

SLEEP APNEA AND CIRCADIAN EXTRACELLULAR FLUID CHANGE AS AN INDEPENDENT FACTOR FOR NOCTURNAL POLYURIA.

Hypothesis / aims of study

Sleep apnea syndrome (SAS) has been suggested to be a major cause of nocturia.[1] However, the precise etiological association of SAS and nocturia is understudied. Additionally, there has been no study that evaluated the body fluid volume in the analysis of the association between SAS and nocturia. Recently, non-invasive techniques to measure body composition, called body impedance analysis (BIA), have been available. The aim of our study was to elucidate the relationship among SAS, nocturnal polyuria, and body fluid volume by utilizing polysomnography, frequency/volume charts (FVC), and BIA.

Study design, materials and methods

104 patients who were suspected of having SAS were enrolled and underwent overnight polysomnography at our institute. IPSS and OABSS for LUTS were obtained. FVC was recorded during the hospital stay. The severity of nocturnal polyuria (NP) was evaluated by the nocturnal polyuria index (NPi). Patients with and without NP were classified into the NP (+) group and NP (-) group by a cut-off NPi value of 0.33 in elderly (age \geq 65) and 0.25 in younger adult (age $<$ 65). Bladder capacity and nocturnal bladder capacity index (NBCi) were also measured. Extra cellular fluid (ECF) was estimated in the morning and at night using bioelectric impedance analysis. 22 patients who started continuous positive airway pressure (CPAP) therapy were invited to post-CPAP evaluation of symptoms and FVC.

Results

NP(+) group showed a higher apnea-hypopnea index (AHI) (33.9 vs. 24.2, $p = 0.03$) and a larger circadian change in extracellular fluid adjusted to lean body mass (Δ ECF/LBM) (0.22 vs. -0.19 , $p = 0.019$) than NP(-) group (Table 2). After adjusting for age, comorbidities, and BMI in the multiple linear regression analysis (Table 3), the independent factors related to NPi were AHI ($R = 0.58$, $p = 0.001$) and Δ ECF/LBM (%) ($R = 0.40$, $p = 0.02$). There was a positive correlation between NPi and AHI ($R = 0.31$, $p = 0.01$). The pre-post change in night-time urinary frequency was negatively correlated with pre-CPAP NPi ($r = -0.536$, $p=0.010$) and positively correlated with the pre-post change of NPi ($r = 0.562$, $p=0.006$). Despite a similar severity of AHI, NP(+) patients alone showed significant improvement in symptom scores on nocturia, night-time urinary frequency, and NPi by CPAP (Table 4).

Interpretation of results

In this study, we have revealed that nocturnal polyuria was independently associated with AHI and circadian body fluid volume change in SAS patients. Although the relationship between two of the three has been studied, our study was the first to concurrently investigate the relationship among these variables. Contrary to our expectations, our study showed no significant association between nocturia frequency and AHI, in despite of distinct correlation between NPi and AHI. This is probably because the increased bladder capacity in NP (+) patients compensated the larger nocturnal urine production as reflected by almost the same values of NBCi. Recent literature highlighted the role of rostral fluid shift in SAS development; shifting of body fluid from the lower half to the upper half of the body may induce neck edema and upper airway obstruction.[2] At the same time, the shift of the accumulated ECF in the leg during daytime to the circulating plasma volume during bed rest causes a night-time overproduction of urine. Therefore, the pathophysiologic relationship among SAS, body fluid retention, and nocturnal polyuria is complicated.

Concluding message

This study identified sleep apnea and circadian change of extracellular fluid as independent factors for nocturnal polyuria.

Table 1. Patient backgrounds

	mean \pm SD	Range	NP (+) (n=78)	NP (-) (n=26)	P Value
Age	63.4 \pm 11.7	28 - 84	63.4	66.4	0.31
Gender (M/F)	86/18		63/15	23/3	0.36
HT, n (%)	45 (43.3%)		33(42.3%)	12(46.2%)	0.29
DM, n (%)	36 (34.6%)		30(38.5%)	6(23.0%)	0.10
CI, n (%)	10 (9.6%)		8(10.3%)	2(7.6%)	0.25
BPH, n (%)	25 (29.0% in male)		19(30.2%)	6(26.0%)	0.95
CHF, n (%)	7 (6.7%)		5(6.4%)	2(7.6%)	0.70
CKD \geq stage3, n(%)	20 (19.2%)		16(20.5%)	4(15.3%)	0.69
Height (cm)	166.0 \pm 7.7	145.0 - 181.0	167.5	164.4	0.18
Weight (kg)	72.2 \pm 14.9	42.49 -104.3	73.8	67.0	0.09
NPi	0.38 \pm 0.13	0.11 - 0.76	0.43	0.24	<0.0001 *

Table 2. Difference in patient background: NP (+) group versus NP (-) group.

