Insight on the Side Effects of Lipid Lowering Agents (Statin) in Iraqi Patients with Ischemic Heart Diseases

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ABSTRACT:

BACKGROUND:

3-hydroxy-3methyl glutaryl co enzyme inhibitor (MMG-COA) (statin) is a very common drug used in many medical conditions regardless of the presence or absence of dyslipidemia. One of these conditions is the cardiac disorders.

OBJECTIVE:

Throwing a light on the prevalence of their side effects in Iraqi patients.

PATIENTS AND METHODS:

Two hundred seventy patients with ischemic heart disease from the period of November 2006-November 2007 referred to Baghdad teaching hospital (the medical city). Those cases were using statin and grouped into two groups.

Group A: patients admitted with acute coronary syndrome (myocardial infarction and unstable angina) (230 patients 77%).

Group B: patients with associated risk factors (Hypertension, diabetes mellitus, smoking and secondary lipidemia) 40 cases 23%, have history of ischemic heart disease on treatment they use the drug in range of (10-40) daily with review monthly for the side effects. All 270 cases were free from other organic disorders (i.e. renal, thyroid, malignancy, or any longstanding disease). All patients went through a questionnaire which includes: age, gender, risk factors (Hypertension, diabetes mellitus, smoking, and lipidemia), routine blood tests, lipid profile, liver function tests, C-reactive proteins, thyroid function tests, chest X-ray, electrocardiography and echocardiography done for all patients, all patients used to take drugs in the range of 10-40mg daily for at least one year.

RESULT:

The side effects noticed in this study were gastric, musculoskeletal, elevated liver enzymes (40%, 28.9%, and 1% respectively from the total number of patients). Other side effects in other systems like skin, respiratory, and cardiac were not encountered.

CONCLUSION:

This study showed that the side effects of statin were not involving all the body systems.

***KEY WORDS*:** statin, side effects, Iraqi patients,

INTRODUCTION:

Endothelial cells dysfunction is the trigger factor for ischemic heart disease by the formation of plaque and thrombus via reduction of nitric oxide syntheses and mitochondrial dysfunction.

Reducates enzyme inhibitor appeared to be significantly effective in improving endothelial function by inhibiting HMGO-Co reducates, there by decreasing the synthesis of mevalonate, a critical intermediary in the cholesterol synthesis[1, 2].

Another biochemical mechanism through the reduction of small guanosine triphosphate-binding protein, reduced production of intramuscular coenzyme-Q10 which is essential for electron transport mechanism and oxidation process inside the mitochondria, regeneration of the active form of antioxidant like ascorbic acid and vitamin (E, tocopherol)[1, 2, 3]. So their benefits against its side effects encourage doctors keep using them especially if not reached their highest dose in most cases.

PATIENTS AND METHODS:

Two hundred seventy patients were admitted in this study over the period of November 2006-November 2007 at Baghdad teaching hospital.

Those ischemic heart disease patients were given statin in the dose range of 10+40mg daily. They were into two groups.

Group A: (230 cases, 77%) patients who came as an emergency referral as acute coronary syndrome (unstable angina and myocardial infarction).

Group B: already having ischemic heart disease and they are under treatment (40 cases 23%). All

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patients went through the same protocol from history taking including age, gender, risk factors (Hypertension, diabetes mellitus, smoking, lipidemia). All have routine blood tests, lipid profile assessment, liver function tests, thyroid function test and C-reactive proteins-also chest X-ray, electrocardiography and echocardiography done for all patients, all patients who were having chronic diseases like malignancy renal, thyroid, and connective tissue disease have been excluded from this study.

The side effects have been distributed according to the body system (i.e. cardiac, renal, respiratory, skin, gastric, hepatic, musculo skeletal…etc)

RESULT:

Number of male in this study was 160 cases (59%). Number of female was 110 cases (41%).

The age range 40-70 years; all patients were in the same range and were distributed according to age and sex as shown in table I.

Table I: Shows the distribution of patients according to age and sex.

Age range (years)	No. of cases and %	Sex
40-50	60 37.5%	Male
50-60	55 34.3%	
60-70	45 28.2%	
40-50	40 36.3%	Female
50-60	38 34%	
60-70	32 29.2%	

Regarding the side effects of statin &systemic involvement have been shown in table II.

