Sleep-disordered breathing and excessive daytime sleepiness in patients with epilepsy – a polysomnographic study

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Abstract

OBJECTIVES: Epilepsy and sleep-disordered breathing (SDB) are relatively common disorders. SDB induces repetitive arousals and sleep fragmentation and may cause symptomatic epileptic seizures or hypoxic encephalopathy. Epileptic seizures change sleep architecture with increase of light sleep and reduction of REM sleep, which may lead to central apneas. The aim of this study was to evaluate the relationship between SDB and daytime sleepiness in patients with epilepsy, who underwent polysomnography (PSG) due to problems with breathing during sleep or due to excessive daytime sleepiness.

METHODS: We enrolled 40 patients with epilepsy. Type, etiology of epilepsy and actual antiepileptic therapy was recorded. All of them underwent overnight PSG. Excessive daytime sleepiness (EDS) was assessed by Epworth Sleepiness Scale (ESS).

RESULTS: SDB (apnea-hypopnea index [AHI]<5) was present in 25 patients, 15 patients had no SDB (AHI≥5). EDS was present in 16 patients (40%). ESS significantly correlated with presence of symptomatic epilepsy (r=0.385, p=0.014), presence of SDB (r=0.524, p=0.001), AHI (r=0.416, p=0.003) and duration of REM sleep (r=–0.476, p=0.002). The presence of SDB (β=0.447, p=0.002) and duration of REM sleep (β=–0.308, p=0.029) were the only independent variables significantly associated with ESS in regression analysis.

CONCLUSION: SDB has negative influence on quality of sleep and daytime vigilility in patients with epilepsy. Sleep fragmentation with the reduction of the REM sleep seems to be the most important mechanism leading to EDS. We suppose that PSG could be beneficial in all patients with epilepsy and EDS.

Abbreviations:
AHI - apnea-hypopnea index
AI - arousal index
BiPAP - bilevel positive airway pressure
BMI - body mass index
CPAP - continuous positive airway pressure
EDS - excessive daytime sleepiness
ESS - Epworth Sleepiness Scale
NREM - non-rapid eye movement
ODI - desaturation index
OSA - obstructive sleep apnea
PSG - polysomnography
REM - rapid eye movement
SDB - sleep-disordered breathing
TST - total sleep time
INTRODUCTION

Both, epilepsy and sleep-disordered breathing (SDB) are relatively common disorders. Their comorbidity has a negative influence on both conditions and is more frequent than expected (Teran-Santos et al. 1999; Höllinger et al. 2006). SDB is present in 24% of men and in 9% of women (Young et al. 1993). Epilepsy is also a common condition with prevalence 0.5−1% of general population (Wallace et al. 1998). About 5% of patients with SDB have also epilepsy (Höllinger et al. 2006). SDB with repetitive episodes of hypoxia and hypercapnia may induce frequent microarousals and lead to fragmentation of sleep, chronic sleep deprivation, excessive daytime sleepiness (EDS) and increase of epileptic seizures in patients with epilepsy (Bateman et al. 2008).

SDB has a negative influence on epilepsy and may lead to cumulation of epileptic seizures. According to literature, one third of patients with refractory epilepsy has mild sleep apnea syndrome with five and more apneas/hypopneas per hour. Repetitive apneas with oxygen desaturation during sleep can also lead to encephalopathy with symptomatic epilepsy (Malow et al. 2000).

On the other hand, epileptic seizures may change the sleep architecture, lead to increase of light sleep and reduction of REM sleep, and negatively influence regulation of breathing during sleep as well (Bazil et al. 2000). Patients with epilepsy often complain of bad quality of sleep and daytime sleepiness. Daytime sleepiness leads to napping, that also rises the risk of epileptic seizures. SDB in patients with epilepsy can be aggravated by antiepileptic therapy (benzodiazepines can lead to relaxation of upper airways, valproate can worsen SDB by weight gain) (Ebben et al. 2008; Joutsa et al. 2015).

