Original Research Article

A study of response to lipid lowering therapy in non-diabetic patients with dyslipidemia at tertiary health care center

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Abstract

Background: In spite of considerable advances in the understanding of the pathophysiology of ischemic stroke, therapeutic options, particularly pharmacological agents for prevention and treatment are still limited. **Aims and Objectives:** To Study of response to lipid lowering therapy in non-diabetic patients with dyslipidemia at tertiary health care center. **Methodology:** All non-diabetic patients with features of stroke admitted to tertiary care hospital from December 2013 to December 2015 were taken for the study. Data will be collected by means of case record form. All non-diabetic patients of cerebrovascular accidents were enrolled in this study with informed consent and detailed patient information were included into study. The clinical outcome after 3 month was assessed by the Modified Rankin Scale (MRS). The statistical analysis done of paired t-test analyzed by SPSS 19 version software. **Result:** The change of serum TG after 3 months is 23.6mg/dl and P value is < 0.01 which is highly significant. The change of LDL levels after 3 months is 12.04mg/dl and P value is < 0.01 which is highly significant. The change of HDL levels after 3 months is 2.76mg/dl and P value is < 0.01which is highly significant. The change of VLDL levels after 3 months is 3.72mg/dl and P value is < 0.01which is highly significant.MRS score showed a good clinical outcome with reduction in LDL levels and the corresponding P value is 0.26 and r value of 0.15 which is significant. **Conclusion:** In the present study there is a significant change in bio-chemical values of lipid profile after treating with statins for a duration of 3 months, but there is no significant improvement in clinical outcome except for LDL. So, it can be concluded that measures to reduce serum LDL levels will be useful in secondary prevention of thrombotic stroke.

Key Words: Lipid lowering therapy, dyslipidemia, Rankin Scale (MRS), Lipid profile, CVA (Cerebrovascular accidents).

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INTRODUCTION

In spite of considerable advances in the understanding of the pathophysiology of ischemic stroke, therapeutic options, particularly pharmacological agents for prevention and treatment are still limited. Stroke is still the third leading cause of death and the most frequent cause of permanent disability in adults worldwide[1]. Systemic and local processes of endothelial dysfunction, thrombogenesis, inflammatory and oxidative stress damage, and angiogenesis play an important role in cerebral ischemic pathogenesis and may represent strategic targets for prevention and treatment of ischemic stroke[2]. Statins lower serum cholesterol level by inhibiting hydroxymethylglutaryl-coenzymeA (HMG-CoA) reductase[3]. Statins have been found to improve endothelial function, modulate thrombogenesis, attenuate inflammatory and oxidative stress damage, and facilitate angiogenesis far beyond lowering cholesterol levels[4-7].

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MATERIAL AND METHODS

All non-diabetic patients with features of stroke admitted to tertiary care hospital from December 2013 to December 2015 were taken for the study. Data will be collected by means of case record form. All non-diabetic patients of cerebrovascular accidents were enrolled in this study with informed consent and detailed patient information were included into study while, Patients having diabetes mellitus type 1 or 2 or impaired glucose tolerance (ADA Guidelines 2014 is used for diagnosis of diabetes mellitus, Patients with history of head injury, Patients on drug therapy such as OCP's, steroids, diuretics and anticoagulant drugs, Patients already diagnosed with dyslipidemia, Patients on lipid lowering agents, Diagnosed case of liver diseases, kidney diseases, pancreatitis, coronary artery disease and thyroid disease, Diagnosed case of malignancy, Patients lost for follow up were excluded from the study. All the patients who fulfilled the inclusion criteria were enrolled in this study Lipid profile after 8 hours of fasting, Serum total cholesterol, Serum triglyceride, Serum HDL, Serum LDL, Serum VLDL was done The MRS is a commonly used scale for measuring the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability and it has become the most widely used clinical outcome measure for stroke in clinical trials,[8]

The Modified Rankin Scale (MRS)

The scale runs from 0-6, running from perfect health without symptoms to death.

0: No symptoms.

1: No significant disability. Able to carry out all usual activities despite some symptoms.

2: Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.

3: Moderate disability. Requires some help, but able to walk unassisted.

4: Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.

5: Severe disability. Requires constant nursing care and attention, bedridden, incontinent.

6: Dead.

The statistical analysis done of paired t-test analyzed by SPSS 19 version software.

RESULT

Lipid level was estimated in ischemic stroke patients at the onset of stroke and after 3 months. Lipid profile testing done after 8 hrs fasting and all the lipid parameters were tested and standard reference value is used as a cut off.

