Journal of Epilepsy and Clinical Neurophysiology

J Epilepsy Clin Neurophysiol 2013; 19 (1): 13-16

The obstructibe sleep apnea screening in patients with epilepsy

Triagem da síndrome da apneia obstrutiva do sono em pacientes com eplepsia

Monique Venturi[1], Lucas Neves de Andrade Lemes[2], Anamélia Costa Faria[3], Marleide da Mota Gomes[4]

ABSTRACT

Objectives: To estimate the accuracy of some obstructive sleep apnea (OSA) screening clinical methods in patients with epilepsy (PWE), besides to report OSA screening issues by literature review. **Methods:** 98 adult PWE were prospectively screened for OSA. The Berlin questionnaire (BQ) performance was compared to the Epworth sleepiness scale (ESS), as well as with some questions about snore from Basic Nordic Sleep Questionnaire (BNSQ), anthropometrical characteristics (BMI, neck circumference-NC), besides variables related to epilepsy by means of the diagnostic odds ratio (OR). **Results:** It was found a remarkable OR for OSA regarding snore frequency (OR=11.2/CI95%=4.2-30/p<0.001), loud snoring (OR=10.7/CI95%=3.6-28.6/p<0.001) and time of snoring in years (OR=14.4 /CI95%=1.6-127.6/p<0.000), BMI(OR=4.1/CI95%=1.8-9.7/p=0.001), male neck circumference (NC) (OR=4.7/CI95%=1.5-14.9/p=0.006), female NC (OR=5.5 /CI95%=1.3-22.7/p=0.015) and generalized epilepsy (OR=3.1/CI95%=1.3-7.1/ p=0.009). **Conclusions:** These questions may help clinicians identify OSA in PWE and the selection of the patients for carrying out polysomnography registration. They can be used for the construction of a predictive rule for the diagnosis of OSA in PWE.The generalized seizure is important for OSA's screening and there is necessity of the better study of this relationship.

Key words- SAOS, epilepsy, screening questionnaires

RESUMO

Objetivos: Estimar acurácia de alguns métodos clínicos de triagem para Síndrome de Apneia Obstrutiva do Sono (SAOS) em pessoas com epilepsia (PCE) e rever literatura sobre assunto. **Métodos:** 98 PCE adultas foram prospectivamente triadas para SAOS. O Questionário Clínico de Berlim (QB) foi comparado através da razão de chances (RC) a: Escala de Sonolência de Epworth (ESE), algumas questões sobre ronco do Questionário Escandinavo Básico do Sono (QEBS), características antropométricas (IMC, circunferência do pescoço (CP), além de variáveis relacionadas a epilepsia. **Resultados:** Foram encontradas RC significativas para o diagnóstico de SAOS em: frequência de roncos (RC=11.2/IC95%=4.2-30/p<0.001), volume de ronco (RC=10.7/IC95%=3.6-28.6/p<0.001), tempo de ronco em anos (RC=14.4/IC95%=1.6-127.6/p<0.000), IMC(RC=4.1/IC95%=1.8-9.7/p=0.001), CP masculina (RC=4.7/IC95%=1.5-14.9/p=0.006), CP feminina (RC=5.5/IC95%=1.3-22.7/p=0.015) e epilepsia generalizada (RC=3.1/IC95%=1.3-7.1/p=0.009). **Conclusões:** Estas questões ajudam o clínico no diagnóstico de SAOS e a seleção dos pacientes para a realização de polissonografia. Elas podem colaborar para construção de uma regra preditiva para diagnóstico de SAOS em PCE. O tipo de crise generalizada é relevante e pode servir para o rastreamento de SAOS e há necessidade de melhor avaliação desta relação.

