Article

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Risk and determinant factors for obstructive sleep apnea in patients with epilepsy

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ABSTRACT

Objective: To evaluate the prevalence of risk of having obstructive sleep apnea (OSA) and its determinants in patients with epilepsy (PE). **Method:** 98 adult PE were prospectively screened for risk of OSA by Berlin questionnaire. Data was also collected about excessive daytime sleepiness, depression, anxiety, clinical and socio-demographic characteristics. **Results:** The PE main characteristics: 59-men/39-women, mean age=39.97, SD=12.3, range 18-66. The prevalence of the risk of OSA was 55.1% (CI 95%, 0.45-0.65). The high risk for OSA was related with body mass index (BMI) (p=0.000), neck circumference (NC) (p=0.000), arterial hypertension (AH) (p=0.000), and anxiety (p=0.006), without relationship with number of seizures, number of antiepileptic drugs, age or depression. The NC was statistically significant regarding risk of OSA, mainly in men. **Conclusion:** We found a high risk of OSA in this sample. The main implicated measures were the large NC, high BMI and anxiety. The anthropometric variables were more relevant than those related to epilepsy itself and similar to those of the general population.

Key words: obstructive sleep apnea, epilepsy, obesity.

Risco e determinantes para apneia obstrutiva do sono em pacientes com epilepsia

RESUMO

Objetivo: Avaliar riscos e fatores determinantes para síndrome da apneia obstrutiva do sono (SAOS) em pacientes com epilepsia (PCE). **Método:** 98 PCE adultos foram avaliados prospectivamente para risco de SAOS pelo questionário Clínico de Berlim, e também para sonolência excessiva diurna, depressão, ansiedade, características socioeconômico e demográficas. **Resultados:** 98 PCE foram estudados (59-homens / 39-mulheres, idade média=39,97, DP=12,3, 18-66 anos). A prevalência de risco para SAOS foi de 55,1% (CI 95%, 0,45-0,65). O alto risco de SAOS estava relacionado com índice de massa corporal (IMC) (p=0,000), circunferência do pescoço (CP) (p=0,000), hipertensão arterial (p=0,000) e ansiedade (p=0,006), sem relação com número de crises, drogas antiepiléptica, idade ou depressão. A CP foi estatisticamente significativa na relação com SAOS, principalmente em homens. **Conclusão:** Encontrou-se alta prevalência de risco de SAOS nesta população. As medidas mais relevantes foram CP principalmente em homens, IMC e ansiedade. As variáveis antropométricas foram mais importantes que aquelas relacionadas à própria epilepsia, o que foi similar à população em geral.

Palavras-Chave: síndrome de apneia obstrutiva do sono, epilepsia, obesidade.

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Obstructive sleep apnea (OSA) and epilepsy are conditions that can be interrelated[1]. The prevalence of OSA in the general adult population in USA (ages 30 to 60) is 24% in men, and 9% in women according to Chihorek et al.[2]. The literature reports that in older adults with epilepsy the presence of OSA is associated with sei-

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zure frequency worsening or late onset seizures[2]. Hollinger et al.[3], are the unique authors that related a possible temporal relationship between onset of OSA symptoms and change in seizure control in about two thirds of their patients. The same authors considered that the change in seizure control is shown by increase in seizure frequency, first onset of seizures or new onset of *status epilepticus*. In this way, several case series have shown that the treatment of OSA may reduce seizures frequency, and lessen daytime sleepiness in adults[1]. Manni et al.[4], indicated that the risk factors for OSA are the same in epilepsy subjects as in the general population. Untreated OSA is associated with a variety of potentially life-threatening conditions including cardiac arrhythmias, arterial hypertension (HA), stroke and myocardial infarction[5]. Regarding the potential importance of the relationship between OSA and epilepsy, the main goal of this paper is to evaluate the prevalence of the risk of OSA in this studied population, and its risk factors (clinical and anthropometrical characteristics, anxiety and depression symptomatology).

METHOD

This is a cross-sectional study based on 98 unselected patient population that were under the care in the Neurology Institute of Rio de Janeiro, all of them fulfilling the eligibility criteria. Patients agreeing to sign an informed consent form were included in the study "*The Sleep disorders in adult patients with epilepsy: study of prevalence, quality of sleep and life",* approved by the Ethics Committee of the Institute of Neurology of the Federal University of Rio de Janeiro. This elicits comprehensive subjective clinical information about sleep from individuals with diagnosis of epilepsy. The auto-applied questionnaires were answered by the patients before the medical consultation. For the purpose of studying the specific topic about risk of OSA in this population, data was collected about: [1] socio-demographic and clinical characteristics; [2] risk of OSA by means of Berlin clinical questionnaire (which was the dependent variable); [3] anxiety and depression symptoms by means of the Beck's Inventories[6]; [4] excessive daytime sleepiness (EDS) by means of the Epworth scale. Berlin questionnaire has three categories: 1st with five questions about snoring: 2nd with four about daytime somnolence: 3rd with 1 question about high blood pressure. High risk for OSA is considered if two or more categories are positive[7,8]. The cut-off points for neck circumference (NC) regarding gender was based on Onat et al.[9].

