HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-106

Case Report

*Corresponding author
Danish Mahmood, M. Pharm, PhD
Lecturer
Department of Pharmacology and Toxicology, Unaizah College of Pharmacy, Qassim University
Unaizah, Saudi Arabia
Tel. +966-594016751
E-mail: ma.alam@qu.edu.sa

Volume 2 : Issue 1
Article Ref. #: 1000HROJ2106

Article History
Received: December 18th, 2014
Accepted: March 17th, 2015
Published: March 18th, 2015

Citation
Mahmood D, Siddique A. A case report of the management of residual cardiovascular risk in a dyslipidaemic patient with metabolic syndrome. *Heart Res Open J*. 2015; 2(1): 35-38. doi: 10.17140/HROJ-2-106

A Case Report of the Management of Residual Cardiovascular Risk in a Dyslipidaemic Patient with Metabolic Syndrome

Danish Mahmood[1*] and Abubakar Siddique[2]

[1]Department of Pharmacology & Toxicology, Unaizah College of Pharmacy, Qassim University, Unaizah, Saudi Arabia

[2]Department of Pharmacy Practice, Unaizah College of Pharmacy, Qassim University, Unaizah, Saudi Arabia

ABSTRACT

Metabolic Syndrome (MS) is a clustering of metabolic and underlying risk factors which doubles the risk of atherosclerotic cardiovascular disease. It is more prevalent in some ethnic groups, especially in the Asian world. Global urbanization and sedentary life habits have increased the underlying risk factors characterised by physical inactivity, atherogenic diet and obesity. Therefore, its detection, prevention, and treatment serve as an important approach for the reduction of cardiovascular risk in the general population and strictly emphasized on strict therapeutic lifestyle changes. In our case report, we present effective management of a dyslipidaemic patient with MS by medication. However, her underlying risk factors were not controlled due to her inability to strictly adopt therapeutic lifestyle changes.

INTRODUCTION

The new worldwide International Diabetes Federation (IDF) defines, Metabolic Syndrome (MS) as having central obesity (defined as waist circumference ≥94 cm for Europid men and ≥80cm for Europid women, with ethnicity specific values for other groups) and any two of the following four factors which include first, raised TG level: ≥150 mg/dL (1.7 mmol/L), Second, reduced High Density Lipoprotein Cholesterol (HDL-C): <40 mg/dL (1.03 mmol/L) in males and <50 mg/dL (1.29 mmol/L) in females, third, the raised blood pressure: systolic BP ≥130 or diastolic BP ≥85 mm Hg, fourth, raised Fasting Plasma Glucose (FPG) ≥100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes. Central obesity and insulin resistance have been regarded as important causative factor, however, the pathogenesis of MS and its components have remained poorly understood (www.idf.org).[1] We present a case report of management of residual CVD risk in a female dyslipidaemic patient with MS.

CASE REPORT

A 62-year old Mexican American woman went to a routine clinical visit. Her Body Mass Index (BMI), waist circumference, FPG, and BP were 31.2 kg/m^2, 36 inches (91.44 cm), 115 mg/dL and 136/77 mm Hg, respectively. She was already on Angiotensin Converting Enzyme (ACE) inhibitor, the antihypertensive medication, which helped to reduce her BP. Her lipid profile revealed borderline elevation of various lipid parameters, including total cholesterol (227 mg/dL), LDL-C (130 mg/dL), HDL-C (40 mg/dL), TG (285 mg/dL), and non-HDL-C (187 mg/dL). Her clinician diagnosed her with impaired fasting glucose and MS and reported her Framingham risk score of 12%. Her 10-year risk of Atherosclerotic cardiovascular disease (ASCVD) was 15.7% as calculated using pooled cohort risk assessment equations. He prescribed atorvastatin (10 mg/day) and suggested to adopt therapeutic lifestyle changes (diet,

exercise) and stop smoking.