Table II: The distribution of side effects according to system involvements.

Side effects systemic involvement	Type of cases according of sex	No. of cases and%
Gastrointestinal	22 male	42 (56%)
	20 female	
Musculoskeletal	16 male	30 (55%)
	14 female	
Elevated liver enzymes	3 male	5 (2%)
	2 female	

From this table it is clear that the musculoskeletal, gastrointestinal, and elevated liver enzymes are the most common side effects detected with the use of HMG-Co reeducates inhibitor while other side effects in other body systems were not detected is our patients. The number of males and females were nearly the same which mean the sex has no effect on the incidence of side effects.

Regarding the types of musculoskeletal side effects are shown in table III: which clearly shows that artharalgia is the most common manifestation in our patients.

Table III: Shows the distribution of musculoskeletal side effects in patients on using statin drug.

Symptoms	No. of cases (%)
Arthralgia	30 (11%)
Myelgia	23 (9%)
Generalized aches	22 (8%)
Achilles tendonitis	0 (0%)

Elevated liver enzymes seen only in 5 cases (2%) from the 270 cases in which liver enzymes increased by >3 times above the normal and this rise of enzyme levels returned back to normal after reducing the dose from 40 to 10mg/d. As a marker that the side effects of statin improved by reducing the dose.

Regarding gastrointestinal side effects were detected in 42 patients (15%) using lipid lowering agents as shown in table IV:

Table IV: Shows gastrointestinal side effects on 270 patients using statin:

Symptoms	No. of cases (%)
Dyspepsia	15 (6%)
Constipation	10 (4%)
Flatulence	10 (4%)
Diarrhea	3 (1%)
Tensmus	2 (1%)

Table V: Shows the distribution of C-reactive protein in people with or without side effects.

Groups of patients	With side effects	Without side effects	p-value
Group A	5.0+0.4mg/l	3.7+0.5 mg/l	<0.005
Group B	5.0+0.2mg/l	3.7+0.5mg/l	<0.005

Table V: showed that correlating the C-reactive protein in both patients with side effect or without, was highly significant in both group (A&B) regardless of the development of this side effects or not, which mean as a good marker of inflammatory process in all ischemic heart patients.

DISCUSSION:

In this study there was no difference in the development of the side effects in correlation to age and sex and this fit with other studies and the third report of the national cholesterol education programme[4, 5].regarding gastrointestinal manifestations, it has been shown that about 15% of cases involved in this study had this effects which considerably a bit higher in comparison to other international studies by about 10-12 %[5]. The liver enzymes elevated more than 3 times above the normal in five cases (2%) only in the first three months which return back to normal levels after reducing the dose to 10 mg daily[6]. This is higher than Jacobson TA study by 1%[6]. Probably these variations in the results to gastrointestinal or liver enzymes could be due to variation of the type of food, alcohol consumption [1, 2], ethnic or genetic variations affecting the cellular enzyme functions [7, 8, 9]. Also discrepancy in the incidence of side effects of statin could be affected by body weight (body mass index) as dimitrios found that elevated liver enzymes was higher in obese patients than none obese patients[10]. In this study the body mass index mean was 26.8%.

Regarding the musculoskeletal manifestations were mainly in the form of myelgia and arthralgia and this probably depend on the dose range used by the patients in this study [3, 10, 11] and this may be due to the effect on mitochondrial function through the effect of statin on serum urobiounone and the level of blood pyruvate which could result in different manifestations from myelgia to rhabdomlysis.

Absence of skin, renal, and cardiac complications could also be related to genetic or racial variations [9].

As C-reactive protein used as marker for many inflammatory processes it was measured in this study and it was higher both in patients with side effects and in those without side effects. HMG-Co reductase inhibitor in some studies showed that it has an anti-inflammatory effect [11, 12, 13, 14, 15]. So C-reactive protein level must regress but not in this study because most of the patients have low dose of statin in comparison to other international studies [9].

CONCLUSION:

Most of the Iraqi patients do well on dose of statin in the range of 10-40 mg/d.

These variations in getting these side effects as compared to different studies was probably related to genetic, racial variations, body weight, type of food, and alcohol consumption.

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