Comparison of efficacy of daily versus every other day dosing of Atorvastatin in patients with atherosclerotic coronary artery disease

Thesis for partial fulfillment of the master degree in cardiology

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Dedication

To the martyrs of October war, 1973

Contents

List of Abreviations

ATP	Adult treatment panel.
LDL-C	Low density lipoprotein cholesterol.
HDL-C	High density lipoproteins cholesterol.

VLDL-C	Very low density lipoproteins cholesterol.
HMG CoA	3-Hydroxy-3-methylglutaryl coenzyme A.
T3	Triiodothyronine.
CHD	Coronary heart disease.
Apo B	Apoprotein B.
Apo A-I	Apoportein A1.
BRHS	The British Regional Heart Study.
TGRLP	Triglyceride-rich lipoproteins.
Hs-CRP	High sensitivity C-reactive protein.
CAMS	Cell adhesion molecules.
Enos	Endothelial nitric oxide synthase.
Fc	C-terminal of immunoglobulin chain.
IL	Interleukin.
PAI-1	Plasminogen activator inhibitor-1.
TNF	Tumor necrosis factor.
tPA	Tissue plasminogen activator.
AHA	American heart association.
CD	Cluster of differentiation.

LRC	The Lipid Research Clinics.
MRFIT	The Multiple Risk Factor Intervention Study.
SPARCL:	Stroke Prevention by Aggressive Reduction in Cholesterol Levels.
ASTEROID:	A Study To Evaluate the Effect of Rosuvastatin on Intravascular Atheroma Burden.
TNT:	Treating to New Targets.
A to Z:	Aggrastat to Zocor.
CARDS:	Collaborative Atorvastatin Diabetes Study.
PROVE IT-TIMI 22:	Pravastatin or Atorvastatin Therapy-Thrombolysis in Myocardial Infarction 22.
REVERSAL	Reversal of atherosclerosis with aggressive lipid lowering.
ASCOT-LLA.	Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm.
HPS:	Heart Protection Study.
AHAT-LLT:	Antihypertensive and Lipid-Lowering Treatment to prevent Heart Attack Trial.
MIRACL:	Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering.

LIPID	Long-term Intervention With Pravastatin in Ischemic Disease.
AF/TexCAPs:	Air Force/Texas Coronary Atherosclerosis Prevention Study.
CARE	The Cholesterol and Recurrent Events Trial.
WOSCOPS	West of Scotland coronary prevention study.
4S	Scandinavian Simvastatin Survival Study.
CVD	Cardiovascular disease.
ACC	American college of cardiology.
IDEAL	Incremental Decrease in Endpoints Through Aggressive Lipid Lowering (IDEAL).

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Abstract

Objective: In this study, we aimed at comparing the effects of standard once daily 10 mg atorvastatin treatment with that of atorvastatin 10 mg administered every other day on serum lipids and high sensitive C-reactive protein (hs-CRP) levels.

Methods: Sixty patients visiting Nasser institute outpatient clinics who were already on daily 10 mg atorvastatin that have already achieved serum LDL cholesterol levels ≤ 100 mg/dl were included in this prospective, randomized study. The patients were randomized to continue their daily treatment of 10 mg atorvastatin (standard treatment) or to shift to 10 mg atorvastatin every other day (every other day treatment) groups. Before the treatment and at a six weeks follow up visit, serum LDL, lipid profile and hs-CRP levels of all patients were measured after 14 hours fasting. Statistical analyses were performed Chi-square, unpaired t tests.

Results: In the reduced (every other day treatment) group, there was a significant rise in total cholesterol and LDL-cholesterol levels by the end of six weeks as compared to standard daily regimen ($p<0.01$), the difference between the changes in the other lipid parameters of the two groups was not found to be of statistical significance., the effects of both treatment arms on hs-CRP levels, did not differ significantly ($p>0.05$).

Conclusions: Alternate-day dosing of atorvastatin causes a significant total cholesterol and LDL –C rise but similar effects on Hs CRP if compared to of daily administration.

Key words: Atherosclerosis, statins, atorvastatin, total cholesterol, low density lipoprotein cholesterol, hs-C reactive protein

INTRODUCTION

Statins play a central role in cardiovascular risk reduction[1]

Their benefit has been demonstrated for a broad spectrum of patients, ranging from those without known vascular disease [2] to those who have recently had a myocardial infarction [3] or have undergone coronary artery bypass surgery.[4]

Not surprisingly, statins are the most widely sold class of drugs in the United States, accounting for $18.4 billion in sales in 2007.[5]

But actually, only half of all patients who have been prescribed a statin actually adhere to this therapy. For example, 42% of Medicare patients enrolled in a pharmacy benefit program were adherent with their prescribed statin 2 years after starting treatment.[6]

Statin adherence rates after acute coronary syndromes do not appear to be much better, [7] nor have they improved substantially over time.[8] Not surprisingly, non adherence is a central reason why many patients do not achieve their low-density lipoprotein goals, and patients who are non adherent have worse clinical outcomes[9] and higher healthcare costs than their adherent counterparts. [10]

The reasons for statin non-adherence are complex and vary from patient to patient. For some, side effects lead them to a legitimate discontinuation of therapy.

Others misunderstand the importance of statin therapy because of the asymptomatic nature of hyperlipidemia, especially when burdened with the complex treatment regimens that many patients with vascular disease receive. Undisputable, for an increasing number of patients, cost is a substantial barrier to appropriate medication use.[11]

AIM OF THE WORK

The aim of this study is to compare the efficacy of "every other day" Atorvastatin regimen with the conventional daily regimen in patients with ischaemic heart disease whose LDL-C levels have already been brought to target levels ≤100 mg/dl by conventional daily 10 mg daily Atorvastatin therapy.

PATIENTS AND METHODS

We will include sixty patients with diagnosed coronary artery disease visiting Nasser institute hospital. Patients will be eligible for enrollment if they have already been on conventional daily 10 mg Atorvastatin regimen and already achieved a target LDL-C level ≤ 100 mg/dl.

Inclusion criteria:

1- Proven coronary artery disease by either :

   a- ECG showing Q waves of infarction.
   b- Previous positive scintigraphy.
   c- Previous positive coronary angiography.
   d- Previous percutaneous coronary intervention (PCI).
   e- Previous coronary artery bypass surgery (CABG).

2- Patients already on 10 mg daily Atorvastatin therapy achieving target LDL-C ≤ 100mg/dl.

Exclusion criteria:

1- Decompensated liver disease.
2- Myalgia attributed to myositis associated with statin therapy.
3- Acute myocardial infarction within six weeks.
4- Pregnancy and lactation.
5- Hypersensitivity to statins.

All patients will be subjected to:

1- Proper history taking:

Attention to history of myocardial infarction, positive scintigraphy, positive coronary angiography, percutaneous coronary intervention or coronary artery bypass surgery.

2- Full general and local examination
3- 12 lead ECG: Looking for Q waves of infarction.
4- Liver and kidney function tests.
5- Triglycerides, Total cholesterol, LDL-C and HDL-C in serum before and after the trial period.
6- High sensitivity "C" reactive protein before and after the trial period.