Sleep disorders in epileptic patients

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ABSTRACT

This study was designed to screen for the presence of sleep disorders in epileptic patients. Subjects and Methods: The study was carried out on 60 adult epileptic patients and 40 normal volunteers as a control group. Patient groups were diagnosed on clinical and EEG basis as generalized and partial epilepsy. Both patients and control groups were subjected to two types of questionnaires to assess sleep disorders; The 1st. one is the Epworth sleepiness scale (ESS) and the 2nd one is the Sleep Disorder Questionnaire (version 2.2) that includes 4 scales measuring the cardinal symptoms of sleep disorders [Sleep apnea scale (SA), Narcolepsy scale (NAR), Periodic limb movement scale (PLM) and Psychiatric sleep disorder scale (PSY)]. Results: Epileptic patients whether generalized or partial types had significant more sleep disorders as detected by the PSY scale, ESS scale and SA scale (P<0.014, P<0.05, P<0.0001) respectively. Another statistically significant sleep disorders in favor of female epileptics was depicted in the PSY scale and SA scale (P<0.05). The outcome measure is the percentage of subjects with scores exceeding the cut-off points of each sleep disorder scale in different groups. Conclusion: Symptoms of sleep disorders are present in epileptic patients either patient with partial or generalized epilepsy with more female affliction. (Egypt J. Neurol. Psychiat. Neurosurg., 2004, 41(1): 161-169).

INTRODUCTION

There is a reciprocal relationship between sleep and epilepsy, where epilepsy affects sleep and sleep in turn affects epilepsy. The existence of such relationship was observed centuries ago. Hippocrates allegedly described "fears, rages, deliria, leaps out of bed and seizures during night".

In patients with generalized seizures, epileptiform discharges are sometimes facilitated by K complex. In addition, NREM sleep facilitates the appearance of focal spikes in patients with partial seizures. On the other hand, focal interictal discharges usually become less frequent and spatially more restricted, although amygdaloid and frontal lobe foci are activated during REM sleep in some patients.

The previous changes are related to the existence of thalamocortical synchronizing mechanism during NREM sleep, while during REM sleep, there is depression of thalamic synchronization and reduction of inter-hemispheric transmission. The changes in firing pattern of brainstem and diencephalic projection neurons that occur with sleep have pronounced effect on EEG activity and neuronal excitability that lead to changes in the frequency and appearance of epileptiform activity during sleep, more frequent in NREM sleep than in wakefulness or REM sleep.

The proportion of patients who have seizures that occur either exclusively or
predominantly during sleep ranged from 7.5%-45%. This wide variation in prevalence may reflect differences in epileptic syndromes among patient population, with seizure more likely to occur during sleep in certain epileptic syndromes.

Hoeppner et al., in a study of self reported sleep patterns of adult subjects with epilepsy found more sleep disorder symptoms in epileptics than in controls. Furthermore, they found that patients with partial epilepsy and frequent seizures had more sleep disturbances such as frequent night waking and parasomnias than did patients with other types of seizures. A link between disorders of arousals and epilepsy has been suggested. Excessive day time sleepiness (EDS) and unrefreshing sleep are allied as frequent adverse effect of antiepileptic medication. However, sleep disorders may coexist with epilepsy, occurring in 0.5-5.0 % of the population.

Antiepileptic drugs (AEDs) play a remarkable role in determining drowsiness in epileptic patients and they are generally viewed as the only cause of sleepiness in these patients. However EDS has been documented in epileptics before starting any drug treatment or after its discontinuation. Both clinical and neuro-physiological studies have clearly documented the possible role of seizure occurrence and of co-morbidity as determinants of EDS in epileptics. Nocturnal sleep fragmentation and day time sleepiness have been reported in temporal and frontal lobe epilepsy, namely nocturnal frontal lobe epilepsy.

**Aim of study:**

To screen for sleep disorders in a group of epileptic patients. Also, to study the effect of chronic antiepileptic medication on sleep in epileptics.

**PATIENTS AND METHODS**

**Patients:**

This study was carried out on sixty adult epileptic patients.

Patients’ age ranged from 16-45yrs old, diagnosed on clinical and EEG basis according to the (1989) classification and terminology of the International League Against Epilepsy (ILAE) into: partial and generalized epilepsy. All subjects should have normal neurological examination.

Subjects included were classified into: group (I): included thirty five patients with generalized epilepsy, group (II): incorporated twenty five patients with partial epilepsy and lastly group (III): forty adult volunteers as normal control.