Palavras chave: triagem, síndrome da apneia obstrutiva do sono, epilepsia

1. Neurologist, Fellow - Post-Graduate Program of the Institute of Psychiatry - Universidade Federal do Rio de Janeiro
2. Otorhinolaryngologist, Associate professor - Universidade do Estado do Rio de Janeiro
3. Pneumologist, Hospital Universitário Pedro Ernesto - Universidade do Estado do Rio de Janeiro
4. Neurologist, Associate professor, Institute of Neurology / Faculty of Medicine - Universidade Federal do Rio de Janeiro

INTRODUCTION

Obstructive Sleep Apnea Syndrome (OSA) is an important public health problem that can be associated with mood disorders, accidents, hypersomnolence, cardiovascular morbidity and metabolic dysfunction.[1,2] Hollinger *et al.,2006*[3] OSA has be found in 5-63% of patients with epilepsy (PWE). The same author justifies that the frequency rates were higher in patients with refractory epilepsy or epilepsy patients referred to a sleep center. In the same context, Chirorek *et al., 2007*[4], sustain that OSA is associated with seizure exacerbation in older adults with epilepsy. The presence of untreated OSA may lead to sleep fragmentation and chronic sleep deprivation, which can facilitate seizures in susceptible individuals according to Chirorek *et al., 2007*[4]. However, there is not a protocol for screening OSA in PWE [5,6]. Once this sleep disorder may worsen the seizures, it is necessary to use non-expensive and available tools for its screening. At the moment, the main clinical screenings for OSA are the clinical-anthropometrical findings and some questionnaires as Berlin Questionnaire (BQ) [6,7]. The BQ presents better accuracy to screen OSA than Epworth Sleepiness Scale (ESS) that is considered the worst [6,7]. Two reviews, one about OSA and epilepsy [5], and other about OSA screening[6] found only one study about OSA screening in PWE: Weatherwax *et al., 2003* [8] used The Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ). The authors considered it an accurate instrument to screen OSA in this specific population mainly if used with lower cut-off because in this way its sensitivity raises. However, Ramachandran and Josephs., 2009[6] reported that SA-SDQ in comparison to BQ had a little worse diagnostic performance because its confidence interval for sensitivity and specificity was larger than in BQ analysis.

The best combination of medical signs, symptoms, and other findings may be important in predicting the probability of OSA, in the scarcity of polysomnography, the gold standard. Regarding this, our intent is to make an exercise regarding the importance of OSA questionnaires analyses in a group of PWE and raises some considerations about their value. In this article, we evaluated the performance of BQ to the ESS and some questions from Basic Nordic Sleep Questionnaire (BNSQ) (snore, time of snoring and apnea) besides anthropometric measures (BMI and neck circumference-NC) [9-11] and number of antiepileptic drug in PWE.

METHODS

This is a cross-sectional study based on 98 unselected patients under Rio de Janeiro Institute of Neurology care. The methodology is presented in other paper by the author Venturi *et al.,* 2011[12]. In this paper, the analyzed data included: 1.Clinical characteristics; 2- Risk of OSA by means of Berlin Clinical questionnaire – BQ (which was the dependent variable)[13]; 3- Excessive daytime sleepiness (EDS) by means of the Epworth sleepiness scale (ESS)[14]; 4-Basic Nordic sleep Questionnaire (BNSQ)[15]. BQ 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[13]. Only some questions of BNSQ were analyzed: snore frequency and loud snoring, time of snoring in years, and apnea.

The diagnostic testing may be used to discriminate subjects with and without the disorder[16]. Then, we propose the use of the diagnostic odds ratio (OR) as a single indicator of diagnostic performance of OSA: the ratio of the odds of the test being positive if the PWE has OSA relative to the odds of the test being positive if the subject does not have it. It facilitates formal meta-analysis of studies on diagnostic test performance[16,17].

The data were analyzed using the Statistical package for social sciences (SPSS 11). All statistical tests were two tailed and p values less than 0.05 were considered significant. To compare proportions between categorical variables we applied the X_2 test or Fisher's exact test. We considered that the OR summarizes the diagnostic accuracy of the index test as a single number that describes how many times higher the OR are of obtaining a positive test result in a PWE with OSA rather than in one without it.

