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DRUG INDUCED MYALGIA IN POST MYOCARDIAL INFARCTION PATIENTS ON ATORVASTATIN AT TERTIARY CARE HOSPITAL OF HYDERABAD,PAKISTAN

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ABSTRACT

Statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) are linked with muscle related illnesses. Statins are worldwide used as a anti lipid lowering agents that are responsible to reduce cardiovascular mortality and morbidity in patients at high risk; and also causing adverse drug reactions (ADRs).The aim of this study to monitor statins (Atorvastatin) induced myalgia in post myocardial infarction patients at tertiary care hospital of Hyderabad, Pakistan. The quantitative descriptive cross sectional study was done and evaluates statins induced myalgia clinically through series of questions asked by patients on predesigned approved questionnaire. A total of 300 patients were enrolled via purposive sampling from Cardiac ward, tertiary hospital, Hyderabad. Out of 300 patients, 72.66% were belonged to male and 27.33 were of female, while 27.33% of the patients were of 50 years of age. Initially observed data of patients on atorvastatin shows 23.66% cumulative myalgia in patients with different %age at different doses. Patients on 10mg showed lowest potential of myalgia expressing in 5%. While 7.66%of patients on 20 mg showed myalgia. Whereas, on 40mg shown (11%) cases of myalgia. There was no patient prescribed with 80mg dose. Among total cases of myalgia, 70%complained for mild myalgia while 30% had moderate level. Initial findings of the study show that statins are causing significant cases of Myalgia which must be taken in to account in local population. %age

of Myalgia at different doses of Atorvastatin shows the potential for causing myalgia increases as the dose increases.

Keywords: Atorvastatin, Statins, Myocardial Infarction, Tertiary Care

INTRODUCTION

Studies have exposed remarkable risks of myositis and myopathy associated with use of statins in various studies, equally in a United States managed care group **[1]** and a UK general practice population **[2]**. Myalgia can be defined as muscle ache or weakness without increases in creatine kinase levels, as defined by the American heart association-/ACC & NHLB; & it is the most frequently occurring adverse effect of statins. Myalgia is reversible on abrupt withdrawal from statins therapy and these symptoms may require 2 to 3 weeks to resolve after therapy is discontinued. Physiogenomic associations of Statin induced myalgia had also been studied in which 3 genes, namely COQ10, ATP2B1 & DMPK, were found as marker of statin induced myalgia, since each one of them were involved in muscle metabolism. Though the exact reason of statin induced myalgia is unknown, but somehow etiological reports showed that due to decline in sarcoplasmic reticular cholesterol level, low production of Ubiquinone also known as CoQ10, declined production of prenylated proteins, alteration in lipid metabolism, elevation in uptake level of phytosterols and inhibition of selenoprotein production **[3]**.

Statins are used as preliminary lipid reducing drugs among the abnormal lipid profile patients, in post Myocardial Infarcted peoples & also for the prevention of atherosclerosis. Initially the statins were attained from fungus named Penicillium citrinum. Whereas, the 1st studied statin was mevastatin. Whereas, lovastatin was primarily approved drug for the use of human beings. Statins are further classified in 3 generations i.e.; 1st generation includes Lovastatin, pravastatin, and fluvastatin etc, 2nd generation includes atorvastatin and simvastatin while 3rd generation includes rosuvastatin. Lovastatin, simvastatin, pravastatin & mevastatin are the metabolites of fungi whereas rosuvastatin, fluvastatin & atorvastatin are synthetic compounds. From chemical point of view, Statins are structural analogs of 3-Hydroxy 3-methyl Glutaryl Coenzyme A, which is a competitive antagonist of the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, (an enzyme which synthesize cholesterol in the liver). This enzyme HMG CoA reductase is responsible to convert

HMG-CoA to another chemical known as mevalonate, which is a precursor in the synthesis of cholesterol. Statins antagonize this enzyme which in turn leads to inhibition of synthesis of cholesterol. By another mechanism statins impede the biosynthesis of apolipoprotein & triglycerides rich lipoprotein thus resulting in decrease levels of atherogenic lipoproteins. Statins are of front position of treatments for elevated lipid levels, coronary artery disease (CAD) and stroke. Patients might not stay to statins therapy for prolong period, due to hepatotoxicity as well as neuromuscular side effects that is comprised on myopathy and neuropathy **[4]**. Decline in the occurrence and rigorousness of cardiovascular risk issues have been noticeable contributors in the direction of the drop in cardiovascular illness and death witnessed in the preceding numerous decades **[5, 6]**. However, an approach that the prolong use of these anti lipidimic agents must be based upon conclusive data that is associated to the safe and effective use of the medication therapy to measure rational risk-benefit. In various references, tolerability and safety are of equal significance as of efficacy in describing the clinical aspects to start a long-term therapy. However, prevalence of rhabdomyolysis with the combined therapy of statins and mibefradil led to the withdrawal of this antihypertensive drug. The current studies have globally shown that withdrawal of cerivastatin causes a relatively high rate of fatal rhabdomyolysis associated with the use of statins **[7]**.