Excluded from this work; patients who had any chronic or current medical illness, psychiatric disorders and their treatment and the presence of non epileptic neurological disorders.

**Methods:**

I. All patients were subjected to full general and neurological examination including the sheet for epilepsy currently used in Kasr El-Aini Hospitals and EEG with 19 channel direct-ink writing Nihon-Kohden machine, microprocessor controlled with black and white video-screen unit. The study was carried out to all patients under standard conditions. The electrodes were placed according to the Ten-twenty international system of electrode placement. Hyperventilation was carried out for 3 minutes during each record.

II. **Sleep Scales:**

Patients were attested by TWO sleep disorder scales; Epworth Sleepiness
Scale (ESS) and Sleep Disorder Questionnaire (SDQ) (version 2.2). The outcome measure is the percentage of subjects with scores exceeding the cut-off points of each sleep disorder scale in different groups.

1. **Epworth Sleepiness Scale (ESS):**
   Validated scale\(^8\) with an eight-item that measures a subjects’ general level of subjective daytime sleepiness. Total score ranged from 0 – 24. An ESS score greater than 10 was used as a cut off point for excessive daytime sleepiness for male and female.

2. **Sleep Disorder Questionnaire (SDQ) (version 2.2):**
   Including the cardinal symptoms of sleep disorders\(^9\). It is divided into 4 scales and each scale score is formed by simply adding together the response values (1–5) of the questions listed in each scale.
   a) **Sleep apnea scale (SA/SDQ):** 12 items survey to measure sleep apnea. Total score ranges from 0-60 and cut off points for apnea is 30 for male and 32 for female.
   b) **Narcolepsy Scale (NAR/SDQ):** 15 items survey to measure narcolepsy. Total score ranges from 0-75 and cut off points for NAR are 36 for male and 32 for female.
   c) **Periodic Limb Movement Scale (PLMS / SDQ):** 9 items survey to measure periodic limb movements. Total score ranges from 0-45 and cut off points for PLM are 22 for both male and female.
   d) **Psychiatric Sleep Disorder Scale (PSY/SDQ):** 9 items survey to measure psychiatric sleep disorders. Total score ranges from 0-45 and cut off points for PSY are 19 for male and 21 for female.

**Statistical Methods:**
Quantitative data were summarized as means and standard deviations. Group means were compared by (student t. test) if they were two groups and by one-way analysis (ANOVA) test if more than two.

Qualitative data were compared by CHI-square or Fisher’s exact tests according to the expected Frequencies.

A 5% probability level (P<0.05) was considered statistically significant.
Calculations were made on the statistical package for social sciences (SPSS) for windows program\(^10\).

**RESULTS**

I. **Clinical Criteria:**
The mean age in group (I) was 23.17±5.73 SD. While in group (II), the mean age was 26.32±8.67 SD. On the other hand, the mean age of group (III) was 25.45±5.38 SD.

As regards sex distribution in the present study, group (I) included 14 males (40%) and 21 females (60%), while group (II) included 11 males (44%) and 14 females (56%). Group (III) included 20 males (50%) and 20 females (50%). However, there was no statistically significant difference in age nor sex between all groups (P>0.05).

II. **Type of seizures:**
In group (I) "generalized epilepsy", there were 7 patients (20%) with generalized tonic clonic seizures (GTC), 24 patients (68.5%) with juvenile myoclonic seizures (JME) and 4 patients (11.4%) with juvenile absence seizures.

In group (II) "partial epilepsy", there were 8 patients (32%) with simple partial
seizure and 17 patients (68%) with partial seizure with secondary generalization.

**III. Frequency of seizures:**
In group I, the most encountered frequency was 1-5 seizures per year (19 patients: 54.31%). While in group II, more than 5 seizures per year was the most common frequency found in (17 patients: 68%).

**IV. Duration of disease:**
In group I, there were 18 patients (51.4%) having the disease for less than 5 years, 10 patients (25.6%) having the disease for 5-9 years and 7 patients (20%) having the disease for 10 years or more. While in group II, there were 12 patients (48%) were having the disease for less than 5 years, 7 patients (28%) were having the disease for 5-9 years and 6 patients (24%) having the disease for 10 years or more.

**V. Drug therapy:**
27 patients (77%) of group I patients were controlled on monotherapy, while patients with partial epilepsy were more controlled on polytherapy (15 patients: 60%).