RESULTS

The patients were composed by 39 women and 59 men, mean age of 39.97 (±12.3), range 18 – 66. There was find a remarkable high OR with snore frequency (OR=11.2/CI95%=4.2-30/p<0.001), loud snoring (OR=10.7 /CI95%=3.6-28.6/p <0.001) and time of snoring in years (OR=14.4 /CI95%=1.6-127.6/ p<0.001) (table 1). In addition, regarding anthropometrical variables, it was found a significant but a comparative lower OR with BMI (OR=4.1 / CI95%=1.8-9.7/ p=0.001), male NC (OR=4.7 /CI95%=1.5-14.9/ p=0.006), female NC (OR=5.5/CI95%=1.3-22.7/p=0.015) and type of epilepsy (OR=3.1/CI95%=1.3-7.1/ p=0.009) (table 1). However, another variables related to snore and epilepsy as seizure frequency (OR=1.29/ /CI95%=0.55-3.1/ p=0.562), number of antiepileptic drugs (OR=0.7 /CI95%=0.31-1.6 /p=0.393) and apnea (OR=4.4/ CI95%=0.89-21.6/p=0.051) do not have important OR (table 1). Regarding specific components of BQ in comparison with EDS/measured by the Epworth Sleepiness Scale, we can see that snore has a reasonable OR (OR=3.4 /CI95%=1.4-8.4/ p=0.008), but not sleepiness, neither arterial hypertension (table 2).

DISCUSSION

Several signals and symptoms showed to be useful for the screening of OSA in PWE as: anthropometrical variables (BMI and NC), type of epilepsy (generalized) and snore variables (frequency, loud snoring and time of snoring). The snore variables demonstrated the higher OR even more than the already know anthropometrical variables. Consequently, we can verify the association's strength and importance between these simple clinical questions about snore and OSA. One exception is about apnea question. This non-significant item is maybe justified by the different level of questions comprehension among the patients and their families. Some of them did not realize what was apnea because it does not disturb the partner's sleep whereas the snore does. Another remarkable finding in our study is the importance of the seizure type for the screening of OSA. The generalized type was more linked to OSA than the focal ones. Probably, the presence of untreated OSA can lead to sleep fragmentation and chronic sleep deprivation which may facilitate seizures in susceptible individuals.[4] However, the contrary can not be rejected: seizure promoting apnea[18], sleep fragmentation, and the patient having both OSA and central apnea as happened in the case report by Dominici *et al.,* 2007[18]. Almost 45% of generalized epilepsies occur during sleep[19]. Consequently, it is important to analyze the type of epilepsy and the risk factors to OSA in this population.

In relation to ESS it is not considered accurate to screen the high risk of OSA in this population as well in the general population, as already stated at the literature [6,7].

The used OSA screening tests in published paper about PWE proved the importance to add questions about snore in anamnesis as presented in the BNSQ besides anthropometrical findings and epilepsy characteristics: BMI, NC, type of epilepsy, loud snoring, frequency and time of snoring. All of them can be important factors for the diagnosis of OSA and its potential preventive / therapeutic measures.

The study has some limitations as the use of BQ as gold standard to OSA diagnoses in order to compare the performance between BQ

with ESS and some questions about snore from BNSQ. We did not use polysomnographic data in this study what is recommended in a future one as the appropriate gold standard.

CONCLUSIONS

There are many screening instruments to evaluate OSA being studied at the moment, but there are rare studies including PWE. It is necessary to use anamnestic questionnaire to screen OSA in PWE, that include the BQ, specific questions about snoring as loud, time and frequency, besides anthropometric data (BMI and NC) and type of epilepsy. Indeed, the ESS performance was poor to indicate the risk of OSA in this population as was expected based in literature. Larger longitudinal studies with the polysomnography appear warranted to study more and validate our findings about the construction of a new screening instrument to OSA in PWE.

Table 1. Diagnostic performance comparison between Berlin questionnaire: Epworth Sleep Scale (ESS), questions about snore by Basic Nordic Sleep Questionnaire (BNSQ) and anthropometric variables.