Table 1: Distribution of the patients as per the STC

	No. of patients (STC at onset)		Total	No. of patients (STC after 3 months of therapy)		Total
	Male	Female	Total	Male	Female	
Normal	24 (62%)	15 (38%)	39 (78%)	25 (60%)	17 (40%)	42 (84%)
Abnormal	6 (55%)	5 (45%)	11 (22%)	5 (63%)	3 (37%)	8 (16%)
Total	**30**	**20**	**50**	**30**	**20**	**50**

STC level was normal in 39 patients (78%) and abnormal in 11 patients (22%) at onset of stroke but after 3 month of therapy STC levels become normal in 42 patients (84%) and abnormal in 8 patients (16%). So there was only 6% improvement in STC values after 3 month of therapy. The minimum STC at onset was found to be 145 mg/dl And maximum was 440 mg/dl with mean STC of 195.8mg/dl. The minimum STC after 3 months of therapy was found to be 141mg/dl And maximum was 380mg/dl with mean value of 182.6 mg/dl. The maximum STC abnormality was observed in male patients (55%) but after 3 month of therapy there is no significant change in parameter in both sexes.

Table 2: Distribution of the patients as per the TG

	No. of patients (Triglycerides at Onset)		Total	Triglycerides after 3 months of therapy		Total
	Male	Female		Male	Female	
Normal	11 (68%)	5 (32%)	16 (32%)	13 (72%)	5 (28%)	18 (36%)
Abnormal	19 (56%)	15 (34%)	34 (68%)	17 (54%)	15 (36%)	32 (64%)
Total	**30**	**20**	**50**	**30**	**20**	**50**

TG levels are normal in 16 patients (32%) and abnormal in 34 patients (68%) at onset but after 3 months of therapy the levels are normal in 18 patients (36%) and abnormal in 32 pts (64%). The minimum TG level at onset was found to be 95mg/dl and maximum TG observed was 310 mg/dl with mean value of 210 mg/dl.

After 3 month of therapy the lowest TG level observed was 92 mg/dl and highest value observed was 270 mg/dl with mean value of 186 mg/dl. The maximum TG abnormality was observed in male patients 19 (56%) but after 3 month of therapy there is 4% improvement in male patients and no improvement in female patients observed.

Table 3: Distribution of the patients as per the LDL

	NO. of patients (LDL at onset)		Total	NO. of Patients(LDL after 3 months of therapy)		Total
	Male	Female		Male	Female	
Normal	13 (73%)	5 (27%)	18 (36%)	20 (67%)	10 (33%)	30 (60%)
Abnormal	16 (50%)	16 (50%)	32 (64%)	9 (45%)	11 (55%)	20 (40%)
Total	**29**	**21**	**50**	**29**	**21**	**50**

TG levels are normal in 16 patients (32%) and abnormal in 34 patients (68%), but after 3 months of therapy the levels are normal in 15 patients (30%) and abnormal in 35 pts (70%). The minimum LDL level observed at onset was 56mg/dl and maximum was 150 mg/dl with mean value of 110.5 mg/dl. The abnormal LDL was observed in equal number of patients (16) in both the sexes. After 3 month of therapy 24% of patients showed significant reduction in LDL concentration. Maximum improvement was observed in male patients (14%) and only 10% improvement in female patients was observed.

Table 4: Distribution of the patients as per the HDL

	No. of patients (HDL at onset)		TOTAL	No. of patients (after 3 months of therapy)		Total
	Male	Female		Male	Female	
Normal	14 (70%)	6 (30%)	20 (40%)	15 (66%)	8 (34%)	23 (46%)
Abnormal	16 (54%)	14 (46%)	30 (60%)	15 (56%)	12 (44%)	27 (54%)
Total	**30**	**20**	**50**	**30**	**20**	**50**

HDL levels are normal in 20 pts (40%) and abnormal in 30 pts (60%) at onset but after 3 months of therapy levels are normal in 23 pts (46%) and abnormal in 27 pts (54%). The minimum HDL at onset was found to be 25 mg./dl and max was 62 mg/dl with mean value of 37.4 mg/dl. After 3 month of therapy the minimum HDL observed was 30mg/dl and maximum HDL level was 65mg/dl with mean value of 41mg/dl. The maximum HDL abnormality was observed in male patients (54%) and maximum improvement observed in female patient (4%) after 3 month of therapy.

Table 5: Distribution of the patients as per the VLDL

	No. of patients (VLDL at onset)		Total	NO. of patients(VLDL after 3 months of therapy)		Total
	Male	Female		Male	Female	
Normal	11 (69%)	5 (31%)	16 (32%)	11 (69%)	5 (31%)	16 (32%)
Abnormal	20 (59%)	14 (41%)	34 (68%)	20 (59%)	14 (41%)	34 (68%)
Total	**31**	**19**	**50**	**31**	**19**	**50**

VLDL levels are normal in 16 pts (32%) and abnormal in 34 pts (68%) at onset but after 3 months of therapy there is no change in biochemical values of VLDL in both sexes The minimum VLDL at onset was found to be 19mg/dl and maximum was 62mg.dl with mean value of 41.5mg/dl. The minimum VLDL after 3 months of treatment was 18 mg/dl and maximum was 54 mg/dl with mean value of 37.8 mg/dl. The maximum VLDL level abnormality was observed in male 20 patients (59%) but after 3 month of therapy there was no change in parameter was observed.