The data were analyzed using the statistical package for social sciences (SPSS 11.01). The Mann-Whitney U-test, Spearman's rank correlation coefficient and Pearson's chi-square tests were applied. All statistical tests were two-tailed, and p values less than 0.05 were considered significant.

RESULTS

There were 98 patients composed of 39 women and 59 men, whose mean age was of 39.97, SD=12.3, range 18-66. In the studied population, the risk of OSA was 55.1% (CI 95%, 0.45-0.65). More than half of the studied patients were overweight, and 28.9% has more than 5 seizures/year (Table 1). High risk for OSA was related with body mass index (BMI) (p=0.000), neck circumference (NC) (p=0.000), AH (p=0.000) and anxiety score (p=0.006), without relationship with number of seizures, number of antiepileptic drugs used, age or depression symptoms (Table 2 and 3). The NC was statistically significant to OSA, mainly in men (p=0.000) (Table 2 and 3). Regarding the relationship analysis between the Berlin questionnaire components and clinical characteristics, we observe significative relationship between EDS and snore (p=0.010), and between AH and BMI (p=0.000) (Table 4).

Table 1. Main characteristics of the studied population.

Variables	Cathegories	n	%	Mean (SD)
Gender	Masculine	59	60.2	–
	Feminine	39	39.8	
Age	<40	49	50	39.97 (12.3)
	≥40	49	50	
Epilepsy type	Focal	37	37.8	–
	Generalized	60	61.2	
Seizure frequency / year	<6	68	70.1	17.12 (55.57)*
	≥6	28	28.9	
AED number	<2	47	48.5	1.63 (0.697)
	≥2	50	51.5	
BMI	Not overweight or obese	46	47	25.79 (4.847)
	Overweight or obese	50	51.3	
Female NC	<35 cm	23	5	33.71 (6.20)
	≥35 cm	14	35.9	
Male NC	<39 cm	25	43.1	34.41 (3.00)
	≥39 cm	33	56.9	
Risk of OSA (Berlin questionnaire)	Low	44	44.9	–
	High	54	55.1	
EDS (Epworth)	<11	51	52	10.11 (5.48)
	≥11	46	46.9	

AED: antiepileptic drugs; BMI: body mass index; NC: neck circumference; EDS: excessive daytime sleepiness; OSA: obstructive sleep apnea; *outlier with more than 1000 seizures/year; SD: standard deviation.

Table 2. Characteristics of patients with low risk and high risk according to the Berlin questionnaire.

	Berlin		
Variable	Low N (Mean-SD)	High N (Mean-SD)	p value
Age	44 (38.32-12.15)	54 (41.31-12.43)	0.233
Seizures frequency / year	44 (34.70-163.32)	53 (22.58-70.84)	0.627
AED's number	44 (1.68-0.71)	54 (1.59-0.69)	0.530
BMI	43 (23.48-3.29)	54 (27.62-5.12)	**0.000**
NC male	42 (35.00-6.35)	53 (38.93-3.44)	**0.000**
NC female	43 (8.53-0.91)	54 (11.37-0.65)	0.074
Depression (Beck Inventory)	43 (9.70-11.09)	54 (13.69-11.80)	0.514
Anxiety (Beck Inventory)	43 (9.05-9.07)	54 (15.31-12.17)	**0.006**

AED: antiepileptic drugs; BMI: body mass index; NC: neck circumference; SD: standard deviation.

Table 3. Relationship between dichotomized important variables and obstructive sleep apnea risk.

		Berlin				
		Low		High		
Variables	Cathegories	n	%	n	%	p value
BMI	Not overweight or obese	29	29.6	18	18.4	**0.001**
	Overweight or obese	14	14.3	36	36.7	
AH	No	40	39	23	22.5	**0.000**
	Yes	2	2	31	30.4	
NC Female	<35 cm	15	38.4	5	12.8	**0.034**
	≥35 cm	6	15.4	11	28.2	
NC Male	<39 cm	14	24	11	19	**0.013**
	≥39 cm	7	12	26	44	

BMI: body mass index; AH: arterial hypertension; NC: neck circumference.

Table 4. Relationship between the Berlin questionnaire components and clinical characteristics.

