Original Article

Sleep in thyrotoxicosis

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ABSTRACT

Objective: Pattern of sleep in hyperthyroid state / thyrotoxicosis has not been systematically studied. It is being characterized as poor without further elaboration. We analyzed the pattern of sleep in a large sample of individuals with thyrotoxicosis who came to our endocrine center in southern India. **Materials and Methods:** We identified individuals with the diagnosis of 'thyrotoxicosis' from our electronic medical record database, and evaluated clinical parameters and pattern of their sleep: difficulty in falling asleep (DFA), difficulty in maintaining sleep (DMS), excess daytime sleepiness). In the first phase, univariate analysis with logistic regression was performed. Multivariate logistic regression was performed in the next phase on variables with a *P*-value < 0.1: these were considered as potential categories/ variables. **Results:** In model response variable with DFA, multivariate logistic regression predicted that subjects with abnormal appetite (more 1.7 or less 2.2), change in bowel motion (loose 1.5 or constipation 2.8), in mood (easy loss of temper 3.4), change of voice -- hoarse 7.4 or moderately hoarse 3.1), tended to have higher chances of difficulty in falling asleep (DFA). Patients with tremor (yes = 5.4) had greater likelihood of difficulty in maintaining sleep (DMS). **Conclusions:** Individuals with hyperthyroidism/thyrotoxicosis principally had difficulty in falling asleep DFA, which was related to hyperkinetic features.

Key words: Difficulty in falling asleep, hypothyroidism, logistic regression

INTRODUCTION

Thyrotoxicosis is the second most frequent functional thyroid disorder at our center.[1,2] Generally individuals with thyrotoxicosis present with hypermetabolic features, but pattern of sleep is not as well studied as in those with hypothyroidism.[1-4] Abnormalities in sleep regulation are often present in thyrotoxicosis[5] even in the neonatal period,[6] which can adversely affect the course of the disease.[7] Owing to the paucity of published information we performed a retrospective analysis of sleep patterns in subjects who presented with thyrotoxicosis to our Center.

MATERIALS AND METHODS

We have a live electronic medical database of subjects who present with endocrine disorders at our Center.[8] We identified individuals with the diagnosis of 'thyrotoxicosis' from our electronic medical record database, and evaluated clinical parameters and the pattern of their sleep (difficulty in falling asleep [DFA], difficulty in maintaining sleep [DMS], excess daytime sleepiness [EDS]) as described previously[4] [Table 1]. Those who did not complain of sleep disturbances were taken as having normal sleep. The aim of this study was to identify factors affecting sleep in this group of subjects at the time of presentation A list continuous variables is presented in Table 1a and of categorical/dichotomous variables in Table 1b.

Statistical analysis

Descriptive statistics are presented in Table 1a for continuous variables and in table 1b for categorical variables. The basic univariate analyses with logistic regression and results are shown in Table 2. From the univariate logistic regression analysis, the variables that had a *P*-value < 0.1

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(90% statistical significance) were considered as potential variables in the multivariate logistic regression done as a second phase analysis. These results are presented in Table 3. The same exercise was adopted for all three models defined earlier namely DFA, DMS and EDS. To minimize the non-identifiably or co-linearity problems, stepwise logistic regression was performed.

In the stepwise logistic regression, a hierarchical forward selection and a backward elimination approach, *P*-value criteria for data inclusion and exclusion were set at 0.05 and 0.09, respectively. The model automatically selected the variable if one of the categories was statistically significant at 95% level.

Odds ratios (OR), values and 95% confidence intervals of

variables associated with the presence of DFA, DMS and EDS were estimated in a final logistic regression model that contained all variables that had entered or had been retained in the stepwise procedures [Table 2]. All analyses were done using SAS v9.2 software.

RESULTS

Out of twenty one variables considered [Tables 1a and b], seventeen were found to be statistically significant either partially or fully attaining at least 90% level of significance with DFA. But only three and ten variables, respectively, were found to be statistically significant at least for 90% significance level when the model response was performed for DMS and EDS, respectively. All models with the statistical significant variables were selected for multivariate logistic regression analysis.

