

Use of Statins in Unstable Angina and their Effect on Recurrent Hospital Admissions

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ABSTRACT

Objective: To determine the effect of lipid lowering with the use of statins on recurrent anginal symptoms.

Study design: Case-control type of study.

Place and duration: The study was conducted in the department of Cardiology, Bahawal Victoria Hospital Bahawalpur from 15th March 2010 to 15th March 2012.

Methodology: During the initial one year of study, patients fulfilling the inclusion criteria were registered. The data regarding the age at the time of presentation, gender, co-morbidities (diabetes mellitus, hypertension, smoking, BMI), baseline lipid levels and drugs taken for symptomatic coronary artery disease was collected on a predesigned proforma. Lipid lowering therapy was optimized in those patients who were having deranged lipid profile. During the second year of study, the data regarding frequency of anginal symptoms and hospital admissions was collected and the relation between serum lipid levels and recurrent hospital admissions was determined.

Results: A total of 1206 patients met the inclusion criteria of the study, 594 having normal lipid levels (group A) and 612 having deranged serum lipid profile (group B). It was found that during the one year follow up time, 99 patients in group B required recurrent hospital admissions for symptomatic angina as compared to 36 in group A, and this difference was statistically found to be significant.

Conclusion: The patients who are having normal lipid levels need a significantly less number of admissions for symptomatic angina as compared to those who are having deranged lipid levels.

Keywords: Statins, unstable angina, serum lipid profile

INTRODUCTION

Acute coronary syndrome (ACS) is the most prevalent cardiac disorder and includes ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina^{1,2}. Atherosclerosis is one of the most common causes of coronary artery disease³⁻⁵. Dyslipidemias are increasingly being recognized as an important contributory factor towards the development of atherosclerosis and cardiovascular disease. Framingham study showed that a 1% increase in total cholesterol causes 2% increase in the incidence of IHD⁶. Atherosclerosis is now considered as an inflammatory disease as it is a result of inflammation and inflammatory cytokines are prevalent in atherosclerotic plaques⁷⁻¹⁰. Statins, inhibitors of 3-hydroxy-3-methyl glutaryl coenzyme A reductase, are potent inhibitors of cholesterol biosynthesis and have greatly improved the management of ischaemic heart disease. Recent studies suggest that direct antithrombotic and anti-

inflammatory effects associated with treatment with statins may at least partly account for the reduction of cardiovascular events¹¹. It is increasingly clear that cardiovascular outcomes depend on an understanding of the biology of atherosclerotic disease, which may involve vascular inflammation, endothelial dysfunction, and plaque instability^{12,14}. Data from observational studies and a randomized controlled trial support the routine use of statins in ACS and highlight the association between early initiation and reductions in recurrent coronary events and mortality. Preclinical and clinical evidence also indicates that, in addition to their lipid-lowering effects, statins may reduce inflammation, improve endothelial function and increase plaque stability².

METHODOLOGY

The study was conducted in the department of Cardiology, Bahawal Victoria Hospital Bahawalpur from 15th March 2010 to 15th March 2012. During the initial one year of study, patients fulfilling the inclusion criteria were registered. Only the patients with the diagnosis of unstable angina were included in the study. The data regarding the age at the time of presentation, gender, co-morbidities (diabetes mellitus, hypertension, smoking, BMI), baseline lipid

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levels and drugs taken for symptomatic coronary artery disease was collected on a predesigned proforma. All such patients who were having one or more of the major identifiable risk factors other than dyslipidemia were excluded from the study as were the patients who had heart failure. All patients were started on atorvastatin at the time of enrollment. The patients were broadly classified into two major groups at the start of follow up period of one year; Group A having the normal baseline serum lipid levels and Group B having deranged lipid profile.

Desirable lipid levels were defined as total serum cholesterol < 200 mg/dl, LDL cholesterol < 130 mg/dl and HDL cholesterol > 60 mg/dl¹³.

