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Research Article

Statin therapy and Vitamin D

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ABSTRACT

Background: Statins are well-known drugs used in dyslipidemia and cardiac disorders since several years. Recently, it has been reported that long-term use of statins reduce serum vitamin D level. When statins are administered to patients with low vitamin D more muscular side effects have been reported. On the contrary, a few studies report that statins might increase vitamin D level competing with its metabolism. Hence, this study was conducted to evaluate the association between statins and vitamin D.
Methods: 125 participants who fulfilled the selection criteria were enrolled in the study. 65 subjects belonged to control group and 60, statin group. The blood sample was collected for Vitamin D estimation. The results were correlated with a demographic profile, nature of statin and the muscular side effects and compared with control group.
Results: The mean vitamin D level in statin group was 15.82 ng/ml±11.51 and 20.57 ng/ml±7.007 in the control group. The difference was found to be statistically significant. 13.85% in the control group and 10% in statin group had sufficient vitamin D level. 18.33% and 36.92 % had insufficient levels and 71.67% and 49.23% had a deficiency in the statin and control groups respectively. Myalgia was reported by 30 among 60 subjects (50%) in statin group and 5 among 65 subjects (7.69%) in the control group.
Conclusion: The present study has shown that statin therapy is associated with low vitamin D level and that this could contribute to the increased incidence of myalgia in the statin group.

Keywords: Vitamin D, Statin, Atorvastatin, Myalgia, Dyslipidemia

INTRODUCTION

Statins are used in dyslipidemia as well as coronary heart disease either with or without significant hyperlipidemia. There are several studies[1-4] favoring the long-term use of statins in ischemic heart disease and peripheral vascular disorders. Statins could also be beneficial in these conditions due to their pleiotropic effects[5] such as "improving endothelial function, enhancing the stability of atherosclerotic plaques, decreasing oxidative stress and inflammation, and inhibiting the thrombogenic response."[5] However, some of the recent studies have shown that statins may cause impairment of cognition, glucose tolerance, and Vitamin D metabolism.[6]

Cholesterol is the precursor for vitamin D synthesis. Statins by reducing cholesterol synthesis may lead to a reduction in vitamin D level. However, recently it has been reported that statins can compete with vitamin D for metabolism and increase its level.[7]

In this background of controversial reports, it is essential to assess vitamin D level in patients who are on statins. Hence, this study has been done with the objective of assessing

vitamin D level in patients who are on statins and those not on statins.

METHODS

- The study was a prospective cross-sectional study
- It was initiated after obtaining approval from the Institutional Human Ethics Committee
- Informed consent was obtained from participants prior to the study
- Selection criteria:
  - Statin group - all subjects who were on any one of statins for more than 1 year
  - Control group - apparently healthy individuals who were not suffering from any known medical disorders.
- From the subjects, the following information was collected:
  - Age, gender, occupation, duration of statin therapy, name of statin taken, medical history including adverse effects such as myalgia and vitamin D supplementation.
- Subjects who were on vitamin D supplementation were excluded from the study in both statin and control groups
- From the eligible subjects, 5 ml of blood was collected by direct venous puncture
- Vitamin D (total) was estimated with the high sensitive chemiluminescence immunoassay method
- The analysis was done in Siemens ADVIA Centaur, standardized with vitamin D Standardization Program
- The results were analyzed for Vitamin D level and status
- Vitamin D level was classified as sufficient, insufficient and deficient based on the following levels:[8,9]
  - Sufficient: 30-100 ng/ml
  - Insufficient: 20-29 ng/ml
  - Deficient: <20 ng/ml.

RESULTS

In this study, a total of 125 subjects participated. 60 subjects were in statin group and 65 in the control group. In statin group, 28 (47%) were males and 32 (53%) females. In control group, 35 (54%) were males and 30 (46%) females. The mean age of the subjects in statin group was 69.35±9.88 years (mean±standard deviation) and control group; it was 54.85±15.26 years. In statin group, 40 subjects were on atorvastatin, 19 on rosuvastatin, and 1 on simvastatin.

The mean vitamin D level in statin group was 15.82 ng/ml±11.51 and in the control group, 20.57 ng/ml±7.07. The gender and age wise summary of vitamin D level in both the groups is provided in Tables 1 and 2.

