

Goal achievement of Low-density lipoprotein cholesterol levels in patients with ischemic stroke and hyperlipidemia at Prasat Neurological Institute

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Introduction

Hyperlipidemia is a healthcare problem in Thai population and one of the important risk factors in coronary heart disease, ischemic heart disease, acute myocardial infarction, peripheral arterial disease, and cerebrovascular disease. Stroke is a major cause of mortality and morbidity in Thailand. The data from the cause of death in 1990 revealed that stroke was a major cause of death in female and a third of death in male Thai people.¹ Moreover, this rate also increases every year in Thailand. Stroke is also a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15% to 30% being permanently disabled. Prevalence of stroke in Thailand is 690 : 100,000 population , approximately almost 500,000 stroke patients per 72 millions of Thai people.²

Large epidemiology studies in ischemic stroke have shown a modest association of elevated total cholesterol or low-density lipoprotein cholesterol (LDL-C) with the increased risk of ischemic stroke and the relationship between low LDL-C and the greater risk of intracerebral hemorrhage.³ The use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) has been approved by regulatory agencies for prevention of ischemic stroke in patients with coronary heart disease (CHD). Statins therapy with intensive lipid-lowering effects is recommended for patients with atherosclerotic ischemic stroke or transient ischemic attack (TIA) and without known CHD to reduce the risk of stroke and cardiovascular events.⁴ For those patients with atherosclerotic ischemic stroke or TIA and history of CHD, it is recommended that clinicians follow the current 2011 the American Heart Association/American Stroke Association (AHA/ASA) guidelines⁵ for lipid management, which emphasize utilization of National Cholesterol Education Panel III guidelines (NCEP III).⁶ Prasat Neurological Institute (PNI), the excellent center of stroke knowledge and treatment in Thailand, serviced amounts of 22,016 out-patients and 1,040 in-patients in cerebrovascular diseases per year (data since 2008 to 2010). Multidisciplinary team and also clinical pharmacist worked in stroke unit since 2010. According to the concept of aggressive reduction in cholesterol level, we undertook retrospective charts review to find out the goal achievement of LDL-C levels in patients with ischemic stroke and hyperlipidemia and prevalence of adverse drug reactions including myalgia and rhabdomyolysis in these patients.

Method

Design and Study Settings ; A cross-sectional descriptive design was employed in this study. This study was conducted at the Inpatient department (IPD) of stroke unit at Prasat Neurological Institute, Bangkok, Thailand, during March to November 2011.

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Sample ; Ischemic stroke patients with hyperlipidemia were enrolled in this study, admitted in stroke unit, Prasat Neurological Institute during March to November 2011. The inclusion criteria for participate in this study were as follow ; (1) patients received statin drug before or during admission (2) the baseline LDL-C level was recorded before hospital discharge . The exclusion criteria were as follow ; (1) patient which diagnosis of cardioembolic stroke (2) loss of connection after hospital discharge.

Data collection procedure; This study was approved by the Institutional Review Board and Independent Ethics Committee Prasat Neurological Institute, Department of Medical Services, Ministry of Public Health, Thailand. Data regarding general, medical and family history were recorded at stroke unit during admission by patient interview and medical chart review. Laboratory data and adverse drug reactions including myalgia and rhabdomyolysis were recorded by medical chart review. First laboratory data were collected at follow-up phase which patients continued the same statin dasages. Medical charts lacked of first laboratory data at follow-up phase, adverse drug reactions including myalgia and rhabdomyolysis were recorded by medical chart review at first follow-up phase after discharged from stroke unit. Medical histories were reviewed to separate patients in 4 groups according to statin drug use history and the underlying disease of diabetes mellitus (DM).

Data Analyses ; The statistics including frequency, percentage, range, mean, and standard deviation were employed to describe demographic data, laboratory data at admission and follow up, mean LDL-C and goal achievement of LDL-C level . Paired t – test was used to compare means of laboratory data and LDL-C at admission and follow-up visit.