**VI. Duration of treatment:**
In group I, there were 21 patients (60%) on treatment for less than 5 years, 7 (20%) on treatment for 5-9 years and 7 (20%) on treatment for 10 years more. In group II, there were 12 patient (48%) on treatment for less than 5 years, 7(28%) on treatment for 5-9 years and 6 patients (24%) on treatment for 10 years or more.

**Results of sleep disorder scales:**
In group I (Generalized epilepsy), according to SDQ, the most common sleep disorder was psychiatric sleep disorders (PSY) (48.6%), followed by periodic limb movements (PLM) (31.4%) and sleep apnea (SA) (14.3%). Excessive day time sleepiness (EDS) was found in (25.6%) of patients.

In group II (Partial epilepsy), according to SDQ, the most common sleep disorder was PSY (36%) followed by PLM (24%) and SA (12%). EDS was found in (28%) of patients.

In group III (Control group), according to SDQ, the most common sleep disorder was PLM (15%) followed by PSY (5%). EDS was found in (5%) of subjects (Table 1).

On comparing the percent of sleep disorder in all groups; the (+ve) cut-off points were significantly higher in epileptic patients (group I&II) ESS scale (P<0.05) in relation to group III being higher in the former. An additional statistically significant difference was also found in the SDQ scale especially in SA scale and PSY scale (P<0.05) & (P<0.0001) respectively; Table (1) and Figure (1).

A significant sleep disorders were detected in females than males in group I & II especially in the PSY and SA scales (P<0.05). However, other sleep scales showed no statistically significant difference in relation to gender (P>0.05). Also, group III, did not show any significant difference between males and females in all scales (Table 2).

In group I, the results did not show significant difference between monotherapy and poly therapy groups regarding all scales. Also In group II, the results did not show significant difference between monotherapy and poly therapy group regarding all scales (Table 3).

The results did not show any significant statistical difference between sleep disorder scales and different types of seizures nor duration of therapy in either group I or II in all scales in relation to control (group III) (p>0.05).
Table 1. Percentages of subjects with positive cut off points of ESS, SDQ scales in group I, II, III.

<table>
<thead>
<tr>
<th>Scale</th>
<th>GROUP I</th>
<th>GROUP II</th>
<th>GROUP III</th>
<th>P. VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESS</td>
<td>10 (25.6%)</td>
<td>7 (28%)</td>
<td>2 (5%)</td>
<td>0.014*</td>
</tr>
<tr>
<td>SDQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SA</td>
<td>5 (14.3%)</td>
<td>3 (12%)</td>
<td>-</td>
<td>0.052*</td>
</tr>
<tr>
<td>NAR</td>
<td>1 (2.9%)</td>
<td>1 (4%)</td>
<td>-</td>
<td>0.482</td>
</tr>
<tr>
<td>PLM</td>
<td>11 (31.4%)</td>
<td>6 (24%)</td>
<td>6 (15%)</td>
<td>0.239</td>
</tr>
<tr>
<td>PSY</td>
<td>17 (48.6%)</td>
<td>9 (36%)</td>
<td>2 (5%)</td>
<td>0.0001**</td>
</tr>
</tbody>
</table>

* Significant  ** Highly significant

Fig. (1): Percentages of subjects with positive cut off points of ESS, SDQ scales in group I, II, III.
Table 2. Relation between gender and +ve cut off points of ESS and SDQ scales in all groups of the present study.

<table>
<thead>
<tr>
<th>Scale</th>
<th>GROUP I (N=35)</th>
<th></th>
<th>GROUP II (N=25)</th>
<th></th>
<th>GROUP III (N=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (n=14)</td>
<td>Female (n=21)</td>
<td>p.value</td>
<td>Male (n=11)</td>
<td>Female (n=14)</td>
</tr>
<tr>
<td>ESS</td>
<td>6(42%)</td>
<td>4(19%)</td>
<td>0.12</td>
<td>5(45.5%)</td>
<td>2(14.3)</td>
</tr>
<tr>
<td>SA</td>
<td>0</td>
<td>5(23.%)</td>
<td>0.04*</td>
<td>2(18.2%)</td>
<td>1(7.1%)</td>
</tr>
<tr>
<td>NAR</td>
<td>0</td>
<td>1(4.8%)</td>
<td>0.407</td>
<td>1(9.1%)</td>
<td>0</td>
</tr>
<tr>
<td>PLM</td>
<td>2(14.3%)</td>
<td>9(42.%)</td>
<td>0.074</td>
<td>4(36.4%)</td>
<td>2(14.3%)</td>
</tr>
<tr>
<td>PSY</td>
<td>2(14.3%)</td>
<td>15(71.%)</td>
<td>0.001**</td>
<td>0</td>
<td>9(64.3%)</td>
</tr>
</tbody>
</table>