Lipid lowering therapy in the second group of patients was intensified by increasing the dose of statins to achieve the desirable lipid levels and the patients who achieved the goal during the follow-up year were also placed under the exclusion criteria. The patients who couldn't achieve the goal, thus constituted the second study group. During the follow-up year, the frequency of admission and the rate of adverse cardiovascular events in both the patient populations were noted. The data was analyzed using the Statistical Package for Social Sciences (SPSS) version 10. Chi square test was applied to determine the significance of difference regarding the admission frequency among the two groups.

RESULTS

A total of 1436 patients were enrolled in the study. During the follow-up year, 98 patients dropped out from study and 116 patients in Group B achieved the goal of serum lipid levels and were thus excluded from study. Meanwhile 16 patients in group B developed myocardial infarction and therefore couldn't fulfill the diagnostic criteria for inclusion in the study. Of the remaining 1206 patients, 594 constituted Group A and 612 constituted Group B. Baseline characteristics of the patients are given in Table 1. It was found that during the one year follow up time, 99 patients in group B required recurrent hospital admissions for symptomatic angina as compared to 36 in group A, and this difference was statistically found to be significant (Table 2).

Table 1. Baseline characteristics of the patients

Parameter	Group A	Group B
Mean Age (years)	53 ± 7	52±8
Male	362	354
Female	232	258
Serum lipid levels		
Total cholesterol (mg/dl)	169 ± 14	234±17
LDL cholesterol (mg/dl)	78 ± 18	153±9
HDL cholesterol (mg/dl)	68 ± 8	30±4

Table 2: Frequency of hospital admissions for recurrent angina

	n=
Group A	
Single admission	558
Recurrent admissions	36
Group B	
Single admission	513
Recurrent admissions	99

P value: 0.001

DISCUSSION

Statins therapies reduce vascular inflammation and improve endothelial function^{14,15}. Various trials have confirmed that statin therapy reduces hs-CRP levels^{14,16} and this has been observed among healthy persons^{14,17} patients with stable coronary artery disease^{14,18} and those with the acute coronary syndrome^{14,19}. Other secondary prevention trials have reported that reduction in hs-CRP levels with statin therapy were associated with regression in atheroma burden^{14,20} as well as reduced cardiovascular events rate like myocardial infarctions, revascularization and deaths^{14,21}. Cholesterol lowering can reduce the lipid content of coronary plaques, making the plaques less active and less likely to rupture. This transformation of an active to less active or inactive plaque is believed to be responsible for the reduction of cardiac events observed during treatment with lipid lowering drugs²².

Our study proved that by keeping the serum lipid levels within desirable limits with appropriate management, dietary as well as medical, the frequency of recurrent symptomatic ischemic events is significantly decreased thus decreasing the need for recurrent hospital admissions.

CONCLUSION

The patients who are having normal lipid levels need a significantly less number of admissions for symptomatic angina as compared to those who are having deranged lipid levels.

REFERENCES

1. Assiri AS. The underutilization of adjunctive pharmacotherapy in treating acute coronary syndrome patients admitted to a tertiary care hospital in Southwest region, Saudi Arabia. Heart Views [serial online] 2010 [cited 2012 Oct 3];11:99-102. Available from: <http://www.heartviews.org/text.asp?2010/11/3/99/76800>.
2. Sacks FM. Do statins play a role in the early management of the acute coronary syndrome? Eur Heart J Suppl (2004) 6 (suppl A): A32-A36. doi: 10.1016/j.ehjsup.2004.01.008.