The peril of rhabdomyolysis and other statins induced side effects can be more worsen by several factors, including renal and hepatic function, hypothyroidism, diabetes, and other related medicines **[8]**. The development in the statin-induced rhabdomyolysis is unusual and can occur in ~0.1% of patients; whereas, the occurrence of fewer severe symptoms is underreported and may be 1–5% or more. Physical exercise can also progress myopathy in the people taking statins **[9]**. Few data are also available regarding the frequency of least severe happenings such as muscle pain and weakness, which may affect 1% to 5% of patients **[9]**.

METHODOLOGY

The aim of this study was to monitor statins induced myalgia in post myocardial infarction patients at tertiary care hospital of Hyderabad, Pakistan. The quantitative descriptive cross sectional study was assessed and approved by board of advance studies and research. Statins induced myalgia was assessed clinically through series of questions asked from patients on predesigned approved

questionnaire. A total of 300 patients were enrolled via purposive sampling from Cardiac ward. The study was conducted for a period of 3 months and then the data was further analyzed by using SPSS software. An informed consent from patients and health care providers was also obtained before inclusion in study.

Inclusion and Exclusion Criteria

Inclusion Criteria

Those Patients who had been reported with myocardial infarction & were taking statin therapy as a secondary prevention were included in this study regardless of age & gender.

Exclusion Criteria

Patients who had HIV-AIDS, Hepatitis B & C, Pneumonia, Pulmonary & Extra-pulmonary tuberculosis, Cancer, Febrile patient who had infection of known or unknown origin, Chronic or History of active muscle pain were not included in the study. Very old, debilitated & wasted patients were also excluded. Any other cause that were expected to cause the myalgia other than statins were also considered as part of exclusion criteria.

RESULTS AND DISCUSSION

For the purpose of this study 300 patients were selected among which 218 patients (i.e. 72.66%) were male and 82 patients (i.e. 27.33%) were females as shown in **Table 1**. The ratio of male and female in this study indicates that male patients were high than the number of female patients. Patients were categorized on the basis of their respective age as patients with 25 up to 60 years of age. It was found that maximum number reported patient's age of 50 years were 82 patients (27.33%), then 70 patients were reported of age group 45 years, while the remaining ages of the patients were in **Figure 1**.

While **Figure 2** showed that maximum numbers were reported belongs to **NSTEMI** (non-ST segment elevation myocardial infarction) i.e. 60 patients, whereas, 45 patients having acute anterior wall myocardial infarction (AAWMI), while 9 patients each representing Antero Septal Myocardial infarction and post myocardial infarction angina respectively.

This study also showed that 43% of the patients were suffering from hypertension and 27% of Diabetes Mellitus. Out of 300 patients, 179 (59.66%) of the patients were smokers and remaining were non-smokers. As far as treatment is concerned, 48.33 % of the patient were taking clopidogrel + simvastatin for secondary prevention, 33.66% were taking Aspirin+Clopidogrel+Atorvastatin and 18% of the patients were taking Aspirin+ Atorvastatin. In other study the most

frequently prescribed throughout United States during 2006 was atorvastatin **[10]**. Now a days, there has been arising interest for the side effects of statin use on patients being seen by physical therapists **[11]**. Out of 300 patients, 71 (23.66%) of the patients reported myalgia due to taken statins therapy (Atorvastatin). 15 patients (5%) presented myalgia complain at the dose of 10 mg, 23 patients (7.66%) who were at 20mg presented the complain. 33 patients (11%) who were at 40mg presented the complain. 70% myalgic cases complained mild intensity while 30% had moderate level. It has been estimated that nearly 25 million peoples use statins **[7]** and 5% to 18% of patients also suffered from certain form of myalgia **[12]**.