		Berlin questionnaire components								
		Snore			Sleepiness			AH		
Variables	Cathegories	Yes	No	p	Yes	No	p	Yes	No	p
Gender	Masculine	43	16	0.126	32	27	1.000	22	37	
	Feminine	22	17		21	18		11	26	0.161
Age	<40	29	20	0.199	27	22	1.000	13	36	0.092
	≥40	36	13		26	23		20	27	
EDS (Epworth)	<11	28	23	0.010	28	23	1.000	15	35	0.407
	≥11	37	9		25	21		18	28	
Epilepsy type	Focal	18	19	0.014	19	18	0.612	8	28	0.242
	Generalized	46	14		33	27		24	35	
Seizures frequency / year	<6	45	23	1.000	37	31	0.828	25	42	0.590
	≥6	19	10		15	14		8	20	
AED number	<2	29	18	0.397	29	18	0.161	16	31	0.389
	≥2	36	15		24	27		17	32	
BMI	Underweight or normal	26	21	0.071	23	24	0.141	37	39	0.000
	Pre obese or obese	38	12		30	20		26	23	

AED: antiepileptic drugs; BMI: body mass index; NC: neck circumference; AH: arterial hypertension; EDS: excessive daytime sleepiness.

DISCUSSION

A high prevalence of risk to OSA was found in the studied population. It was similar to a Brazilian study carried out by Tufik et al.[10] about the general population in São Paulo, where it was found 32.8% of prevalence of OSA diagnosed by polysomnography. The authors justified the results regarding their population that presents high age, obesity, and, also, using the criteria of the most recent International Classification of Sleep Disorders (ICDS-2) from American Academy of Sleep Medicine and more sensitive polysomnography's canula evaluation[10,11].

In another study using Berlin questionnaire, also in a Brazilian setting, the authors found high risk of OSA: 78% in cases with resistant AH *vs.* 48% in those with controlled AH. It is also important to remember that AH is one component of Berlin questionnaire and, consequently, in a setting of high prevalence of AH, like in Brazil, the rate of high risk for OSA by the Berlin questionnaire can be overestimated. This questionnaire ranges from 68% to 86% of sensitivity, and 49% to 77% of specificity as mentioned by Friedman et al.[12] which can overestimate the risk to OSA, even more in a setting like ours, as already mentioned.

The main risk factors for OSA were partially similar in our study when compared to the literature[1-3]. It was expected that the number of seizures, the number of antiepileptic drugs used (meaning pharmacoresistant epilepsy), age and depression score were proportionally related to high risk of OSA[1-3] but we did not find this relations statistically significant in our study. Maybe because only 1/3 of the studied sample has more than 5 seizures / year, which would make necessary studying a larger sample size.

The strongest relationship is with anthropometric risk factors, as seen in most of the studies[4,5,9-13]. Therefore, the main measures that we found were the EDS, the large NC mainly in men, and the high BMI that are related to obesity. Deegan and McNicholas[13] said that in male patients according to age, abdominal girth was a closer correlate with apnea-hipopnea index (AHI) than NC and BMI, but, in the other hand, the NC was the best correlate of AHI in female patients, suggesting a possible sex difference in fat distribution and its effect on AHI. In the same article the authors affirm that BMI was a significant independent that correlates with AHI on multiple linear regression analysis while NC was not. However, in our study both the NC (especially NC from male patients) and BMI were strongly correlated to the high risk to OSA as demonstrated in Table 2 and 3.

Another point is the fact that patients that slept predominantly on their back were found to be at increased risk of having OSA. In another study, Lambert et al, payed attention to the development of OSA, the rapid weight gain, following treatment with antiepileptic drugs, especially vigabatrin. In spite of the rare link between epilepsy, namely, central apnea, as cause to OSA, Dominici et al.[14] presented a case of central and obstructive sleep apnea due to epileptic seizures and report that this condition may be neglected in most instances. In this way the authors suggested also the video-EEG-polysomnography to respiratory events associated to seizures.

Furthermore, it is shown in our study the significant relation between anxiety and risk of OSA. In this context, the psychiatric comorbidities can be consequence or the cause of OSA, and then we have a complex mechanism to be understood in each case. Consequently, it is necessary a good knowledge and control of all these associated comorbidities.

There are many determinant factors for OSA being studied at the moment as BMI and NC for example and certainly these findings can help epileptic and non epileptic patients, mainly the overweight ones. Therefore, the comorbidities and the seizures can be avoided or lessened by the correct management of these variables. Weight loss, dietary advice, bariatric surgery and alcohol consumption reduction are important measures to decrease OSA and its consequences, such as hypertension. Besides, larger longitudinal studies with the use of polysomnography appear warranted to study more thoroughly our Brazilian population with epilepsy.

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