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Original Article

Frequency of Myopathy in Cases of Diabetes Mellitus Using Atorvastatin

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Abstract

Objective: The prime objective of this study was to determine the frequency of myopathy in diabetes mellitus patients using atorvastatin.

Methods: This cross-sectional study was conducted in the department of medicine at Gulab Devi Hospital, Lahore, after the approval of ethical committee and informed consent of the participants. Sample of 107 diabetic patients of both genders, aged between 20-70 years were included through non-probability consecutive sampling method. Electromyography was performed on selected participants and their serum creatinine kinase (CK) levels were assessed. Data analysis was done through SPSS version 16.

Results: The mean age in this study was 51±10.8 years. Majority of the patients were male 59(55%) while female were 48(44.9%). Mean duration elapsed from diagnosis of diabetes was 9.42±2.15 years. It was observed that patients were on statin therapy from last 6.26±1.46 months. Myopathy was present in the 66(61%) cases while 41(38.3%) did not have this condition.

Conclusion: The study concluded that symptoms of myopathy are highly prevalent in diabetic patients on statin therapy and the frequency of myopathy rises with the atorvastatin dosage. The study provides valuable insights into the potential musculoskeletal side effects of statin therapy in this specific patient population.

Keywords: Statin, Diabetes Mellitus, Myopathy, Creatinine Kinase, Electromyography

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Introduction

The prevalence of noncommunicable diseases, such as diabetes and cardiovascular conditions, is increa-sing globally.[1] Statins, which are known for their diverse effects, are frequently prescribed to reduce the risk of cardiovascular and cerebrovascular complications.[2] Statins helps to reduce cholesterol levels along with reduction in disease and death rate secondary to cardiovascular diseases.[3] Statins are generally considered to be safe to use with minimum side effects.[4] However, statin-related adverse drug reactions (ADRs) can manifest as problems related to brain function, issues with the muscles and skeleton[5] and in very uncommon cases, damage to the kidneys or liver.[6] New side effects have been raised including increasing body weight[7]. Problems related to musculoskeletal system represent the most common form of statin intolerance. The use of statins has increased in the past two decades resulting in increased incidence of muscle toxicity.[8] The severity of these adverse drug reactions varies widely from mild myalgias or myositis to involvement of multiple systems as in rhabdomyolysis.[9]

Clinically, statin-induced muscle toxicity can be diagnosed on the basis of 2 variables, firstly muscle pain and secondly the serum levels of creatine kinase (CK) enzyme. Among both, CK levels are used as markers of severity of the muscle damage.[10]

Statins, also known as HMG-CoA reductase inhibitors, are a class of lipid-lowering medications that reduce illness and mortality in those who are at high risk of cardiovascular disease. They are the most common cholesterol-lowering drugs.[11] Statins have been found to be one of the most important drugs with pleotropic drug action. Specifically, atorvastatin is likely to increase the occurrence and development of myopathy according to previous studies. It was also demonstrated the presence

of myopathy in patients treated with atorvastatin and the concurrent increase in the risk of myopathy with increased doses of atorvastatin (i.e.40mg/day to 80mg/day).[12,13] According to a study the incidence of myopathy reported in patients on statin therapy was 65%.[14] The symptoms of myopathies vary from mild myalgia to severe rhabdomyolysis which may cause cessation of the drug therapy. These adverse effects are increased in older adults, female gender, hepatic and renal insufficiency, and hypothyroidism. Use of different drugs along with statins also causes increased risk of myopathy associated with statins.[9]

Currently we lack the ability to identify patients at high risk of developing the complications associated with statin treatment particularly Atorvastatin. Thus, current study will focus on these gaps and will try to unveil the possible consequences of using Atorvastatin. The present study has therefore been undertaken to investigate the frequency of myopathy. Results of this study may help us to reduce the morbidity related to use of atorvastatin.

Methods

The current cross-sectional study was conducted over 107 patients diagnosed with diabetes mellitus at Department of Medicine, Gulab Devi Hospital Lahore after approval from the research committee of the institute from March 2022 to Nov 2022. The sample size was calculated by using the WHO Sample size calculator for estimating a population proportion with specified absolute precision. Confidence interval of 95% and absolute precision of 9% was used with anticipated frequency of myopathy as 65%.[14] The data was collected through convenient sampling technique. Date from patients taking doses of Atorvastatin 10, 20 and 40mg was collected.

The study included diabetic patients of both genders aged between 20-70 years, while those having history of liver disease, myopathy, polyneuropathy, peripheral vascular disease, and pregnant females were excluded from the study.[15] Electromyography was performed on selected participants and their serum creatine kinase (CK) levels were assessed. The values were recorded in a pre-designed performa including demographic data.

Data analysis was done by using SPSS version 16. Mean and standard deviation were calculated for quantitative data while frequency and percentages were calculated for qualitative data. Stratification was done for age, gender, duration of DM, duration and dose of atorvastatin. Post stratification chi-square test was applied. P value of <.05 was considered significance.