In control group, vitamin D status was insufficient level (30-100 ng) in 9 subjects (13.85%), insufficient in 24 (36.92%), and deficient in 32 (49.23%) subjects. In statin group, vitamin D status was sufficient in 6 (10%) subjects, insufficient in 11 (18.33%) and deficient in 43 (71.67%) subjects (Table 3).

The data of vitamin D level and vitamin D status is graphically represented in figure 1 and 2 respectively

Statistical comparison was made for vitamin D level using independent samples t-test as well as vitamin D status using Chi-square test which indicated a significant difference between the two groups (p=0.006 and 0.033, Table 4).

Age and gender difference did not have any influence on vitamin D level in both the groups.

Table 1: Summary data of vitamin D level in statin group.

Age (Years)	n (%)	Mean vitamin D (ng/ml)	SD
<40	0		
40-60	14	15.03	12.22
>60	46	15.26	12.35
Gender			
Male	28	16.65	10.02
Female	32	13.94	13.90

SD: Standard deviation

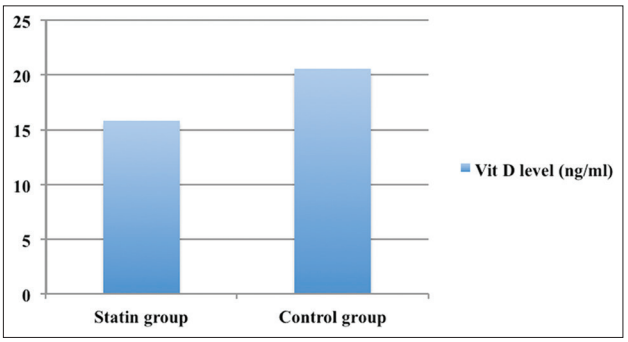

Figure 1: Vitamin D level in stain and control group.

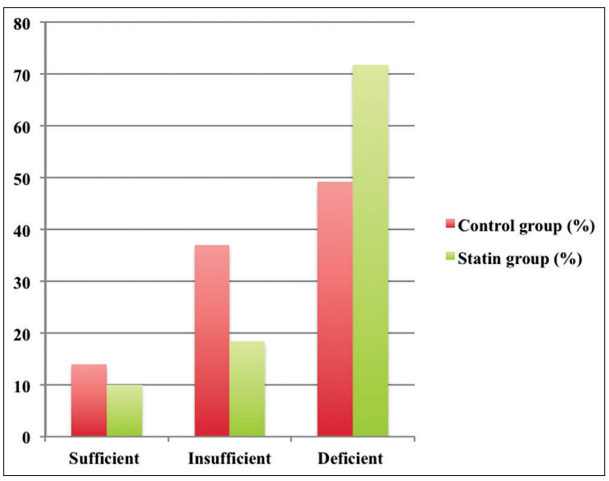

Figure 2: Vitamin D status in stain and control group.

Within the statin group, there was no difference between atorvastatin and rosuvastatin. As there was a single patient in simvastatin group, it was not included for statistical comparison (Table 5).

Myalgia was reported by 30 out of 60 subjects (50%) in statin group and 5 out of 65 subjects (7.69%) in controls. The difference was found to be highly significant (p=0.00).

Table 2: Summary data of vitamin D level in control group.

Age (Years)	n (%)	Mean vitamin D (ng/ml)	SD
<40	12	15.13	6.46
40-60	29	20.64	7.11
>60	24	23.04	6.53
Gender			
Male	35	22.48	6.68
Female	30	18.20	7.29

SD: Standard deviation

Table 3: Vitamin D status.

Vitamin D status	n (%)	
	Statin group	Control group
Sufficient	6 (10.00)	9 (13.85)
Insufficient	11 (18.33)	24 (36.92)
Deficient	43 (71.67)	32 (49.23)

Table 4: Comparison of vitamin D status in statin and control groups.

