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Incidences of insomnia sleep disturbances and nightmares in patients receiving statins as treatment in urban Mumbai, India

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ABSTRACT

Objective - To study the incidences of insomnia, sleep disturbances and nightmares in patients receiving statins as treatment. **Methodology** – A self constructed semi-structured questionnaire was prepared and distributed amongst 300 patients on atorvastatin at the Medicine and Hypertension OPDs at B.Y.L. Nair Charitable Hospital, Mumbai. The questionnaire was designed to note the quality of sleep, incidence and frequency of sleep disturbances and nightmares. The dosage and duration of atorvastatin treatment was also noted and then co-related with the above. Further, 30 patients with the above symptoms were asked to stop taking atorvastatin for 15 days and were asked to report improvements, if any. **Results:** A definite co-relation was found between atorvastatin and sleep disturbance and nightmares. 13.33% of the patients complained of poor quality of sleep. 22.33% of the patients complained of sleep disturbances. 11.67% of the patients complained of nightmares. There is no significant co-relation between dosage of atorvastatin and the sleep-related side effects. There is a definite and significant co-relation between the duration of atorvastatin treatment and sleep-related side effects. On withdrawal of atorvastatin for 15 days, there was a definite improvement in quality of sleep, sleep disturbances and incidence and frequency of nightmares with complete cessation of nightmares in a majority of cases. **Conclusion:** There is a definite derogatory effect of atorvastatin on quality of sleep with increase in sleep disturbances and nightmares. There is a significant co-relation between the duration of treatment with atorvastatin and the occurrence of sleep-related side effects. On cessation of the drug, the effects also decrease to a large degree.

Key words: Atorvastatin, Statins, Sleep, Nightmares, Myocardial Infarction

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Introduction:

"Statins" or HMG-CoA reductase inhibitors are a class of drugs that lower the level of cholesterol in the blood. They block the enzyme hydroxymethylglutaryl-coenzyme A reductase (HMG-CoA reductase) in the liver which is responsible for making cholesterol. The important role of cholesterol in atherosclerosis is widely accepted by scientists. Statins are used for preventing and treating atherosclerosis that causes chest pain, heart attacks, strokes, and intermittent claudication in individuals.

There have been claims worldwide in the last few years of increasing sleep related disorders in patients on statins and several case reports have been noted for the same^{1,2,3}. Parmar and Luque-Coqui speculated in 1998 that an association between dreams and sudden death may occur². They state that an intense alteration in autonomic activity during dreaming can have adverse effects in those with cardiovascular disease. This study was conducted in order to observe the incidence of insomnia, sleep disturbances and nightmares in patients on atorvastatin treatment as well as to correlate it with their dose and duration of

therapy.

Materials And Methods:

A self constructed semi-structured questionnaire was given to 300 patients who were on atorvastatin, who came to the Medicine Out Patient Department of B.Y.L. Nair Charitable Hospital, Mumbai. Patients pre-diagnosed with psychiatric disease, anxiety, stress or panic and those habituated with alcohol, cigarettes and/or coffee before sleeping, by self report, were excluded from the study.

The questionnaire was designed to measure the incidence of sleep disturbances and nightmares in the patients on atorvastatin, along with grading their sleep quality. These were then co-related with the dosage of atorvastatin taken by these patients and the duration of treatment. 30 of the patients with poor quality of sleep, frequent night-awakenings or nightmares were asked to stop taking the drug for 15 days and the results were noted.

The data so collected was tabulated and analysed using the SPSS (version 17) package. Both, the SPSS Software and Graph Pad Instat 3 Software were used for Chi Square Analysis of the data. Graphs were created in MS-Excel.

Results And Interpretations:

A total of 300 patients were taken for the study and asked to fill up a questionnaire. On the basis of the questions answered, the following results were obtained.

40 patients complained of poor Quality of Sleep, 67 patients complained of frequent night-awakenings per week and 35 patients complained of nightmares during statin treatment.