3. Antman EM, Selwyn AP, Braunwald E, Lascialzo J. Ischemic heart disease. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, *et al.* editors. *Harrison's principles of internal medicine*. 17th ed. New York: *McGraw-Hill*; 2008. p. 1514-26.
4. Libby P. The pathogenesis, prevention and treatment of atherosclerosis. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, *et al.* editors. *Harrison's principles of internal medicine*. 17th ed. New York: *McGraw-Hill*; 2008. p. 1501-08.
5. Mujibul Haq AM, Giasuddin ASM, Mahbulul Huque Md. Serum Total Homocysteine and Lipoprotein (a) Levels in Acute Myocardial Infarction and Their Response to Treatment with Vitamins. *J Coll Physicians Surg Pak* 2011, Vol. 21 (5): 266-270.
6. Spellman CW. Strategies for optimizing lipid treatment outcomes. *J Am Osteopath Assoc* 2003; 103:S12-5.
7. Shoenfeld Y, Gerli R, Doria A, Matsuura E, Cerinic MM, Ronda N, *et al.* Accelerated atherosclerosis in autoimmune rheumatic disease. *Circulation* 2005; 112:3337-47.
8. Turesson C, Jacobsson LT, Matteson EL. Cardiovascular co-morbidity in rheumatic diseases. *Vasc Health Risk Manag* 2008; 4:605-14.
9. Anila N, Uzma R, Wajahat A, Abid ZF. Prevalence of dyslipidemias in autoimmune rheumatic diseases. *J Coll Physicians Surg Pak* 2012, Vol. 22 (4): 235-9.
10. Muhammad AB, Azhar MK, Naseer AS. Frequency of Risk Factors in Male Patients with Acute Coronary Syndrome. *J Coll Physicians Surg Pak* 2011, Vol. 21 (5): 271-275.
11. Brugaletta S, Biasucci LM, Pinnelli M, Biondi-Zoccai G, Giannuario GD, Trotta G, *et al.* Novel anti-inflammatory effect of statins: reduction of CD4⁺CD28^{null} T lymphocyte frequency in patients with unstable angina. *Heart* 2006; 92:249-250.
12. Calabro P, Golia E, Yeh ET. CRP and the risk of atherosclerotic events. *Semin Immunopathol* 2009;31:79-94.
13. Zellner C. Lipid disorders. In: Michael HC. *Current diagnosis & treatment (Cardiology)*. New York: *Mc Graw Hill*; 2009. p.14-24.
14. Samiullah K, Hafizullah M, Amjad K, Ibrahim S, Nadeem M, Hikmatullah J, *et al.* Short term effects of Rosuvastatin on plasma concentration of high sensitivity C-reactive protein in patients with chronic stable angina. *Pak Heart J* 2012; Vol. 45 (01):53 – 58.
15. Robinson JG. Models for describing relations among the various statin drugs, lowdensity lipoprotein cholesterol lowering, pleiotropic effects, and cardiovascular risk. *Am J Cardiol* 2008;101:1009-15.
16. Ridker M, Morrow DA, Rose LM, Rifai N, Cannon CP, Braunwald E. Relative efficacy of atorvastatin 80 mg and pravastatin 40 mg in achieving the dual goals of low-density lipoprotein cholesterol <70 mg/dl and c-reactive protein <2 mg/l: an analysis of the PROVE-IT TIMI-22 trial. *J Am Coll Cardiol* 2005;45:1644-8.
17. Ridker PM, Fonseca FAH, Genest J. Baseline characteristics of participants in the JUPITER trial: a randomized placebo-controlled primary prevention trial of statin therapy among individuals with low-density lipoprotein cholesterol and elevated high-sensitivity C-reactive protein. *Am J Cardiol* 2007;100:1659-64.
18. Oren H, Erbay AR, Balci M, Cehreli S. Role of novel biomarkers of inflammation in patients with stable coronary heart disease. *Angiology* 2007;58:148-55.
19. Kumar A, Sivakanesan R. Does plasma fibrinogens and C-reactive protein predict the incidence of myocardial infarction in patients with normal lipids profile? *Pak J Med Sci* 2008;24:336-9.
20. Nissen SE, Tuzcu EM, Schoenhagen P, Brown BG, Peter Ganz P, Vogel RA, *et al.* Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis. *JAMA* 2004; 291:1071-80.
21. Cannon CP, Braunwald E, McCabe CH, McCabe, Daniel JR, Jean L, *et al.* Comparison of intensive and moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;350:1495-1504.
22. Tzivoni D, Klein J. Improvement of myocardial ischaemia by lipid lowering drugs. *European Heart Journal* (1998) 19, 230–234.