During her follow up visit after 3 months (Visit 1), she reported that her smoking habits were reduced from 1 pack to half pack a day. However, there was no change in her BMI (31.8 kg/m^2) and waist circumference (36.5 inches). Her BP was slightly raised (from 136/77 mm Hg to 138/80 mm Hg). To normalize her BP, the clinician prescribed amlodipine, a calcium channel blocker, in addition to existing ACE inhibitor. After the use of atorvastatin a change in her lipid profile was observed. Her total cholesterol, LDL-C, non-HDL-C, and TG were reduced from 227 to 181 mg/dL; 130 to 89 mg/dL; 187 to 139 mg/dL, and 285 mg/dL to 248 mg/dL, respectively and HDL-C levels were increased from 40 to 42 mg/dL. She reached her target goal of LDL-C (<100 mg/dL) but did not reach target goal of non-HDL-C (<130 mg/dL) as per ATP III guidelines (Table 1). Though there was an overall improvement in the metabolic parameters, her FPG was elevated (132 mg/dL) and was diagnosed with type 2 diabetes. The clinician prescribed metformin (500 mg, twice a day) to reduce her FPG levels and added fenofibrate (145 mg/day) to existing atorvastatin therapy to further elevate HDL-C and lower TG levels. He explained the importance of lifestyle changes and again stressed her to strictly adopt lifestyle changes.

Three months after Visit-1, no change in BMI and waist circumference was observed in spite of her reduced smoking habit. The combination of amlodipine plus ACE inhibitor normalised her BP (from 138/80 mm Hg to 122/74 mm Hg) and metformin reduced her FPG (from 132 mg/dL to 114 mg/dL). After treatment with fenofibrate and atorvastatin her lipid profile was further improved. Her total cholesterol, LDL-C, non-HDL-C, and TG reduced to 158 mg/dL, 80 mg/dL, 110 mg/dL, and 148 mg/dL, respectively, and her HDL-C increased to 48 mg/dL. Since she did not experience any adverse muscle, liver, or kidney events, the treatment was continued. The medications helped her lower presence of most of her metabolic and major risk factors. However, no changes in underlying risk factors were observed owing to her inability to adopt to a strict lifestyle changes.

DISCUSSION

The two most widely accepted criteria for the diagnosis of MS in the United States have been proposed by the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI). International Diabetes Federation (IDF) was similar to NCEP ATP III and AHA/NHLBI criteria except that it included central obesity plus two or more than two criteria (Table 2).[1] Enlarged waist plus elevated triglycerides serves as a stronger predictor of cardiovascular mortality and all-cause mortality after adjustment of age, smoking status, and LDL-C levels.[1,2] In our report, the patient was a 62-year old female of Mexican American descent with enlarged waist (91.44 cm) and borderline elevation of lipid parameters with elevated TG levels (285 mg/dL), and was diagnosed with MS.

Central (abdominal) obesity can be easily assessed using waist circumference which is independently associated with all components of MS including insulin resistance, and is a prerequisite risk factor for the diagnosis of the syndrome in the new definition of IDF. Table 2 present the IDF recommended cut-points for waist circumference for diagnosis of MS in different ethnic group. In reference to the IDF cut-point on waist circumference as presented in here in table 2, the cut point defining abdominal obesity and those of Central American ancestry is 80 cm and the so patient in the present case study has a waist circumference far above that, and hence she meets the criteria

NCEP III	NHLBI/AHA Criteria	IDF Criteria
	Any 3 or more criteria	Central obesity + any 2 or more criteria
Waist circumference: men ≥102 cm (40 in); women ≥35 in (88 cm)	Waist circumference: men ≥102 cm (≥40 inches); women ≥88 cm (≥35 inches); lower cut-points for insulin-resistant individuals	Waist circumference ethnicity specific
TG ≥150 mg/dL (1.7 mmol/L)	TG >150 mg/dL (1.7 mmol/L) or on specific treatment	TG >150 mg/dL (1.7 mmol/L) or on specific treatment
HDL-C: men <40 mg/dL (1.03 mmol/L) Women <50 mg/dL (1.3mmol/L)	HDL-C: men <40 mg/dL (1.03 mmol/L); women <50 mg/dL (1.29 mmol/L)	HDL-C: men <40 mg/dL (1.03 mmol/L); women <50 mg/dL (1.29 mmol/L) or on specific treatment
SBP ≥130 mm Hg or DBP ≥85 mm Hg	SBP ≥130 mm Hg or DBP ≥85 mm Hg or antihypertensive medication	SBP ≥130 mm Hg or DBP ≥85 mm Hg or antihypertensive medication
FBG ≥110 mg/dL	FBG ≥100 mg/dL (5.6 mmol/L) or on drug treatment for elevated glucose	FBG ≥100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 DM