The aim of this study was to evaluate the relationship between daytime sleepiness and SDB in patients with epilepsy, who underwent polysomnography (PSG) due to problems with breathing during sleep or due to EDS.

METHODS

The study population consisted of 40 patients with epilepsy, who were examined in Sleep laboratory of the 1st Department of Neurology, Bratislava, Slovakia for suspected SDB, or EDS. Type, etiology of epilepsy, as well as actual antiepileptic therapy was recorded on admission. Only the patients without a history of epileptic seizure during the month prior to enrollment were included. Excessive daytime sleepiness (EDS) was assessed by Epworth Sleepiness Scale (ESS) (Johns 1991). ESS ≥10 was considered as EDS. All patients underwent standard overnight video-polysonmography (PSG) using Alice 5 device (Philips Respironics, Netherland). Sleep parameters and respiratory events were recorded and scored according to The American Association of Sleep Medicine Manual for the Scoring of Sleep and Associated Events (Iber et al. 2007). Parameters of sleep architecture and respiration during sleep were assessed. Apnea-hypopnea index (AHI), arousal index (AI), desaturation index (ODI) as well as duration of N1,N2,N3 NREM and REM sleep (as proportion of total sleep time [TST]) were recorded. Apnea was defined as the cessation of the reduction of airflow of ≥90% for >10 seconds and hypopnea as a reduction of airflow ≥50% for 10 seconds with oxygen desaturation of ≥3%. The statistical analyses were performed using SPSS version 18 (SPSS Inc., USA). Categorical variables were expressed as numbers and proportions (%), continuous variables as means ± standard deviation or median, interquartile range, minimal and maximal values. Chi-squared test, Student t test and Mann–Whitney test were used for group comparison. Pearson or Spearman correlation coefficients were used to determine the relationships between particular study characteristics. Stepwise multiple linear regression analysis was used to identify factors that contributed to ESS. A p-values less than 0.05 were considered statistically significant.

RESULTS

Baseline characteristics of two groups (epileptic patients with SDB and without SDB) are shown in Table 1. Sleep disordered breathing (AHI≥5) was diagnosed in 25 patients (62.5%). In this group, 7 patients (28%) had central sleep apnea, 4 patients (16%) had mild obstructive sleep apnea (OSA) with AHI 5–15, 8 patients (32%) had moderate OSA (AHI 15–30) and 6 patients (24%) had severe OSA (AHI over 30). The group without SDB (AHI<5) consisted of 15 patients (37.5%). Patients with SDB, compared to patients without SDB, were significantly older (52.5±12.8 years vs. 36±8.8 years, p=0.006), had significantly higher body mass index (BMI) (31±18.6 kg/m² vs. 25.7±15.8 kg/m², p=0.03), significantly higher proportion of symptomatic epilepsy (60% vs. 20%, p=0.015), significantly higher ESS (9.8±4.3 vs. 5.6±2.5, p=0.001, see Figure 1) and had significantly higher proportion of EDS (52% vs. 20%, p=0.046). Sleep fragmentation measured by AI was significantly higher in the group of epileptic patients with SDB than in the group without SDB (18.9±7.9/h vs. 5.9±3.6/h, p=0.001). Significant differences were found also in sleep architecture. Patients with SDB had significantly higher proportion of N1 NREM sleep (35.2±18.5% vs. 20.4±17.1%, p=0.009) and significantly lower proportion of N3 NREM sleep (27.1±14.6% vs. 38.8±22.3%, p=0.02). Patients with SDB had also lower proportion of REM sleep, but this difference was not statistically significant.

We found, that ESS significantly correlated with the presence of idiopathic epilepsy (r=−0.385, p=0.014), presence of symptomatic epilepsy (r=0.385, p=0.014), presence of SDB (r=0.524, p=0.001), AHI (r=0.416, p=0.003) and duration of REM sleep (r=−0.476, p=0.002) (see Table 2). Presence of SDB (beta=0.447, p=0.002) and duration of REM sleep (beta=−0.308, p=0.029) were the only independent variables signifi-
Sleep-disordered breathing and epilepsy significantly associated with ESS in stepwise multiple linear regression analysis (see Figure 2).