Table 6: Paired Differences

Lipids	Mean	Std. Deviation	Std. error	P Value
Serum Total cholesterol	13.1400	18.30023	5.077	<.001 vhs
TG	23.6600	12.36347	6.886	<.001 vhs
LDL	12.0400	12.36347	6.886	<.001 vhs
HDL	2.7600	4.00286	4.876	<.001 vhs
VLDL	3.7200	7.53235	3.492	<.001 vhs

The change of serum Total cholesterol after 3 months is 13.14mg/dl and P value is < 0.01 which is highly significant. The change of serum TG after 3 months is 23.6mg/dl and P value is < 0.01 which is highly significant.

The change of LDL levels after 3 months is 12.04mg/dl and P value is < 0.01 which is highly significant.
The change of HDL levels after 3 months is 2.76mg/dl and P value is < 0.01which is highly significant.
The change of VLDL levels after 3 months is 3.72mg/dl and P value is < 0.01which is highly significant.

Table 7: Co-relation between MRS (Modified Rankin Scale) (After 3 month of therapy) and Lipid profile

MRS	Serum cholesterol	Triglycerides	LDL	HDL	VLDL
R (pearson value)	.123	.130	.150	.100	.129
P (p value)	0.397	0.370	0.26	0.490	0.373
N (no. of patients)	50	50	50	50	50

MRS score showed a good clinical outcome with reduction in LDL levels and the corresponding P value is 0.26 and r value of 0.15 which is significant.

DISCUSSION

Statins have also been proved to significantly decrease cardiovascular risk and to improve clinical outcome[8]. Could statins be the new candidate agents for the prevention and treatment of ischemic stroke? In recent years, a vast expansion in the understanding of the pathophysiology of ischemic stroke and the pleiotropic effects of statins has occurred. Clinical trials involving statins for prevention and treatment of ischemic stroke have begun. Treatment with statins either before, or early after cerebral arterial occlusion has been proved to associate with reduced infarct volume and improved neurological function in animal models[9-11]. In several large clinical trials, the effects of statins on stroke prevention and treatment have also been well established[12-14]. Statins may have surpassed other pharmacologic medicine in the reduction of the incidence of stroke and total mortality[15,16]. These facts force us to revisit ischemic stroke and consider new strategies for prevention and treatment and The relationship between stroke and cholesterol becomes even more complex with the notion that stroke outcome might be negatively associated with cholesterol levels. For example, the Lausanne Stroke Registry demonstrated that stroke patients with higher cholesterol levels had better outcomes after 1 month. In agreement with this, a retrospective study performed by Dyker *et al* (1997) found more patients dead or disabled after stroke with low cholesterol levels at stroke onset, Taken together, there are many open questions regarding the relationship between cholesterol and stroke. The American Heart Association (AHA) does not list cholesterol as a risk factor.[17,18] The present study showed no significant relationship with cholesterol levels and stroke incidence which correlates with studies conducted by Prospective studies collaboration 1995; Dauber *et al*, Kagan *et al*, Harmisen *et al*.[19]In our study the cholesterol levels after 3 months of statins showed no significant fall and no significant clinical improvement. After treatment with statins, study revealed a significant fall in the triglyceride level but was not significant in the clinical scenario in accordance with MRS scale. Njolstal *et al* study states that in patients with ischaemicstroke hypertriglyceridemia affects males more than females which is correlated in the present study with 56% males affected.[20] In the present study the LDL levels declined after starting with statins and showed a significant improvement in the clinical outcome (p value=0.026).Hachinski *et al*study states that patients have a high risk of thrombotic stroke with high LDL levels at onset which correlates with our study.[21] In present study after 3 months of therapy with statins there was no significant change in the HDL levels and with no improvement in the clinical outcome.
After starting therapy with statins the outcome at 3 months showed a no change in the VLDL levels and also no significant improvement in the clinical outcome. Garg RK *et al* stated increased risk of thromboembolic stroke with high serum VLDL levels which correlate in the present study with VLDL level abnormality seen in 68% population.[22]

CONCLUSION

In the present study there is a significant change in bio-chemical values of lipid profile after treating with statins for a duration of 3 months, but there is no significant improvement in clinical outcome except for LDL. So it can be concluded that measures to reduce serum LDL levels will be useful in secondary prevention of thrombotic stroke. However we feel that it is too premature to draw definite conclusion in view of 3 month follow up. This may need larger duration of prospective study to draw more definite conclusion and also help us in prevention and treatment of dyslipidemia which goes a long way in stroke management.

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