Results

The mean age in this study was 51±10.8 years. Majority of the patients were male 59(55%) while 48(44.9%) were female. Mean duration elapsed from diagnosis of diabetes was 9.42±2.15 years. It was observed that patients were on statin therapy from last 6.26±1.46 months. Myopathy was present in the 66(61%) cases while 41(38.3%) did not have this condition (Table #1).

Table 1: *Summary of descriptive statistics (N=107)*

Characteristic		Mean ± SD	
Age of patients		51±10.8 years	
Duration of DM		9.42±2.15 year	
Duration of statin therapy		6.26±1.46 months	
		Frequency (n)	**Percentage (%)**
Gender	Male	59	55.1
	Female	48	44.9
Myopathy	Present	66	61.7
	Absent	41	38.3

*DM: Diabetes Mellitus

Data stratification revealed that 13(61%) patients from age group of <40 years and 53(61%) patients from age group >40 year had myopathy. Of 59 males patients, 35(59%) had myopathy and of 48 female patients, 31 (64%) reported to had myopathy which shows greater frequency in females than males. The variables of age and gender were not significantly associated with myopathy as p value of both was > 0.05. Incidence of Myopathy was higher in those having DM from more than 7 years [59(65%)], those who were on statin therapy from more than 5 months [38(62.3%)] and those having atorvastatin dosage of 20 mg [41(91.1%)].

Table 2: *Stratification of the Presence of Myopathy in Diabetic cases using Statin with different variables*

Variables		Myopathy		P-value
		Present N (%)	**Absent (%)**	
Age Group	20-40 year	13 (61.9%)	8 (38.1%)	0.59
	41-70 year	53 (61.6%)	33 (38.4%)	
Gender	Male	35 (59.3%)	24 (40.7%)	0.36
	Female	31 (64.6%)	17 (35.4%)	
Duration of DM	<7 years	7 (41.2%)	10 (58.8%)	0.05*
	>7 years	59 (65.6%)	31 (34.4%)	
Duration of Statin therapy	<5 months	28 (60.9%)	18 (39.1%)	0.023*
	>5 months	38 (62.3%)	23 (37.7%)	
Dose of Statin	10mg	2 (5.7%)	33 (94.3%)	0.00*
	20mg	41 (91.1%)	4 (8.9%)	
	40mg	23 (85.2%)	4 (14.8%)	

*Denotes significant values
*DM: Diabetes Mellitus

The results showed significant association with duration of DM (0.05), Duration of statin therapy (0.023) and dosage of atorvastatin (0.00) as P-value of all were < 0.05. (Table # 2)

Discussion

Statins are particularly beneficial lipid lowering drugs which may reduce cardiovascular morbidity and mortality. The so-called "statin intolerance" is a major contributor to non-adherence, primarily due to symptoms associated to the muscles. Myalgia is the most common symptom of these conditions. Myositis or rhabdomyolysis with elevated creatine kinase levels have also been seen in patients less often.

In the current study 61.7% diabetic patients receiving statin therapy reported to have symptoms of myalgia, with increased prevalence by increasing the dosage and duration of statin therapy. The current prevalence of myalgia during statin therapy is slightly higher than that reported in previous studies

The results of the current study were contrary to a pilot study conducted in 2017 by k. Monaj et al on 200 patients using atorvastatin, the results showed that incidence of myopathy was 7.5% overall while the current study showed greater prevalence of myopathy (61.7%). The results of preceding study were concurrent with the current study as it showed higher prevalence of myopathy in females and increasing prevalence with increasing dosage of statin which were similar with the results of current study.[13]

The current study showed non-significant association among presence of myalgia and age of the patients, denoting that symptom of myalgia is not age dependent, however in contrast, a previous study in 2019 reported to have increased prevalence in older age group patients (>42%).[16] On the other hand in 2005, PRIMO concluded that symptoms of myopathy are more prevalent in those individuals who are physically active rather than older adults who spend a sedentary lifestyle.[17]

Waddah abed et al in 2022 conducted a prospective cohort study, the results of which showed that the overall prevalence of myopathy was 27.8% with 34% incidence among older adults aged > 60years.[18] The prevalence was much lower than that of current study where the incidence rate was 61.7%. However, both the current and previous studies reported to have increased incidence with increasing dosage and duration of statin therapy.

In 2021, M. K. Saeed et al. Conducted a retrospective study on patients who reported to the lipid clinic between 2009 to 2012. They studied 535 patients, including those who had reported muscle symptoms secondary to statin therapy. The results showed that statin-associated muscle symptoms (SAMS) were present in 11% of the cases reported, with increased prevalence in older adults.[19] The results of this study were in contrast with the current study where non-significant association was present among age group and myopathy (p-value >0.05).