Some other important observations :-

Table 1: Co-relation between the dosage of statin taken and the Quality of Sleep [QOS] of the patient.

Daily Dosage	QOS			Total
	Good	Average	Poor	
10mg	57	9	13	79
20mg	117	21	23	161
40mg	50	5	5	60
Total	224	35	41	300

P value (Chi square) – 0.5 [Hence, non significant as it is > 0.05]

Of the 300 patients ; 16.45% of the patients [79 patients] taking 10mg statins daily, 14.28% of the patients [161 patients] taking 20mg statins daily and 8.33% of the patients [60 patients]taking 40 mg statins daily rated their own sleep as “poor”.

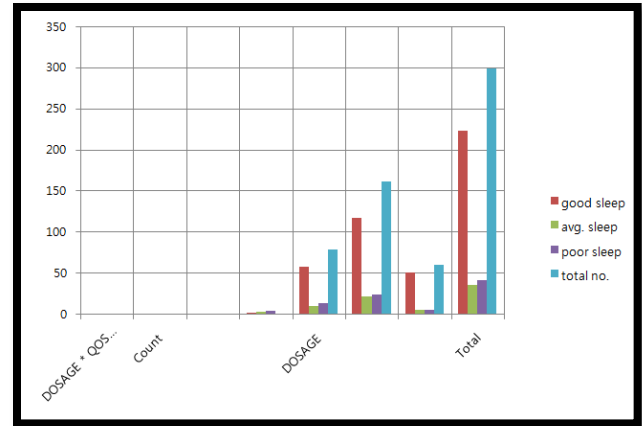
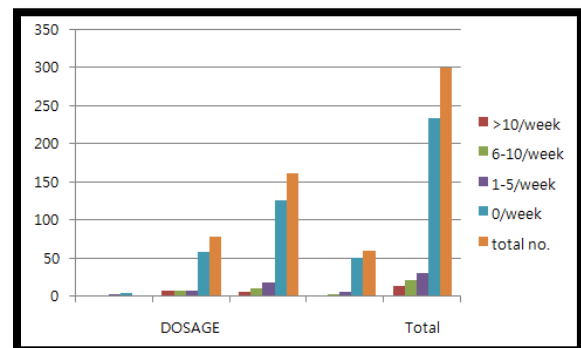


Table 2: Co-relation between Dosage of statins and Frequency of Night Awakenings/week by the Patient

Daily Dosage	FREQUENCY				Total
	>10/week	6-10/week	1-5/week	0/week	
0mg	7	7	7	58	79
20mg	6	11	18	126	161
40mg	1	3	6	50	60
Total	14	21	31	234	300

P value (Chi Square) – 0.43 [Hence, non significant as it is > 0.05]

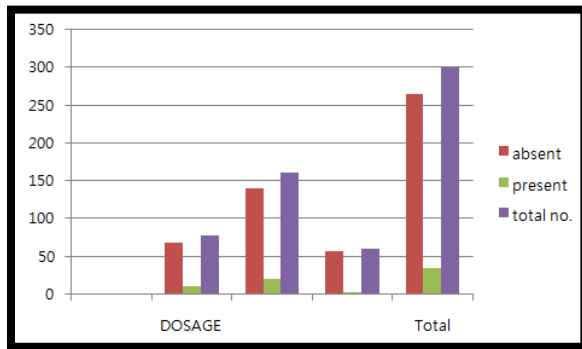


Out of the 300 patients: 17.72% of the patients taking 10 mg statins daily [79 patients], 10.56% of the patients taking 20 mg statins daily [161 patients] and 6.67% of the patients taking 40 mg statins daily [60 patients] woke up more than 5 times in a week at night during statin treatment.