Results ; One hundred and ninety seven patients were enrolled in this study, admitted at stroke unit during March to November 2011. Four groups were separated according to LDL-C goal accomplishment. There were group A (patient without diabetes mellitus (DM) and never used statins), group B (patient without DM and have been used statins), group C (patient with DM and never used statins) and group D (patient with DM and have been used statins). Demographic data of these groups was described in Table 1. Laboratory data including mean of cholesterol , high density lipoprotein (HDL) , triglyceride (TRI) ,alanine transaminase (ALT) , aspartate transaminase (AST) , creatine phosphokinase (CPK) , glucose and hemoglobin A1c(HbA1c) blood level , before admission and follow up phase were recorded in table 2.

The baselines of LDL-C level in group A,B,C and D were 140.93 , 106.05, 141.38, and 113.37 mg/dL, respectively. The mean duration of follow up phase in group A,B,C and D were 133.17 , 136.60 , 91.45 and 112.92 days as shown in table 3.

According to LDL-C goal accomplishment (LDL-C < 100 mg/dL), Goal achievement of LDL-C levels in group A and group B were 82.22% (average LDL-C=77.76 mg/dL) and 68.89% (average LDL-C=75.00 mg/dL), as shown in table 4 .

According to LDL-C goal accomplishment (LDL < 70 mg/dL), Goal achievement of LDL-C levels in group C and group D were 21.74% (average LDL-C = 55.60 mg/dL) and 37.04% (average LDL-C = 57.10 mg/dL) as shown in table 5.

Table 1. Demographic data of 197 patients with ischemic stroke and hyperlipidemia separated in 4 groups.

Demographic data	group A	group B	group C	group D
	N=68	N=59	N=32	N=38
SEX (%)				
- Male	47 (69.11%)	33(55.93%)	17(53.13%)	14(36.84%)
- Female	21(30.89%)	26(44.07%)	15(46.87%)	24(63.16%)
Mean age (years)				
- Standard deviation	13.29	12.68	10.94	9.66
- Range	16 - 85	35 - 83	44 - 85	43 - 78
Smoking history (%)				
- No	35 (51.47%)	39 (66.11%)	14 (43.75%)	30 (78.95%)
- Smoking in the past	3 (4.41%)	1 (1.69%)	5 (15.63%)	1 (2.63%)
- Smoking in the present	30 (44.12%)	18 (30.51%)	13 (40.62%)	7 (18.42%)
- Unknown	0 (0.00%)	1 (1.69%)	0 (0.00%)	0 (0.00%)
Alcohol drinking (%)				
- No	39 (57.35%)	36 (61.02%)	18 (56.25%)	32 (84.21%)
- Drinking in the past	3 (4.41%)	4 (6.78%)	3 (9.38%)	1 (2.63%)
- Drinking in the present	26 (38.24%)	18 (30.51%)	11 (34.37%)	5 (13.16%)
- Unknown	0 (0.00%)	1 (1.69%)	0 (0.00%)	0 (0.00%)

- Note ; group A ; patient without diabetes mellitus (DM) and never used statins , group B; patient without DM and have been used statins, group C; patient with DM and never used statins and group D; patient with DM and have been used statins, Smoking in the past ; Smoking was discontinued more than 1 year , Drinking in the past ; Drinking was discontinued more than 1 year

Table 2 Laboratory measures at admission and follow-up in 4 groups of patients.