DBP = Diastolic Blood Pressure; FBG = Fasting Blood Glucose; HDL-C = High-Density Lipoprotein Cholesterol; IDF: International Diabetes Federation; NHLBI/AHA: National Heart Lung Blood Institute/American Heart Association; SBP = Systolic Blood Pressure; TG = Triglyceride

Table 1: NHLBI/AHA and IDF Diagnostic Criteria for Metabolic Syndrome.[1,2]

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-106

for the diagnosis of MS as per new IDF definition. Although, there are inadequate data in other racial groups, such as Hispanics, Asians, and American-Indian populations. It has been reported that in comparison to non-Hispanic white or Caucasians, the risk of ASCVD is generally found to be lower among Hispanic-American and Asian-American populations, and generally higher among American-Indian populations.[3] Our results corroborated with earlier reports where females aged >60 years, enlarged waist, elevated TG and the Mexican American descent have higher predisposition to MS.

Non-HDL-C reported as a stronger predictor of CVD risk than LDL-C[4,5] and was considered as a secondary target after attainment of LDL-C goal with TGs ≥200 mg/dL (5.17 mmol/L).[6,7] During her follow up visit her LDL-C, total cholesterol, TG got reduced by 31.5%, 20.2%, and 13%, respectively, and HDL-C goal was elevated by 5% after the use of atorvastatin (10 mg/day). Our results were in agreement with the previous study where standard doses of statins (simvastatin 10-40 mg/day, pravastatin 40 mg/day and lovastatin 20-40 mg/day) reduced total cholesterol by 18-26%, LDL-C by 25-30% and TG by 11-17%, and increased HDL-C by 5-7%.[6] However, other studies reported statins to be inadequate in the residual CVD risk associated with lipid abnormalities, especially above TG >220 mg/dL.[7-9]

As per NCEP ATP III guidelines, statins or TG lowering drugs, such as fibrates or niacin served a vital role in achieving non HDL-C and LDL-C goals where the non-HDL-C goal was always 30 mg/dL higher than the LDL-C goal.[10] In our report too, we observed that the patient after treatment with fenofibrate and atorvastatin achieved the largest goal of LDL-C and non-HDL-C. In the present case, the patient calculated ASCVD risk was 27.8% indicating that this patient was at elevated 10-year risk (≥7.5%) for ASCVD. In diabetics (40-75 years, LDL 70-189 mg/dL), a high-intensity statin should be considered with a 10-year ASCVD risk ≥7.5%. The 2013 ACC/AHA guidelines recommend either a high-intensity or moderate-intensity statin regimen in patients who have an elevated ASCVD risk (≥7.5%) for primary prevention of cardiovascular disease. The recommended doses of moderate intensity atorvastatin dose ranges between 10-20 mg. Hence, this patient was prescribed atorvastatin dose of 10 mg, and advised to adopt therapeutic lifestyle changes as the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guideline have emphasized that lifestyle modification (i.e., adhering to a heart healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight) constitutes an important element in the health promotion and ASCVD risk reduction, both prior to and in concert with the use of cholesterol lowering drug therapies.[11,12] The new ACC/AHA guideline emphasizes matching the intensity of statin treatment to the level of ASCVD risk and replaces the old paradigm of pursuing LDL-C targets (Table 3).

During her follow up visit after 3 months that there was no change in her BMI (31.8 kg/m^2) and waist circumfer-

Gender	Waist Circumference (cm)					
	Europids	South Asian	Chinese	Japanese	Ethnic South and Central Americans	Eastern Mediterranean & Middle East (Arab)
Male	≥94	≥90	≥90	≥90	≥90	≥94
Female	≥80	≥80	≥80	≥80	≥80	≥80

Table 2: Waist circumference cut-point for diagnosis of metabolic syndrome in different ethnic group[1]

Clinical risk categories	Treatment
Those with clinical ASCVD	High-intensity statin therapy. If 50% reduction is not reached drug combination may be considered
Diabetes mellitus (Type I or Type II) without ASCVD but with LDL-C between 1.8 and 4.9 mmol/L	Diabetes with high risk: High-intensity statin therapy. Diabetes with low risk: Moderate-intensity statin therapy
Those with primary elevation of LDL-C >4.9 mmol/L	High-intensity statin therapy, aimed at achieving at least 50% reduction of LDL-C
If none of the above but with estimated 10-year ASCVD risk of 7.5% or more using a pooled populations risk calculator If risk-based assessment treatment decision uncertain assessment of 1 or more of family history, hs-C-reactive protein, CAC Score or ABPI may be considered, contribution of Apo B, CKD, microalbuminuria or cardio-respiratory fitness is uncertain and CIMT is not recommended for routine assessment of individual patients	Moderate-to-high-intensity statin therapy if ASCVD risk >7.5%. If risk 5-7.5% risk of CVD event: Reasonable to consider moderate-intensity statin therapy