		mean \pm SD	Range	NP (+) (n=78)	NP (-) (n=26)	P Value
PSG	AHI	34.7 \pm 18.9	8.5 - 88.5	33.9	24.2	0.033*
Questionnaire	PSQI	7.4 \pm 3.9	2 - 17	7.1	8.3	0.61
	IPSS total	7.6 \pm 7.5	0 - 31	8.8	8.7	0.99
	IPSS question 7	1.9 \pm 1.4	0 - 6	1.9	2.4	0.21
	IPSS QOL index	3.3 \pm 1.4	0 - 5	3.4	3.4	0.98
	OABSS question2	1.6 \pm 0.9	0 - 3	1.6	1.8	0.38
	OABSS total	2.9 \pm 2.5	0 - 11	3.3	3.3	0.99
FVC	Daytime urinary frequency	6.4 \pm 2.0	3 - 13	5.9	7.4	0.0044*
	Nocturnal urinary frequency	1.5 \pm 1.4	0 - 6	1.6	1.1	0.20
	24h urinary frequency	7.8 \pm 2.7	3 - 16	7.5	8.5	0.14
	Daytime urinary volume(ml)	1090.2 \pm 441.2	175 - 2150	988.9	1372.9	0.0008*
	Nocturnal urinary volume(ml)	663.6 \pm 345.6	200 - 1950	746.8	431.6	0.0004*
	24h urinary volume(ml)	1682.0 \pm 675.3	894 - 3500	1733.8	1804.5	0.66
	Bladder capacity (ml)	364.4 \pm 160.1	100 - 900	396.3	272.4	0.0056*
	Nocturnal bladder capacity index (NBCi)	0.44 \pm 0.82	-3.33 - 2.87	0.436	0.440	0.986
	NPI	0.38 \pm 0.13	0.11 - 0.76	0.43	0.24	<0.0001*
	BIA	BMI	26.3 \pm 4.5	16.4 - 36.3	26.5	23.6
LBM(kg)		53.2 \pm 9.4	32.5 - 78.7	53.9	51.4	0.38
ECF morning (kg)		15.6 \pm 1.9	9.9 - 20.8	15.8	15.4	0.36
ECF night (kg)		15.7 \pm 1.9	10.1 - 19.1	16.0	15.3	0.19
ECF/TBF morning		0.427 \pm 0.03	0.38 - 0.48	0.424	0.435	0.24
ECF/TBF night		0.425 \pm 0.04	0.38 - 0.49	0.424	0.439	0.24
Δ ECF		0.05 \pm 0.66	-2.6 - 1	0.22	-0.19	0.019*
Δ ECF/LBM(%)		0.11 \pm 1.21	-4.1 - 1.7	0.45	-0.38	0.011*

Table3 Association of factors with nocturnal polyuria index on multiple linear regression analysis

variables	Regression Coefficient	p value	t	95% CI	VIF
Age	-0.25	0.21	-1.28	-0.01 - 1.38	2.24
AHI	0.58	0.001*	3.55	0.002 - 0.02	1.52
HT (yes/no)	-0.0003	1.00	0	-0.05 - 0.05	1.77
DM (yes/no)	0.21	0.20	1.31	-0.02 - 0.08	1.52
BPH (yes/no)	0.01	0.94	0.08	-0.07 - 0.08	1.65
CHF(yes/no)	0.12	0.42	0.82	-0.08 - 0.19	1.30
CKD (yes/no)	0.13	0.45	0.76	-0.03 - 0.08	1.57
BMI	1.41	0.34	0.98	-0.05 - 0.14	1.20
Δ ECF/LBM(%)	0.40	0.020*	2.41	0.02 - 0.08	1.55

Table4. Effect of CPAP on nocturia and nocturnal polyuria.

	NP(+) (n=16)			NP(-) (n=6)		
	before CPAP	after CPAP	P value	before CPAP	after CPAP	P value
Age	68.2			70.0		
AHI	38.7			40.4		
IPSS Question 7	2.4 \pm 1.2	1.6 \pm 0.9	0.008*	2.2 \pm 0.4	1.6 \pm 0.5	0.18
OABSS Question 2	1.9 \pm 1.0	1.2 \pm 0.8	0.008*	1.8 \pm 0.4	1.8 \pm 0.8	1.00
Nocturnal urinary frequency by FVC	2.0 \pm 1.7	0.9 \pm 1.1	0.042*	1.2 \pm 0.8	1.7 \pm 1.4	0.48
NPi	0.46 \pm 0.13	0.35 \pm 0.17	0.023*	0.27 \pm 0.6	0.33 \pm 0.16	0.60

References

- Umlauf MG Obstructive sleep apnea, nocturia and polyuria in older adults. Sleep27:139,2004
- Friedman O, Bradley T D, Chan CTet al. Relationship between overnight rostral fluid shift and obstructive sleep apnea in drug-resistant hypertension. Hypertension 56:1077, 2010

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