In model response with variable DFA, multivariate logistic regression predicted that patients with abnormal appetite (more 1.7 or less 2.2), bowel movement abnormality (loose 1.5 or constipation 2.8), change in mood (easy loss of temper 3.4), changes in voice (hoarse 7.4 or moderately hoarse 3.1), had greater chances of difficulty in falling asleep (DFA) when compared to patients with normal

Table 1a: Descriptive statistics for continuous variable

Variable	DFA Mean (SD)	DMS Mean (SD)	EDS Mean (SD)
Age	36.18 (11.04)	35.65 (11.46)	34.96 (11.32)
Dyspnea	0.67 (0.47)	0.61 (0.49)	0.61 (0.49)
Pulse	99.08 (19.22)	98.10 (19.09)	97.48 (18.64)
BMI (Kgs/m^2)	19.73 (4.24)	19.64 (3.99)	19.86 (4.15)

DFA: Difficulty in falling asleep, DMS: Difficulty in maintaining sleep, EDS: Excessive daytime sleeping

Table 1b: Frequencies and percentages of categorical variables

Variable	Category	DFA N (%)	DMS N (%)	EDS N (%)	Variable	Category	DFA N (%)	DMS N (%)	EDS N (%)
Anxiety	No	111 (22.38)	80 (27.21)	91 (29.64)	Palptn	Yes	368 (74.19)	202 (68.71)	206 (67.10)
	Yes	385 (77.62)	214 (72.79)	216 (70.36)		No	128 (25.81)	92 (31.29)	101 (32.90)
Appetite	More	63 (12.65)	29 (9.83)	36 (11.58)	Sex	Female	152 (30.46)	92 (31.08)	88 (28.12)
	Normal	197 (39.56)	105 (35.59)	103 (33.12)		Male	347 (69.54)	204 (68.92)	225 (71.88)
	Less	238 (47.79)	161 (54.58)	172 (55.31)	Skin Sweating				
Body pain	Missing	320 (64.13)	183 (61.82)	186 (59.42)		Increased sweating	102 (20.86)	48 (16.55)	46 (15.03)
	No	94 (18.84)	53 (17.91)	66 (21.09)		Normal	10 (2.04)	6 (2.07)	11 (3.59)
	Yes	85 (17.03)	60 (20.27)	61 (19.49)	Skn				
Eyes	Abnormal	278 (55.94)	154 (52.38)	162 (52.77)		Abnormal	6 (1.23)	1 (0.34)	3 (0.97)
	Equivocal	88 (17.71)	52 (17.69)	53 (17.26)		Normal	295 (60.33)	167 (57.39)	167 (54.22)
	Normal	131 (26.36)	88 (29.93)	92 (29.97)	Temperature	Normal	300 (60.12)	194 (65.54)	207 (66.13)
						Unable to tolerate heat	177 (35.47)	90 (30.41)	89 (28.43)
					Tremor	Yes	355 (71.43)	196 (66.44)	196 (63.64)
Hair loss	Yes	323 (64.86)	182 (61.69)	191 (62.01)		No	142 (28.57)	99 (33.56)	112 (36.36)
	No	175 (35.14)	113 (38.31)	117 (37.99)	Tremors	Termor+	347 (70.53)	200 (68.26)	200 (65.36)
HIF	Easy loss of temper	11 (2.21)	5 (1.69)	13 (4.17)		No hand termor	145 (29.47)	93 (31.74)	106 (34.64)
	Normal	343 (68.88)	176 (59.66)	181 (58.01)					
Motion	Loose	41 (8.23)	13 (4.39)	19 (6.07)		Normal	15 (3.01)	3 (1.01)	10 (3.19)
	Normal	203 (40.76)	110 (37.16)	109 (34.82)	Weight	Gained Wt	96 (19.24)	65 (21.96)	72 (23.00)
						No change	375 (75.15)	215 (72.64)	220 (70.29)
						Lost Wt	28 (5.61)	16 (5.41)	21 (6.71)

DFA: Difficulty in falling asleep, DMS: Difficulty in maintaining sleep, DMS: Difficulty in maintaining sleep, EDS: Excessive daytime sleeping

Table 2: Univariate logistic regression, odd ratios and *P*-values by each model: Patients diagnosed as Thyrotoxicosis disorder between 1992 and 2004 in EDC