ABPI: Ankle Brachial Pressure Index; ASCVD: Atherosclerotic cardiovascular disease; Apo B: Apoprotein B; CAC: Coronary Artery Calcification; CKD: Chronic Kidney Disease; CIMT: Coronary Intima Media Thickness; LDL-C: Low Density Lipoprotein Cholesterol

Table 3: 2013 ACC/AHA guidelines on the treatment of blood cholesterol to reduce ASCVD risk in adults[12]

ence (36.5 inches) despite reducing her smoking from 1 pack to half pack a day. The current cut-points for overweight (BMI 25.0-29.9 kg/m^2) and obesity (BMI ≥30 kg/m^2) compared with normal weight (BMI 18.5 to <25 kg/m^2) has been associated with elevated risk of combined fatal and nonfatal coronary heart disease. The new ACC/AHA guideline on obesity recommends healthcare providers to develop individualized weight loss plans that should include three key components - a moderately reduced calorie diet, a program of increased physical activity and the use of behavioral strategies to help patients achieve and maintain a healthy body weight. In order to better manage weight reduction and obesity, physician should advice patients to undertake multiple sessions with dietician. No change in BMI as reported by the patients after 3 months underscores inadequate instruction on weight reduction plan was provided by the healthcare provider.

The NCEP ATP III and the AHA/NHLBI recognized HDL-C as a tertiary target but did not set an HDL-C goal level. These two organisations including ADA advocated the use of fibrates to reduce TG and elevate HDL-C in patients with the MS or diabetes and suggested that fenofibrate combination with statin may be an effective and safer alternative than statin alone. We also observed that the patient did not experience any side-effects with the combination therapy of atorvastatin and fenofibrate and hence prescribed to continue her treatment.

In conclusion, the metabolic risk factors for MS in dyslipidaemics can be well managed by appropriate treatment but the underlying risk factors could only be managed by adopting strict therapeutic life style changes.

REFERNCES

1. International Diabetes Foundation. The IDF consensus worldwide definition of the metabolic syndrome. http://www.idf.org/webdata/docs/MetS_def_update2006.pdf. 2007; Accessed 2007.

2. Tankó LB, Bagger YZ, Qin G, Alexandersen P, Larsen PJ, Christiansen C. Enlarged waist combined with elevated triglycerides is a strong predictor of accelerated atherogenesis and related cardiovascular mortality in postmenopausal women. *Circulation*. 2005; 111: 1883-1890. doi: 10.1161/01.CIR.0000161801.65408.8D

3. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics-2013 update: a report from the American Heart Association. *Circulation*. 2013; 127(1): e6-e245. doi: 10.1161/CIR.0b013e31828124ad

4. Cui Y, Blumenthal RS, Flaws JA, et al. Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. *Arch Intern Med*. 2001; 161: 1413-1419. doi: 10.1001/archinte.161.11.1413

5. Ridker PM, Rifai N, Cook NR, Bradwin G, Buring JE. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. *JAMA*. 2005; 294: 326-333. doi: 10.1001/jama.294.3.326

6. LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med*. 2005; 352: 1425-1435. doi: 10.1056/NEJMoa050461

7. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*. 2006; 3: 2011-2030. doi: 10.1371/journal.pmed.0030442

8. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet*. 2002; 360: 7-22. doi: 10.1016/S0140-6736(02)09327-3

9. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002; 106: 3143-3421.

10. Grundy SM, Cleeman JI, Merz BN, et al. Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. *Circulation*. 2004; 110: 227-239. doi: 10.1161/01.CIR.0000133317.49796.0E

11. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014; 129(25 Suppl 2): S1-S45. doi: 10.1161/01.cir.0000437738.63853.7a

12. Ray KK, Kastelein JP, Boekholdt SM, et al. The ACC/AHA 2013 guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: the good the bad and the uncertain: a comparison with ESC/EAS guidelines for the management of dyslipidaemias 2011. *Eur Heart J*. 2014; 35: 960-968.