Table 3: Co-relation between Dosage and occurrence of Nightmares in patients

Daily Dosage	NIGHTMARES		Total
	absent	present	
10mg	68	11	79
20mg	140	21	161
40mg	57	3	60
Total	265	35	300

P value (Chi Square) – 0.19 [Hence, non significant as it is > 0.05]



Of the 300 patients; 13.92% of the patients taking 10 mg statins daily [79 patients], 13.04% of the patients taking 20 mg statins daily [161 patients] and 5% of the patients taking 40 mg statins daily [60 patients] suffered from nightmares during statin treatment.

Table 4: Co-relation between Dosage of statins and Frequency of Nightmares in Patients

Daily Dosage	FREQUENCY			Total
	6-10/week	1-5/week	0/week	
10mg	5	6	68	79
20mg	9	12	140	161
40mg	2	1	57	60
Total	16	19	265	300

P value (Chi Square) – 0.46 [Hence, non-significant as it is > 0.05]

Of the 300 patients who were part of the study; 6.32% of the patients taking 10mg statins daily [79 patients], 5.59% of the patients taking 20 mg statins daily [161 patients] and 3.33% of the patients taking 40 mg statins daily [60 patients] suffered from 6 nightmares and above per week during statin treatment.

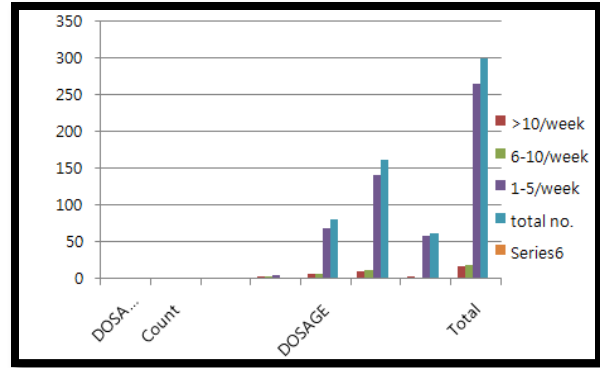
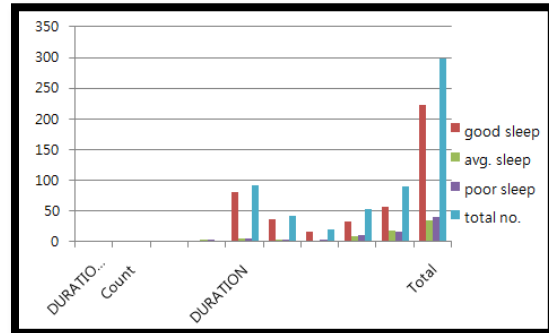


Table 5: Co-relation between Duration of Statin treatment and Quality of Sleep [QOS] of patients

Duration in months	QOS			Total
	Good	Average	Poor	
0-6	81	5	6	92
6-12	37	3	3	43
12-18	16	1	4	21
18-24	33	9	12	54
>24	57	17	16	90
Total	224	35	41	300

P value (Chi Square) – 0.002 [Hence, significant as it is < 0.05]

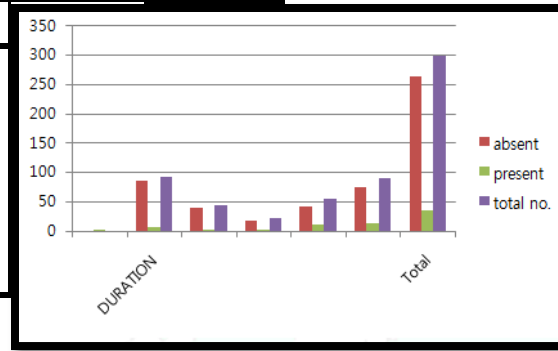


Of the 300 patients who were part of this study; 11.95% of the patients on statin therapy for upto 6 months [92 patients], 14.28% of the patients on statin therapy for 6-12 months [43 patients], 23.8% of the patients on statin therapy for 1-1.5 years [21 patients], 38.88% of the patients on statin therapy for 1.5-2 years [54 patients] and 36.67% of the patients on statin therapy for >2 years [90 patients] had less than satisfactory sleep during statin treatment.