Variable (Effect)	DFA	DMS	EDS			
	OR	*P*-value	OR	*P*-value	OR	*P*-value
BMI	1.003	0.8999	0.939	0.2907	1.071	0.0906
AGE	1.016	0.0599	1.031	0.1072	0.976	0.1219
Anxiety (Yes vs No)	2.326	0.0003	4.021	0.0649	0.680	0.3037
Appetite (More vs Normal)	1.902	0.0010	1.767	0.2121	0.688	0.3735
Body pain (Yes vs No)	1.833	0.0481	1.404	0.5942	3.706	0.0100
Dyspnea in grades	1.902	0.0013	0.927	0.8672	0.942	0.8663
Eyes (Abnormal vs Normal)	0.587	0.0142	0.602	0.3471	0.690	0.3762
Eyes (Equivocal vs Normal)	0.807	0.3843	0.612	0.4556	0.519	0.2492
Hair loss (Yes vs No)	1.435	0.0581	1.360	0.5168	1.385	0.3975
HIF (Easy loss of temper vs Normal)	3.269	<.0001	1.424	0.4561	1.208	0.6323
Bowel Movement (Loose vs Normal)	1.850	0.0013	1.636	0.2685	0.711	0.3944
Palpitation (Yes vs No)	2.099	0.0006	1.599	0.3714	0.705	0.3437
Pulse rate	1.008	0.0942	1.012	0.2876	0.993	0.4751
Sex (Female vs Male)	0.982	0.9279	0.628	0.3041	2.954	0.0292
Skin (Increased sweating vs Normal)	2.108	0.0010	2.515	0.0589	0.963	0.9408
SKN (Abnormal vs Normal)	1.361	0.1033	0.875	0.7642	0.350	0.0048
Temp in tolerate (Hot vs Normal)	0.589	0.0056	0.922	0.8665	2.075	0.1208
TREMORS (Yes vs No)	2.192	0.0002	5.511	0.0233	0.735	0.3975
TREMORS (Yes vs No)	1.226	0.3079	0.800	0.6286	0.305	0.0013
Weight (Gained vs No change)	1.444	0.3964	0.800	0.8439	2.000	0.2298
Weight (Loss vs No change)	1.474	0.0985	0.965	0.9464	0.528	0.1018

The underline shows 90%, **bold** one shows at 95% level, and **underline and bold** shows at 99% statistical significance, DFA: Difficulty in falling asleep, DMS: Difficulty in maintaining sleep, EDS: Excessive daytime sleeping

Table 3: Multivariate logistic regression, odd ratios, *P*-values and 95% CI by each model: Patients diagnosed as Thyrotoxicosis disorder between 1992 and 2004 in EDC

Model / Variable (Effect)	OR	*P*-value	95% CI	
			Lower	Upper
Difficulty in falling asleep (DFA)				
Appetite (More vs Normal)	1.7	0.0259	1.062	2.572
Bowel Movement (Loose vs Normal)	1.5	0.0649	0.976	2.271
HIF (Easy loss of temper vs Normal)	3.4	<.0001	2.096	5.628
Eyes (Abnormal vs Normal)	0.5	0.0017	0.279	0.743
Eyes (Equivocal vs Normal)	0.8	0.3751	0.443	1.359
Age in years	1.0	0.0057	1.008	1.047
Difficulty in maintaining sleep (DMS)				
Tremor (Yes vs No)	5.4	0.0253	1.232	23.578
Excessive daytime sleeping (EDS)				
HIF (Easy loss of temper vs Normal)	1.2	0.6617	0.514	2.851
Tremors (Termors+ vs No hand termor)	0.4	0.0119	0.162	0.798
Sex (Female vs Male)	3.8	0.0381	1.075	13.266

The **bold** one shows at 95% level, underline shows 90% statistical significance

appetite, normal bowel movements, normal affect or normal voice, respectively. Patients with tremor (yes = 5.4) are likely having the difficulty in maintaining sleep (DMS). Patients with hand tremors were as expected, less likely to have excessive daytime sleeping (EDS).

Discussion

Sleep disorders have been described in a variety of endocrine disorders and span across entire age spectrum.[5,6] Earlier studies focused on sleep disturbances in thyrotoxicosis in relation to organic movement disorders[9,10] and periodic paralysis[11] but did not address sleep in general. A rare association of somnambulism was reported with hyperthyroidism.[3] Studies of patterns of sleep disturbances *per se* other than sleep apnea are lacking

In the current study, we found an association of hyperkinetic features (tremor, appetite change, bowel disturbances) with difficulty in falling asleep DFA and with difficulty in maintaining sleep DMS.

The sleep disturbances can potentially add to poor physical health of those with thyrotoxicosis,[12] which could be associated with increased percentage of sleep time spent in stages 3 and 4 (non-REM sleep).[13] A modification of sleep behavior has potential to improve overall wellness of patients with hyperthyroidism. Disturbances of sleep may directly or indirectly contribute to glucose dys-metabolism often reported in patients with hyperthyroidism. Thus understanding of patterns of sleep in hyperthyroid state begs attention. Our study is a step in that direction.

In conclusion, we have shown that thyrotoxicosis is associated principally with difficulty in falling asleep (DFA). Rather than merely affecting the quality of life in untreated thyrotoxicosis, there are potential adverse consequences for behavioral and cardiovascular performance as well.[14,15] It would be instructive to study the latter association in future in larger well well-designed prospective studies.

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