Disease or characteristics		BQ High	BQ Low	OR IC 95% P value
EDS /ESS	≥11 <11	30 (30.9) 24 (24.7)	16 (16.5) 27 (27.8)	2.11 (0.93-4.8) 0.072
Snore while sleeping/ BNSQ	≥3x week <3x week	38 (40.9) 14 (15)	8 (8.6) 33 (35.5)	**11.2 (4.2-30) <0.001**
Loud snoring/ BNSQ	Righ Low	32 (35.5) 18 (20)	6 (6.7) 34 (37.7)	**10.1 (3.6-28.6) <0.001**
Apnea/ BNSQ	≥1x week < 1x week	9 (9.8) 41 (44.6)	2 (2.2) 40 (43.5)	4.4 (0.89-21.6) 0.051
Time of snoring/ BNSQ	>2 years ≤2 years	7 (12.3) 16 (28.1)	1 (1.8) 33 (57.9)	**14.4 (1.6-127.6) <0.001**
BMI	Overweight or obese Not overweight or obese	36 (37.1) 18(18.6)	14 (14.4) 29 (29.9)	**4.14 (1.8-9.7) 0.001**
NC (men)	≥39 cm <39 cm	26 (44.8) 11 (18.9)	7 (12.1) 14 (24.1)	**4.7 (1.5-14.9) 0.006**
NC (women)	≥35 cm <35 cm	11 (29.7) 5 (13.5)	6 (16.2) 15 (40.5)	5.5 (1.3-22.7) 0.015
Epilepsy	Generalized Focal	39 (40.2) 14 (14.4)	21 (21.6) 23 (23.7)	**3.1 (1.3-7.1)** **0.009**
Number of epileptic drugs	≥2 1	26 (26.5) 28 (28.6)	25 (25.5) 19 (19.4)	0.7 (0.32-1.6) 0.393
Seizure frequency/ Year	>3 ≤3	19 (19.8) 34 (35.4)	13 (13.5) 30 (31.2)	1.29 (0.55-3.1)* 0.562

BQ (Berlin Questionnaire); EDS (Excessive daytime sleepiness); Epworth Sleep Scale (ESS); BNSQ (Basic Nordic sleep Questionnaire); BMI (body mass index); NC (Neck circumference), CI (Confidence interval) and OR(Odds Ratio). * we excluded one outlier with more than 1000 seizures/year

Table 2. Diagnostic performance comparison between Berlin questionnaire components and Epworth Sleep Scale

ESS	Berlin questionnaire components								
	Snore			Sleepiness			Arterial hypertension		
	Yes	No	OR (CI 95%) P value	Yes	No	OR (CI 95%) P value	Yes	No	OR (CI 95%) P value
≥11	37(38.1)	9(9.3)	**3.4(1.4-8.4) 0.008**	25 (25.8)	21(21.6)	0.97 (0.44-2.2) 0.95	18(18.8)	15(15.6)	1.5 (0.64-3.5) 0.340
<11	28(28.9)	23(23.7)		28 (28.9)	23(23.7)		28(29.2)	35(36.5)	

ESS (Epworth Sleep Scale), EDS (Excessive daytime sleepiness), CI (Confidence interval), OR (Odds Ratio).

REFERENCES

1. Tufik S, Santos-Silva R, Taddei JA, Bittencourt LRA. Obstructive Sleep Apnea Syndrome in the Sao Paulo Epidemiologic Sleep Study. Sleep Med 2010;11:441-6.

2 .Gus M,Gonçalves SC, Martinez D, de Abreu Silva EO, Moreira LB, Fuchs SC, Fuchs FD. Risk for Obstructive Sleep Apnea by Berlin Questionnaire, but not daytime sleepiness, is associated with resistant hypertension: a case-control study. Am J Hypertens 2008;21(7):832-5.

3. Hollinger P, Khatami R, Gugger M, Hess CW, Bassetti CL. Epilepsy and obstructive sleep apnea. Eur Neurol 2006;55(2):74-9.