Laboratory measures	Group A			Group B			Group C			Group D		
	at admission	at follow-up	P-value	at admission	at follow-up	P-value	at admission	at follow-up	P-value	at admission	at follow-up	P-value
Total cholesterol (mg/dL)												
Mean (SD)	206.24 (36.44)	147.61 (28.26)	< 0.001	170.20 (44.48)	159.91 (28.27)	0.604	214.47 (52.31)	172.23 (32.83)	< 0.001	174.33 (52.20)	161.71 (59.71)	0.148
Range	119 - 332	98 - 236		84 - 267	106 - 214		130 - 323	119 - 236		84 - 328	95 - 324	
No. of patients (%)	67 (98.53%)	28 (41.18%)		54 (91.53%)	32 (54.24%)		32 (100.00%)	13 (40.63%)		36 (94.74%)	17 (44.74%)	
HDL cholesterol (mg/dL)												
Mean (SD)	43.29 (14.18)	48.06 (14.31)	0.023	39.14 (12.90)	46.94 (12.58)	0.002	37.09 (11.72)	45.07 (13.11)	0.001	36.95 (11.67)	46.63 (16.91)	0.008
Range	17-88	24 - 81		10 - 82	32 - 81		16 - 63	33 - 85		20 - 83	26 - 95	
No. of patients (%)	68 (100.00%)	34 (50.00%)		56 (94.92%)	35 (59.32%)		32 (100.00%)	15 (46.88%)		37 (97.37%)	19 (50%)	
Triglyceride (mg/dL)												
Mean (SD)	133.63 (72.09)	104.23 (37.22)	0.194	117.61 (71.03)	120.24 (59.29)	0.985	172.38 (84.78)	149.60 (76.22)	0.181	130.11 (43.43)	157.32 (95.21)	0.236
Range	55 - 475	42 - 198		40 - 397	37 - 300		65 - 336	60 - 336		54 - 240	52 - 456	
No. of patients (%)	68 (100.00%)	31 (45.59%)		57 (96.61%)	37 (62.71%)		32 (100%)	15 (46.88%)		37 (97.37%)	19 (50%)	
ALT (IU/L)												
Mean (SD)	22.52 (18.89)	27.73 (18.88)	0.366	25.26 (17.01)	24.86 (15.18)	0.747	27.08 (14.49)	30.32 (24.30)	0.456	28.47 (14.88)	24.26 (10.66)	0.277
Range	9 - 103	10 - 103		8 - 82	10 - 81		6 - 61	10 - 119		9 - 66	10 - 56	
No. of patients (%)	23 (33.82%)	33 (48.53%)		27 (45.76%)	37 (62.71%)		12 (37.50%)	19 (59.38%)		17 (44.74%)	19 (50%)	
AST (IU/L)												
Mean (SD)	27.45 (12.23)	26 (8.30) (68.66)	0.110	30.56 (17.01)	28.03 (9.45)	0.804	25.92 (5.18%)	25.37 (8.76)	0.834	31.59 (11.12)	23.37 (7.48)	0.014
Range	14 - 56	11 - 56		12 - 86	13 - 57		18 - 34	13 - 48		15 - 54	13 - 39	
No. of patients (%)	22 (32.35%)	32 (47.06%)		27 (45.76%)	35 (59.32%)		12 (37.50%)	19 (59.38%)		17 (44.74%)	19 (50.00%)	
Creatine kinase (IU/L)												
Mean (SD)	88.33 (8.96)	117 (68.66)	-	80.25 (45.04)	134.27 (54.12)	0.295	85 (5.18)	99.50 (45.74)	-	77 (9.90)	95 (58.62)	-
Range	78 - 94	43 - 240		29 - 126	21 - 208		49 - 121	34 - 140		70 - 84	35 - 165	
No. of patients (%)	3 (4.41%)	6 (8.82%)		4 (6.77%)	11 (18.64%)		2 (6.25%)	4 (12.5%)		2 (5.26%)	5 (13.16%)	
Fasting blood sugar (mg/dL)												
Mean (SD)	97.90	101.26	0.268	102.33	101.21	0.139	160.38	152.48	0.71	136.97	128.35	0.576

	(15.26)	(15.14)	(25.85)	(15.28)	(66.69)	(56.92)	(47.50)	(40.41)		
Range	65 – 137	78 – 145	71 – 200	74 – 151	60 – 375	86 – 322	70 – 261	46 – 228		
No. of patients (%)	67 (98.53%)	39 (57.35%)	58 (98.31%)	33 (56.93%)	32 (100.00%)	23 (71.88%)	38 (100.00%)	31 (81.58%)		
HbA1c (%)										
Mean (SD)	6.28 (1.63)	6.4 (0.96)	5.98 (0.68)	5.7 (0.28)	9.15 (2.51)	8.85 (3.33)	0.779	7.95 (2.10)	6.9 (0.83)	0.427
Range	5.10 – 13.00	5.8 – 8	5 – 6.8	5.5 – 5.9	4.9 – 13.4	5.5 – 13.7	6 – 13	6 – 8.2		
No. of patients (%)	21 (30.88%)	5 (7.35%)	10 (16.95%)	2 (3.39%)	22 (68.75%)	6 (18.75%)	21 (55.26%)	5 (13.16%)		

