 2010; 3:1-8.
51. Zhao Y, Marcel YL. Serum albumin is a significant intermediate in cholesterol transfer between cells and lipoproteins. Biochemistry. 1996; 35:71747180.
52. Zhou YT, Grayburn P, Karim A, Shimabukuro M, Higa M, Baetens D, *et al*. Lipotoxic heart disease in obese rats: implications for human obesity. Proc Natl Acad Sci D S A. 2000; 97:1784-89.