4. Chihorek AM, Abou-Khalil B, Malow BA. Obstructive sleep apnea is associated with seizure occurrence in older adults with epilepsy. Neurology 2007;69(19):1823-7.

5. Venturi M, Valois A, Pontes IM, Gomes MM. Relação da epilepsia com a síndrome de apneia obstrutiva do sono: revisão. J Epilepsy Clin Neurophysiol 2010;16(1):18-22.

6. Ramachandran SK, Josephs LA. A meta-analysis of clinical screening tests for obstructive sleep apnea. Anesthesiology 2009;110(4):928-39.

7. Friedman M, Wilson MN, Pulver T, Pandya H, Joseph NJ, Lin HC, Chang HW. Screening for obstructive sleep apnea/hypopnea syndrome: subjective and objective factors. Otolaryngol Head Neck Surg 2010;142(4):531-5.

8. Weatherwax KJ, Wang L, Song Y. Obstructive sleep apnea in epilepsy patients: the Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ) is a useful screening instrument for obstructive sleep apnea in a disease-specific population. Sleep Med 2003;4(6):517-21.

9. Onat A, Hergenc, Yuksel H, Can G, Ayhan E, Kaya Z, Dursunoglu D. Neck circumference as a measure of central obesity: associations with metabolic syndrome and obstructive sleep apnea syndrome beyond waist circumference. Clin Nutr 2009;28(1):46-51.

10. Lemes LNA. Efeitos antropométricos, clínicos, laboratoriais e polissonográficos do CPAP nasal por 12 semana sem pacientes com Síndrome da apneia obstrutiva do sono de moderada a grave intensidade: Associações com índice de massa corporal, com a faixa etária e com a morfologia do pescoço. Universidade Estadual do Rio de Janeiro, UERJ, Brasil. Tese de doutorado. Ano de obtenção: 2007.

11. Bittencourt LRA, Academia Brasileira de Neurologia, Associação Brasileira de Otorrinolaringologia e Cirurgia Cervico-Facial, Associação Brasileira de Sono, Sociedade Brasileira de Pediatria, Sociedade Brasileira de Pneumologia e Tisiologia, Sociedade Brasileira de Neurofisiologia Clínica. Diagnóstico e tratamento da Síndrome da Apnéia Obstrutiva do Sono. Guia Prático, 2ª edição. São Paulo: Livraria Médica Paulista Editora, 2009.

12. Venturi M, Neves GSM, Pontes IM, Valois A, Gommes MM. Risk and determinant factors for obstructive sleep apnea in patients with epilepsy. Arq Neuro-Psiquiat. 2011; 69(6):924-927

13. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome.AnnIntern Med. 1999;131(7):485-91).

14. Bertolazi AN, Fagondes SC, Hoff LS, Pedro VD, Menna Barreto SS, Johns MW. Portuguese-language version of the Epworth sleepiness scale: Validation for use in Brazil. J Bras Pneumol 2009;35(9):877-83.

15. Partinen M, Gislason T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. J Sleep Res. 1995;4(1):150-155.

16. Glas AS, Lijmer JG, Prins MH, Bonsel GJ, Bossuyt PM. The diagnostic odds ratio: a single indicator of test performance. J Clin Epidemiol 2003;56(11):1129-35

17. Macaskill P, Gatsonis C, Deeks J, Harbord R, Takwoingi Y.Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy. Chapter 10 Analysing and Presenting Results. Version 1.0 Released December 23rd 2010.

18. Dominici M, Filho FP, Gomes MM. Probable causal link between epilepsy and sleep apnea: case report. Arq. Neuro-psiquiatr. 2007; 65(1)

19. Malow BA. Sleep and epilepsy. Neurol Clin. 2005;23(4):1127-47.

CORRESPONDENCE

Dra Monique Venturi - Programa de Epilepsia do Instituto de Neurologia Deolindo Couto/Universidade Federal do Rio de Janeiro (UFRJ)
Av. Venceslau Braz 95 - 22290-140
Rio de Janeiro RJ - Brazil.
E-mail: moni_venturi@hotmail.com