Table 3. Relation between drug therapy and +ve cut off points of ESS, SDQ scales.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Group I (N=35)</th>
<th></th>
<th>Group I (N=25)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Monotherapy</td>
<td>Polytherapy</td>
<td>P. Value</td>
<td>Monotherapy</td>
</tr>
<tr>
<td>ESS</td>
<td>7(25.9%)</td>
<td>3(37.5%)</td>
<td>0.524</td>
<td>4(40%)</td>
</tr>
<tr>
<td>SA</td>
<td>4(14.8%)</td>
<td>1(12.5%)</td>
<td>0.869</td>
<td>1(10%)</td>
</tr>
<tr>
<td>NAR</td>
<td>1(3.7%)</td>
<td>0</td>
<td>0.581</td>
<td>0</td>
</tr>
<tr>
<td>PLM</td>
<td>9(33.3%)</td>
<td>2(25%)</td>
<td>0.656</td>
<td>2(20%)</td>
</tr>
<tr>
<td>PSY</td>
<td>14(51.9%)</td>
<td>3(37.5%)</td>
<td>0.476</td>
<td>5(50%)</td>
</tr>
</tbody>
</table>

DISCUSSION

Sleep in epileptic patients is altered in a large percentage of patients\(^{11}\). A variety of sleep disturbances have been observed in epileptics including a reduction in REM sleep, an increase in wake after sleep onset (WASO), increased instability of sleep states, an increase in NREM stage 1 and 2, a reduction in NREM stage 3 and 4, a reduction in the density of sleep spindles and an increase of sleep onset latency\(^{12}\).

In the present study, sleep disorder symptoms were found in epileptic patients either patients with generalized epilepsy or patients with focal epilepsy and this is in agreement with Broughton\(^{11}\), who reported a variety of treatable sleep disorders including inadequate sleep, insomnia, obstructive sleep...
apnea, periodic limb movements (PLMs) and excessive daytime sleepiness (EDS) in epileptic patients.

In the present study, sleep disorder symptoms such as psychiatric sleep disorders, EDS, PLMs and SA were the most frequently encountered symptoms reported by epileptic subjects.

The control subjects showed some sleep disorder symptoms like PSY, EDS and PLMs. Epileptics were more likely to report sleep disorder symptoms in the (PSY, EDS & SA scales) when compared with normal controls. While in the PLM scale, no statistically significant difference was noted between epileptics and normal controls but epileptic patients were only somewhat more likely than controls to have elevated PLM score presumably because increased number of patients having myoclonic seizures. This type of seizures has a strict relationship to the sleep-wake cycle particularly to transition phases (awakening) as reported by Broughton\(^1\), who observed that morning awakening and to less extent nocturnal awakening and sleep onset activate myoclonic jerks because of increased cortical excitability during these periods, while manifestations of myoclonic epilepsy are deactivated during sleep.

In the present study, the age could not be correlated with the presence of sleep disorder symptoms because the age of subjects was similar in the three groups. Going with other studies, no correlation was found between age and sleep disorder symptoms\(^1\).\(^2\).

Hoeppner et al.\(^4\), reported that there was no significant sex difference in presence of sleep disorder symptoms in either control or epileptic subjects. However, the present study showed significantly more PSY sleep disorder symptoms reported by female epileptic patients either with generalized or focal epilepsy.

In our study, sleep disorder symptoms were not significantly different between patients with focal epilepsy and those with generalized epilepsy. This is in accordance with Vaughn et al.\(^1\)\(^3\), who observed that there was no real relationship between sleep disorders and type of epilepsy.

In the present study, the results showed no significant difference between various types of seizures in number of sleep disorder symptoms, but there was a trend toward patients with generalized tonic clonic seizures (GTC), juvenile myoclonic epilepsy (JME) and partial seizures with secondary generalization to have more sleep disorder symptoms than other types of seizures. This goes in accordance with Janz\(^1\)\(^4\), who observed that sleep deficits are more marked in primary generalized epilepsy and partial epilepsy with secondary generalization than other types.

Our study showed that the number of antiepileptic drugs did not affect the presence of sleep disorder symptoms and this going in agreement with Hoeppner\(^4\), who observed that the number and types of antiepileptic medications were not considered significant predictors of sleep disorders. Our study did not have a sufficient number of patients allowing correlation between specific antiepileptic medication and sleep disorder symptoms.