Statin intake	Vitamin D level			Total
	Deficient	Insufficient	Sufficient	
Yes				
Count	43	11	6	60
Row %	71.67	18.33	10.00	100.00
Column %	57.33	31.43	40.00	48.00
No				
Count	32	24	9	65
Row %	49.23	36.92	13.85	100.00
Column %	42.67	68.57	60.00	52.00
Total				
Count	75	35	15	125
Row %	60.00	28.00	12.00	100.00
Column %	100.00	100.00	100.00	100.00

Chi-square value: 6.853; Significant: 0.033

DISCUSSION

Marwaha et al., studied vitamin D level in 1346 healthy Indians above 50 years of age and reported vitamin D deficiency in 91.2% and insufficiency in 6.8% of the study population. The authors suggested that vitamin D deficiency is universal, and the population may need higher amounts of vitamin D supplementation to prevent complications of vitamin D deficiency.[10]

Ritu and Gupta reported that the prevalence of vitamin D deficiency is 70-100% among Indians and in both urban and rural population. The sociocultural and religious practices in India may be a contributing factor for highly prevalent vitamin D deficiency. Moreover, food fortification with vitamin D is not carried out in India. Chronic deficiency of vitamin D may play a role in rickets, osteoporosis, cardiovascular diseases, diabetes, cancer and infections such as tuberculosis.[9]

Relationship between vitamin D level and statin-induced myalgia is not well-established. Palamaner Subash Shantha et al., (2014) reported that low level of vitamin D (<15 ng/ml) during the initiation of statin therapy is found to be associated positively with myopathy.[11]

Gupta and Thompson suggested that patients who have low vitamin D level while on statin therapy might benefit with vitamin D supplementation in preventing myalgia. They were cautious in recommending that supplementation of vitamin D could prevent statin-induced muscular problems and suggested that further research studies are needed to provide any such recommendation.[12]

The present study has revealed that subjects on statin therapy had low vitamin D level compared to normal control subjects. The reason for such low level of vitamin D could be that statins reduce synthesis of cholesterol which is the precursor of vitamin D and make less cholesterol available for vitamin D synthesis. On the contrary, Schwartz[7] reported that statin increases vitamin D level as both undergo hepatic metabolism through the same pathway. Due to competitive inhibition of vitamin D metabolism by statins, its level is rather increased with concomitant statin therapy.

In our study, the statin group had at least 25% lower vitamin D level compared to control group. The mean vitamin D level in patients taking statins for more than 1 year was 15.82 ng/ml and in controls, 20.57 ng/ml. 71.67% of

Table 5: Vitamin D status in statin and control groups.

Vitamin D status	n (%)			
	Atorvastatin	Rosuvastatin	Simvastatin	Control
Sufficient	4 (10.00)	2 (10.53)	0.00	9 (13.85)
Insufficient	7 (17.50)	4 (21.05)	0.00	24 (36.92)
Deficient	29 (72.50)	13 (68.42)	1 (100.00)	32 (49.23)

subjects in statin group had vitamin D deficiency while only 49.23% of subjects in the control group had deficiency of vitamin D.

Vitamin D more than 30 ng/ml is considered to be sufficient. In our study only 13.85% of the control subjects had sufficient vitamin D level, and the remaining subjects (86.15%) had either insufficient or deficient vitamin D level. This observation is in accordance with the data reported in different studies,[9,10] which have observed that vitamin D is not sufficient in more than 70% of Indian population.

10% of subjects in statin group had sufficient vitamin D level, and the remaining 90% of subjects were in insufficient or deficient status.

Though there is no significant difference between statin and control group with regard to percentage of patients having normal vitamin D level, the percentage of patients having vitamin D deficiency was very high in statin group (71.67%) compared to control group (49.23%).

It can be postulated that vitamin D deficiency could have additionally contributed to stain induced myalgia and whether vitamin D supplementation can be recommended to all patients on statin therapy has to be explored. This is especially important when vitamin D deficiency is reported to be highly prevalent in normal subjects[8,9] and whether universal vitamin D supplementation will prevent vitamin D deficiency related health issues is not known.[13-16]

Though this cross-sectional study observes that statin produces lower vitamin D level, long-term studies are required to investigate the changes in vitamin D level at multiple time points in response to statin therapy.

CONCLUSION

In this study carried out in 125 subjects, 10% of control subjects and 13.85% of statin group had normal vitamin D level. Statin group had significantly lower vitamin D level, compared to control. 71.67% of subjects in statin group had vitamin D deficiency while only 49.23% of control subject had vitamin D deficiency. It is concluded that statin therapy results in significant reduction in vitamin D level compared to normal control subjects.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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