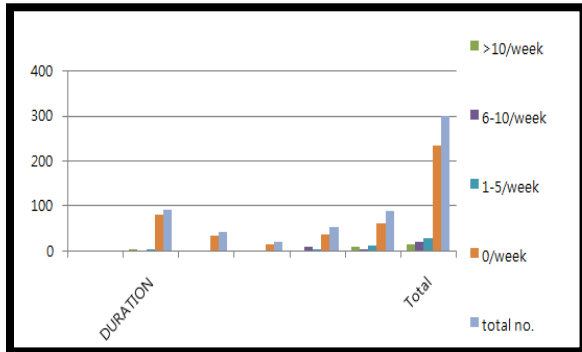
Table 6: Co-relation between duration of treatment and Frequency of Night-Awakings by patients

Duration in months	FREQUENCY
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	>10/week	6-10/week	1-6/week
0-6	3	2	5
6-12	2	2	3
12-18	0	2	3
18-24	1	10	6
>24	8	5	14
Total	14	21	31



P value (Chi Square) – 0.005 [Hence, significant as it is < 0.05]



Of the 300 patients; 6.52% of the patients on statin therapy for upto 6 months [92 patients], 4.65% of the patients on statin therapy for 6-12 months [43 patients], 9.52% of the patients on statin therapy for 1-1.5 years [21 patients], 20.37% of the patients on statin therapy for 1.5-2 years [54 patients] and 15.55% of patients on statin therapy for >2 years suffered from nightmares during statin treatment.

Table 8: Co-relation between Duration of treatment and Frequency of Nightmares in Patients

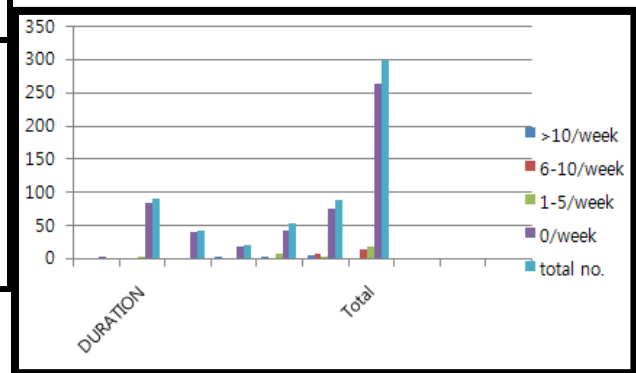
Duration in months	FREQUENCY			Total
	6-10/week	1-5/week	0/week	
0-6	2	4	86	92
6-12	2	0	41	43
12-18	0	2	19	21
18-24	3	8	43	54
>24	9	5	76	90
Total	16	19	265	300

Of the 300 patients; 5.43% of the patients on statin therapy for upto 6 months [92 patients], 9.30% of the patients on statin therapy for 6-12 months [43 patients], 9.52% of the patients on statin therapy for 1-1.5 years [21 patients], 20.37% of the patients on statin therapy for 1.5-2 years [37 patients] and 14.44% of the patients on statin therapy for > 2 years [90 patients] woke up more than 5 times in a week at night during statin treatment.

Table 7: Co-relation between Duration of treatment and occurrence of Nightmares in Patients

Duration in months	NIGHTMARES		Total
	Absent	Present	
0-6	86	6	92
6-12	41	2	43
12-18	19	2	21
18-24	43	11	54
>24	76	14	90
Total	265	35	300

P value (Chi Square) – 0.025 [Hence, significant as it is < 0.05]



P value (Chi Square) – 0.04 [Hence, significant as it is < 0.05]

Of the 300 patients, 2.17% of patients on statin therapy for up to 6 months [92 patients], 4.65% of patients on statin therapy for 6-12 months [43

patients], 0% of patients on statin therapy for 1-1.5 years [21 patients], 5.55% of patients on statin therapy for 1.5-2 years [54 patients] and 10% of patients on statin therapy for >2 years suffered from 6 or more nightmares per week during statin treatment.