Hoeppner et al.\(^4\), reported that there is lack of a significant correlation between seizure frequency and number of sleep disorder symptoms in epileptic patients and this in agreement with our study which showed no significant difference between frequency of seizures in either generalized or focal epilepsy and the presence of sleep disorder symptoms. In addition, duration of disease and of treatment did not change the results significantly.
The study is unique in that we examined the relation between symptoms of sleep disorders and type of epilepsy, duration of disease, drug therapy, age and sex of patients. In spite of this, it has several limitations; firstly, our study had been conducted in patients on anticonvulsants, thus adding the confounding effect of these medications on sleep architecture. Second, polysomnography was not done to assess objectively the presence of sleep disorders. Thirdly, no follow up on the questionnaire responses was done.

Recognizing and treating sleep disorders in epileptic patients has important implication not only for improving the quality of life of these patients population but also for seizure control\textsuperscript{15}. Once coexisting cases of sleep disorders are treated, we can add higher doses of existing medications or other medications needed to control seizure.

In summary; our data support the premises that symptoms of sleep disorders are present in epileptic patients. Before attributing sleep disorders in epilepsy to the disease itself, clinicians should consider the possibility of underlying disorders.

**REFERENCES**

الملخص العربي

تم تصميم هذا البحث لدراسة العلاقة بين النوم ومرض السرعة ووجود اضطرابات في النوم لدى مرضى السرعة. وقد تم إجراء الدراسة على 60 مريضاً بالسرعة و40 شخصًا طبيباً وقد تم تقسيم مجموعة المرضى إلى مجموعة تعاون من مرضى السرعة العام وأخرى تعاني من مرض السرعة البؤري.

وقد تم إجراء تقييم طبي وعنصبي مع قياس مدى وجود اضطرابات في النوم من خلال تقييم إجابات كل المشاركين في الدراسة على نوعين من الاستبيانات خاصة بتحديث وجود نعاس شديد في فترة النهار (عامل كيوبوراث) والآخر يشمل أربع عناصر تقييم اضطرابات النوم الرئيسية مثل (الاختناق أثناء النوم – الخدرات – الأطراف أثناء النوم – اضطرابات النوم النفسية) (استبيان اضطرابات النوم). وتم عمل رسم مسح لجميع المرضى.

أظهرت نتائج البحث أن:

1. وجود اضطرابات في النوم لدى مرضى السرعة العام خاصة اضطرابات النوم النفسية (48.6%) والاختناق أثناء النوم (3.4%) وحركات الأطراف أثناء النوم (31.4%) والشعور الشديد أثناء النوم (28.6%).

2. وجود اضطرابات في النوم لدى مرضى السرعة البؤري خاصة اضطرابات النوم النفسية (36%) والاختناق أثناء النوم (26%) وحركات الأطراف أثناء النوم (24%).

هناك فارق ذو دلالة إحصائية بين مجموعتين مرضى السرعة العام ومجموعة المتوقفين في كلاً من مقياس اضطرابات النوم النفسية وقياس النعاس الشديد أثناء النهار وقياس الاختناق أثناء النوم. ليس هناك فارق ذو دلالة إحصائية بين مجموعتين مرضى السرعة البؤري ومجموعة المتوقفين عند قياس حركات الأطراف أثناء النوم ولكن المرضى ظهرت فيهم حركات الأطراف أثناء النوم بشكل أكثر وضوحًا من المرضى المتوقفين.

هناك فارق ذو دلالة إحصائية بين مجموعتين مرضى السرعة البؤري ومجموعة المتوقفين في كلاً من مقياس اضطرابات النوم النفسية وقياس النعاس الشديد أثناء النهار وقياس الاختناق أثناء النوم.

هناك فارق ذو دلالة إحصائية بين المرضى ومجموعتين من مرضى السرعة البؤري في جميع مقاييس اضطرابات النوم.

هناك فارق ذو دلالة إحصائية بين المرضى ومجموعتين من مرضى السرعة البؤري في جميع مراحل النوم. وủaوUV

أظهرت النتائج أن فترة النوم ودرجة العلاج لم تؤثر على وجود اضطرابات النوم لدى مرضى السرعة البؤري.

لم يكن هناك فارق ذو دلالة إحصائية في جميع مقاييس اضطرابات النوم بين مجموعة المرضى التي تتبع أطرو

دواء ومجموعة المرضى متعددة الأدوية.