Table 1: Number of Patients Based on Gender

S. No.	Gender	Number of patients with percentage
1	Male	218 (72.66%)
2	Female	82 (27.33%)

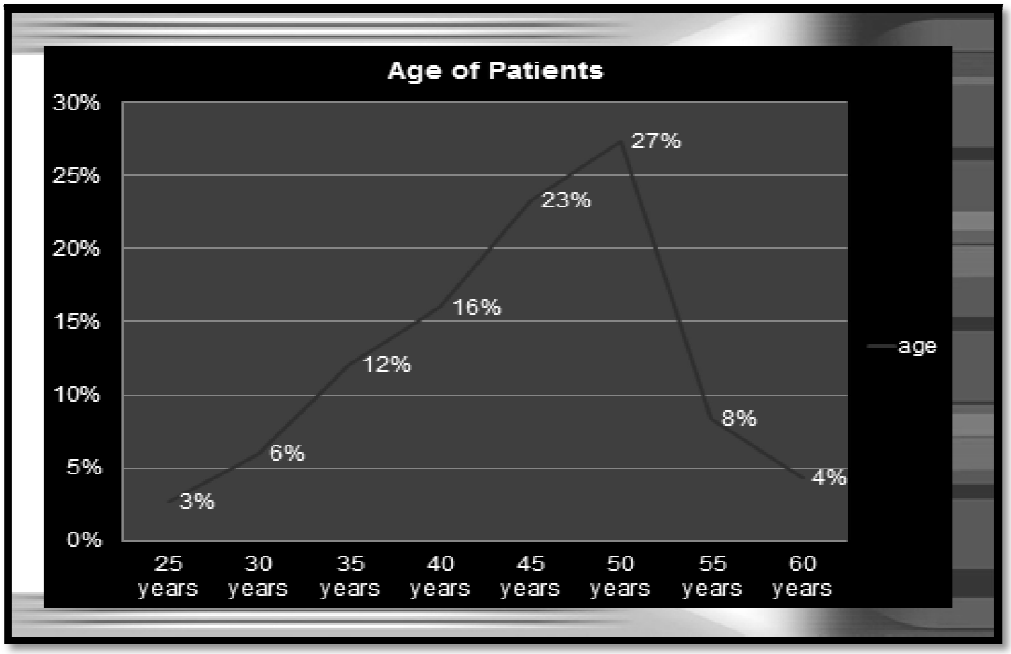

Figure 1: Age of the Patients

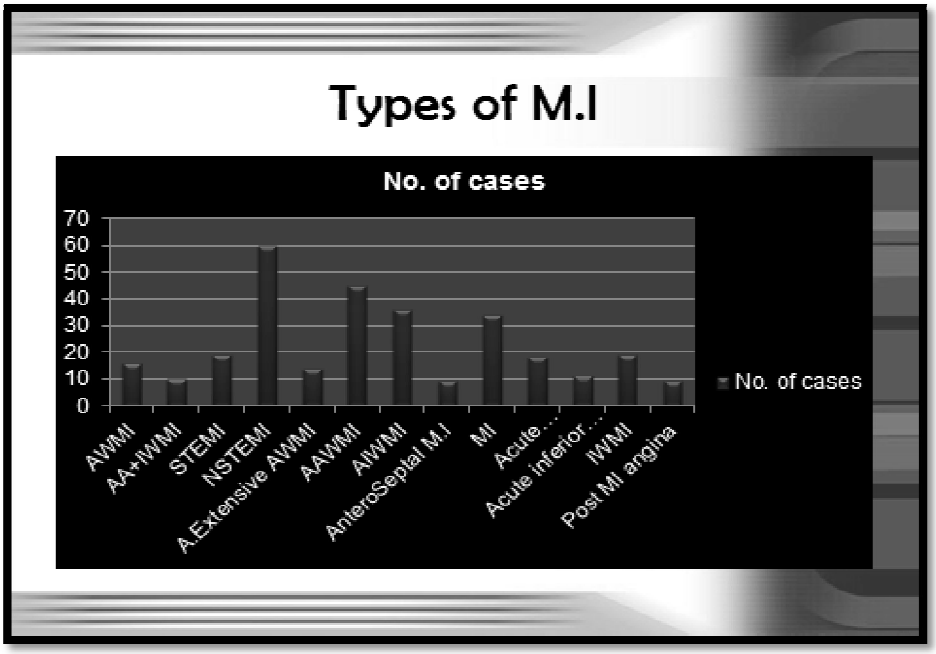

Figure 2: Types of Post Myocardial Infarction

CONCLUSION

From the findings of the above study, it has been concluded that the statin induced myalgia and myopathy can be occurred due to different factors either due to abrupt withdrawal from the therapy or it might be responsive myalgia that can be occurred at different doses, whereas irrational therapy is also a noticeable factor, so dose management plays a keen role in prevention of such hazardous and fatal conditions. However, it is utmost responsibility of all members of the health care team i.e. Doctor, Pharmacist and Paramedical staff to have keen look ahead for statins therapy in order to prevent such happenings.

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