There isn't any standard guideline for managing myopathy secondary to statin therapy. According to all standards, serum creatine kinase (CK) levels should only be measured in patients who exhibit symptoms of myopathy and not in those who do not. It is recommended to stop taking the medication right away if there is a symptomatic increase in serum CK levels that is greater than ten times the upper limit of normal. Regarding stopping statins until symptoms improve if CK levels are three to ten times higher than usual, different guidelines have differing viewpoints.[20]

Conclusion

The study concluded that symptoms of myopathy are highly prevalent in diabetic patients on statin therapy and the frequency of myopathy increases somewhat with dose increments but definitely with a longer duration of use. The study provides valuable insights into the potential musculoskeletal side effects of statin therapy in this specific patient population. To lower the frequency of myopathy, however, alternative measures such as switching statins, using medications other than statins, and adjusting dosage schedules may also be taken into account. Further research and monitoring may be necessary to better understand and manage these effects in clinical practice.

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References

1. Eldor R, Raz IJDc. American diabetes association indications for statins in diabetes: Is there evidence? 2009;32(Suppl 2):S384.
2. Oesterle A, Laufs U, Liao JKJCr. Pleiotropic effects of statins on the cardiovascular system. 2017; 120(1): 229-43, Ruscica M, Ferri N, Banach M, Sirtori CR, Corsini AJCR. Side effects of statins: From pathophysiology and epidemiology to diagnostic and therapeutic implications. 2022;118(17):3288-304.
3. Diamantis E, Troupis T, Mazarakis A, Kyriakos G, Troupis G, Skandalakis PJRPoCDD. Primary and secondary prevention of acute coronary syndromes: The role of the statins. 2014;9(2):97-105.
4. Iwere RB, Hewitt JJBJoCP. Myopathy in older people receiving statin therapy: A systematic review and meta-analysis. 2015;80(3):363-71, Sillars A, Sattar NJCCR. Management of lipid abnormalities in patients with diabetes. 2019;21:1-8.

5. Selva-O'Callaghan A, Alvarado-Cardenas M, Pinal-Fernández I, Trallero-Araguás E, Milisenda JC, Martínez MÁ, et al. Statin-induced myalgia and myositis: An update on pathogenesis and clinical recommendations. 2018;14(3):215-24.
6. Mach F, Ray KK, Wiklund O, Corsini A, Catapano AL, Bruckert E, et al. Adverse effects of statin therapy: Perception vs. The evidence–focus on glucose homeostasis, cognitive, renal and hepatic function, haemorrhagic stroke and cataract. 2018;39(27):2526-39.
7. Thompson PD, Panza G, Zaleski A, Taylor BJJotACoC. Statin-associated side effects. 2016;67(20):2395-410.
8. Tiniakou EJT, Management CR. Statin-associated autoimmune myopathy: Current perspectives. 2020:483-92, Seshadri S, Rapaka N, Prajapati B, Mandaliya D, Patel S, Muggalla CS, et al. Statins exacerbate glucose intolerance and hyperglycemia in a high sucrose fed rodent model. 2019;9(1):8825.
9. Nikolic D, Banach M, Chianetta R, Luzzu LM, Pantea Stoian A, Diaconu CC, et al. An overview of statin-induced myopathy and perspectives for the future. 2020; 19(5):601-15.
10. Alfirevic A, Neely D, Armitage J, Chinoy H, Cooper RG, Laaksonen R, et al. Phenotype standardization for statin-induced myotoxicity. 2014;96(4):470-6.
11. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. Guidelines: Editor's choice: 2016 european guidelines on cardiovascular disease prevention in clinical practice: The sixth joint task force of the european society of cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of 10 societies and by invited experts) developed with the special contribution of the european association for cardiovascular prevention & rehabilitation (eacpr). 2016;37(29):2315.
12. Pergolizzi Jr JV, Coluzzi F, Colucci RD, Olsson H, LeQuang JA, Al-Saadi J, et al. Statins and muscle pain. 2020;13(3):299-310.
13. Manoj K, Jain N, Madhu SJIJoE, Metabolism. Myopathy in patients taking atorvastatin: A pilot study. 2017; 21(4):504.
14. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart J-C, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. 2005; 352(14):1425-35.
15. Butt KR, Khan A, Muhammad A, Khan J, Ali E, Zubair UBJPAFMJ. Frequency and correlates of myopathy in patients with diabetes taking atorvastatin. 2021; 71(2): 482-85.
16. Salman Roghani R, Delbari A, Asadi-Lari M, Rashedi VJPr, treatment. Neuropathic pain prevalence of older adults in an urban area of iran: A population-based study. 2019;2019.
17. Bruckert E, Hayem G, Dejager S, Yau C, Bégaud BJCd, therapy. Mild to moderate muscular symptoms with high-dosage statin therapy in hyperlipidemic patients — the primo study. 2005;19:403-14.
18. Abed W, Abujbara M, Batieha A, Ajlouni KJAoM, Surgery. Statin induced myopathy among patients attending the national center for diabetes, endocrinology, & genetics. 2022;74:103304.
19. Saeed M, Shah J, Damani R, Rahman F, Patel P, Gupta PJJol. Risk factors associated with statin-associated muscle symptoms in patients attending a specialized regional lipid clinic. 2021;2021.
20. Tournadre AJJBS. Statins, myalgia, and rhabdomyolysis. 2020;87(1):37-42.