30 patients out of the above 300, with reported poor QOS, frequent Night-Awakening and/or Nightmares were asked to stop taking statins for 15 days.

Of the 30 patients who were asked to stop taking statins for 15 days; 88.46% of the patients with previous poor sleep [26 patients] reported improvement in QOS with 38.46% reporting marked improvement.

Of the 30 patients who were asked to stop taking statins for 15 days; 71.42% of the patients who previously reported 6-10 nightmares/week [7 patients] and 88.88% of the patients who previously reported 1-5 nightmares/week [18 patients] now reported complete cessation of nightmares.

Of the 30 patients who were asked to stop taking statins for 15 days; 78.57% of patients with more than 10 night-awakenings /week [14 patients], 92.3% of patients with 6-10 night-awakenings /week [13 patients] and 50% of the patients with 1-5 night-awakenings/week [2 patients] said there was a definite reduction in number of times they got up at night with 14.28%, 23.07% and 50%, respectively, reporting complete cessation of night-awakenings.

Discussion:

There has been an increased use of statins over the last few years and physicians have gone so far as to call statins the “new aspirin”⁵. However, the fear about the side effects of statins has remained. Although myopathy is the most widely studied side effect of statins, there have been several studies as well as case reports about the association between nightmares and various statins including lovastatin and simvastatin. On comparing lovastatin and pravastatin and their effects on sleep Tonstad *et al* found that neither drug had any effect on the quality of life or sleep scores after 24 months of treatment⁶. A large randomised placebo controlled study in Oxford found no adverse effects of prolonged treatment with simvastatin on sleep⁷.

However, the case reports linking statins and nightmares have continued to pour in. Cham *et al* have reported an improvement in sleep apnoea associated with a switch from simvastatin to pravastatin⁸. Similarly Boriani, Gregoor and Ebben have also reported cases of sleep disturbances and sleep apnoea in patients on statins^{1,2,3}.

This study found that there was a significant

association between the duration of atorvastatin use and sleep disturbances as well as nightmares. Patients who had been using atorvastatin for several months reported nightmares as well as frequent awakening at night and poor quality of sleep. We also found that there was no significant association between the dosage of the drug taken and sleep disturbances.

It is interesting to note that 88% of subjects who were asked to stop taking atorvastatin for 15 days had an improvement in quality of sleep and more than 70% patients reported a cessation of nightmares. Over 50% of the patients also reported a complete cessation of night awakenings while over 78% reported a reduction in number of night time awakenings. This was similar to Gregoor’s result of improved sleep and reduction in nightmares after stopping Atorvastatin for 5 days¹

Atorvastatin has an immunomodulatory effect, by which it causes inhibition of the tryptophan-degrading enzyme. This leads to serotonin non-availability. The relation found between nightmares and intake of atorvastatin may refer to this immunomodulatory effect or a direct effect of the drug on the central nervous system.

Conclusion

Atorvastatin has a definite derogatory effect on the quality of sleep of patients. This is a known side effect of statins which often underestimated due to it being a ‘non-serious’ one. About 1/5th of the patients taking atorvastatin reported less than satisfactory sleep which is a significant percentage. Approximately 1 in every 4 patients in the study complained of frequent disturbances in sleep up to more than 6/week. On stopping the drug in 30 of these patients, a significant improvement in sleep was reported. Further studies need to be done on this as atorvastatin is commonly used in asymptomatic patients without a significant past history, as well. Side effects affecting quality of life can have a devastating effect.

35 patients out of 300 reported nightmares after the onset of atorvastatin therapy. That means approximately one in every ten patients taking atorvastatin suffers from nightmares. 21 out of these 25 patients, after stopping atorvastatin for 15 days, reported complete cessation of nightmares. The fact that the drugs given to reduce cardiac risk and mortality in patients may be the cause or trigger of the same cardiac risk is something which needs to be investigated in greater detail and with a larger sample size.

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