* paired t test, significance level of 0.05

Note: Group of patients: group A = patients without diabetes mellitus (DM) and never used statins; group B = patients without DM and have been used statins; group C = patients with DM and never used statins; group D = patients with DM and have been used statins.

Abbreviation: HDL = high density lipoprotein; ALT = alanine aminotransferase; AST = aspartate aminotransferase; HbA1C = glyceated hemoglobin.

Table 3 Comparability of the means LDL-C level at admission and follow-up separated in each group

DATA	Mean LDL-C at admission ,mg/dL (SD) (Range)	No. of patients at admission,%	Mean Duration (days), SD	Mean LDL -C at follow-up ,mg/dL (SD) (Range)	No. of patients Follow-up,%	P-value
Group A	140.93 (34.98) (62 – 283)	68 (100.00%)	133.17 (93.55)	85.18, (22.75) (11 – 326)	45 (66.18%)	<0.001
Group B	106.05 (36.91) (35 -185)	59 (100.00%)	136.60 (99.00)	87.71(25.54) (10 – 406)	45 (76.27%)	<0.01
Group C	141.38 (39.04) (81-236)	32 (100.00%)	91.45 (70.68)	100.43 (43.03) (14-262)	23 (71.88%)	<0.001
Group D	113.37 (43.96) (43-223)	38 (100.00%)	112.92 (90.34)	89.85 (41.21) (14 – 327)	27 (71.05%)	<0.01

Note ; * pair t – test, group A ; patient without diabetes mellitus (DM) and never used statins , group B; patient without DM and have been used statins, group C; patient with DM and never used statins and group D; patient with DM and have been used statins

Table 4 Goal achievement of LDL-C levels according to LDL-C goal accomplishment

Group	LDL-C < 100 mg/dL			LDL-C ≥100 mg/dL		
	Number of patients (%)	Mean LDL-C (SD)	Range	Number of patients (%)	Mean LDL-C (SD)	Range
Group A (N=45)	37 (82.22%)	77.76 (14.38)	42 - 99	8 (17.77%)	119.50 (23.48)	100 - 168
Group B (N=45)	31 (68.89%)	75.00 (15.92)	38 - 98	14 (31.11%)	115.86 (19.60)	100 - 152

Implications of the study

The findings from this study utilize for improvement the health care of patients with ischemic stroke and hyperlipidemia in this stroke unit and others. Multidisciplinary team and also clinical pharmacist who work in stroke unit should be pay attention to assess the efficacy to achievement of NCEP goal of LDL-C level especially patients in group B, C and D.

Limitations

Firstly, this study was not excluded some patients who reached the goal of LDL-C level at admission visit that made the goal achievement of LDL-C level in this study was rather overestimated. Secondly, retrospective study from medical chart review, adverse drug reactions of statin were not found which likely underreported.

Conclusion

This study discovered the goal achievement of LDL-C in patients with ischemic stroke and hyperlipidemia at Prasat Neurological Institute, separated patients groups according to statin drug use history and the underlying disease of diabetes mellitus (DM). According to LDL-C goal accomplishment (LDL-C < 100 mg/dL), Goal achievement of LDL-C levels in group A and group B were 82.22% (average LDL-C=77.76 mg/dL) and 68.89% (average LDL-C=75.00 mg/dL). According to LDL-C goal accomplishment (LDL < 70 mg/dL), Goal achievement of LDL-C levels in group C and group D were 21.74% (average LDL-C = 55.60 mg/dL) and 37.04% (average LDL-C = 57.10 mg/dL). In aspect of adverse drug reaction, myalgia or rhabdomyolysis were not found in this study.

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