**DISCUSSION**

EDS and sleep disorders are frequently reported by patients with epilepsy. Prevalence of subjective sleep disturbances is two times higher in patients with partial epilepsy than in controls and is associated with impaired quality of life (De Haas et al. 2002; Del-Rosso et al. 2016). There are several possible reasons for EDS and disrupted sleep in patients with epilepsy. They include insufficient sleep due to inadequate sleep hygiene, coincidence of sleep disorders, effect of epileptic seizures, antiepileptic medication or pathology underlying epilepsy (symptomatic epilepsy).

In patients with epilepsy, coincidence of primary sleep disorders is quite common (Im et al. 2016). Several studies used PSG to diagnose sleep disorders in patients with epilepsy. Sleep apnea was found in 44% to 71% of patients, who underwent PSG (Malow et al. 1997b; Beran et al. 1999) We diagnosed SDB in 62.5% of 40 patients with epilepsy, but our patients were referred due to some problems with breathing while sleeping or due to EDS, so the prevalence in common population of patients with epilepsy could be lower.

Although ESS in our study significantly correlated with the presence of symptomatic epilepsy (r=0.385,
p = 0.014), presence of SDB (r = 0.524, p = 0.001), AHI (r = 0.416, p = 0.003) and the duration of REM sleep (r = 0.476, p = 0.002), presence of SDB (beta = 0.447, p = 0.002) and duration of REM sleep (beta = -0.308, p = 0.029) were the only independent variables significantly associated with ESS in regression analysis. We failed to find any association of EDS with antiepileptic drugs.

It is known that EDS is common in both, epilepsy and SDB. Our results are consistent with previous studies and association of EDS with SDB is well known (Malow et al. 1997a). We suppose SDB could be one of the most important predictors of EDS in patients with epilepsy. Physiological architecture of sleep is important for restorative function of sleep and disruption of sleep has negative consequences on daytime vigilance. We found significantly higher proportion of N1 sleep and significantly lower proportion of N3 sleep in patients with SDB and epilepsy. These results are similar to findings of our previous studies, where changes of sleep architecture (decrease of N3 sleep and REM sleep) were associated with poor quality of sleep and EDS (Kloebucnikova et al. 2014; Kloebucnikova et al. 2009). Sleep fragmentation in patients with epilepsy could be caused not only by SDB, but also by nighttime seizures. No seizure was recorded during PSG in our population. Impact of epileptic seizures could be bigger in patients with decompensation of epilepsy. Our study included only patients without a history of epileptic seizure during the month prior to PSG. On the other hand, it is known, that SDB in patients with epilepsy should be adequately treated to improve seizure frequency in patients with epilepsy (Carreno & Fernandez 2016; Pornsriniyom et al. 2014). All patients in our study with AHI over 15 were indicated for noninvasive continuous positive airway pressure (CPAP) or bilevel positive airway pressure therapy (BiPAP). Influence of this therapy on daytime sleepiness and compensation of epilepsy should be evaluated in our next study. In our study, we also found positive correlation between ESS and the presence symptomatic epilepsy. Exact underlying conditions causing symptomatic epilepsy and their association with EDS and SDB should be investigated in future studies.

CONCLUSION

Sleep disorders are common in patients with epilepsy. Despite SDB has negative influence on quality of life, it is often under-diagnosed in patients with epilepsy. Our results suggest, that SDB could be one of the most important predictors of EDS in patients with epilepsy. Sleep fragmentation with the reduction of the REM sleep seems to be the most important mechanism leading to EDS. Screening for sleep apnea could be beneficial in every patient reporting problems with nocturnal breathing or EDS.

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