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Review article

Insomnia in people with epilepsy: A review of insomnia prevalence, risk factors and associations with epilepsy-related factors

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ABSTRACT

Background: Insomnia is a common sleep complaint in the general population, and sleep loss may be a trigger for epileptic seizures.
Objectives: To conduct a comprehensive review of the literature of insomnia symptoms and insomnia disorder, their prevalence and epilepsy-related risk factors in people with epilepsy (PWE).
Methods: A PUBMED search was performed for articles indexed to June 2016 involving human subjects, excluding papers in languages other than English, Spanish and Portuguese and case reports. Eligible studies were those using a clear definition of insomnia and reporting quantitative data on prevalence rates and risk factors. The search included the following terms: insomnia, sleep disorder(s), sleep disturbance(s) and sleep-wake in the title and abstract; and epilep* in the title. 425 papers were reviewed and 31 were selected for the final analysis (21 adult and 10 paediatric). Twenty-one studies used a control group. Two reviewer authors independently extracted all data and a third author resolved disagreements.
Results: Most studies were hospital-based, cross-sectional and evaluated convenience samples representing highly select populations. Various insomnia inventories were used. Fourteen assessed insomnia (10 in adults, four, children), but only five as primary outcome (none in children). Four evaluated insomnia disorder based on international classification criteria (International Classification of Sleep Disorders − ICSD-2–in 3, and DSM-IV-TR, in 1). In adults, insomnia prevalence was 28.9-51% based on the Insomnia Severity Index ≥15 and 36–74.4% based on DSM-IV-TR or ICSD-2. The prevalence of insomnia in children was 13.1-31.5% using the Sleep Disturbance Scale for Children and 11% based on ICSD-2 diagnostic criteria. Compared to control groups, PWE usually had higher frequencies of insomnia symptoms and disorder. Insomnia was associated with greater impairment in quality of life and higher degree of depressive symptoms in several studies, and was inconsistently related to female gender, poor seizure control and antiepileptic drug polytherapy. In children, insomnia was associated with developmental delay, focal epilepsies and poor seizure control.
Conclusion: Insomnia symptoms and insomnia disorder are highly prevalent among PWE based on a limited number of studies with variable inclusion criteria and methodology. Excessive daytime sleepiness (EDS) was not found to be related to insomnia disorder or symptoms, and the exclusion of individuals with EDS may explain the higher frequencies of insomnia found in some studies. Additional investigations are needed given the potential impact of insomnia on seizure control, mood and QOL in PWE.

1. Introduction

Epilepsy is a brain disorder characterized by an enduring predisposition to generate epileptic seizures with consequences on neurobiological, cognitive, psychological, and social performance (Fisher et al., 2014). Sleep-wake complaints are at least twice as common in people with epilepsy (PWE) compared with the general population (Gutter et al., 2013; Jain et al., 2013; Xu et al., 2006) and comorbid sleep disturbances have been associated with additional impairment in quality of life (QoL) (de Weerd et al., 2004; Garcia-Morales et al., 2014; Gutter et al., 2013; Piperidou et al., 2008; Vendrame et al., 2013), worsening seizure control (Batista and Nunes, 2007; Piperidou et al.,

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2008) and psychiatric conditions (Vendrame et al., 2013).

Insomnia symptoms and disorders are exceedingly common in the general population with a prevalence of 35–50% and 12–20%, respectively, sometimes due to comorbid medical or psychiatric conditions, medications or substance use (Buysse, 2013; Sateia, 2014). Known risk factors include female gender, older age, lower socioeconomic status, comorbid psychiatric and medical conditions, substance abuse, unemployment, divorce and widowhood (Buysse, 2013). Insomnia is a known risk factor for the development of depression and anxiety, as well as to impaired QoL and people with insomnia are at risk for a number of adverse health outcomes including hypertension, diabetes, and cardiovascular events (Buysse, 2013; Lewis et al., 2014; Sofi et al., 2014; Vgontzas and Fernandez-Mendoza, 2013). Untreated insomnia has an impact in health care economics, with direct costs (outpatient encounters, drug prescription, cognitive behaviour therapy, procedures) and indirect costs (lost workplace productivity, higher accident risks) exceeding 100 billion dollars annually in the USA alone (Ohayon, 2002; Wickwire et al., 2015). Despite this burden and the high costs, insomnia is still undervalued by most health professionals and patients (Buysse, 2013; Manni and Terzaghi, 2010; Ohayon, 2002).

The relationship between sleep and epilepsy have been explored in previous studies and the existence of a detrimental effect of sleep deprivation on epileptiform activity is undeniable (Derry and Duncan, 2013; Manni and Terzaghi, 2010). Moreover, sleep disorders are common in PWE, possibly due to the sleep disruption lead by the occurrence of an epileptic attack or as a consequence of antiepileptic drug therapy (AED) (Manni and Terzaghi, 2010). However, little research was performed to assess insomnia in epileptic population, therefore prompting a literature review of the prevalence of insomnia disorder and symptoms in PWE, as well as to identify possible risk factors related to this comorbid sleep disorder.

2. Methods

A PUBMED search was performed to identify publications involving human subjects with epilepsy exploring sleep-wake disorders and complaints through June 2016 (Fig. 1). This search used the terms insomnia, sleep disorder(s), sleep disturbance(s) and sleep-wake in title and abstract; and epilep (sy,tic), in the title, but not in different languages other than English, Spanish and Portuguese. Case reports were excluded. Abstracts were reviewed by two investigators (PJOMM and PSO) for data regarding insomnia symptoms, insomnia disorders and sleep disturbances. Full text analysis was performed with the purpose of identifying those papers fulfilling standard insomnia disorder diagnostic criteria, using validated insomnia instruments, such as the Insomnia Severity Index (ISI) and the Athens Insomnia Scale (AIS), and those evaluating insomnia symptoms.

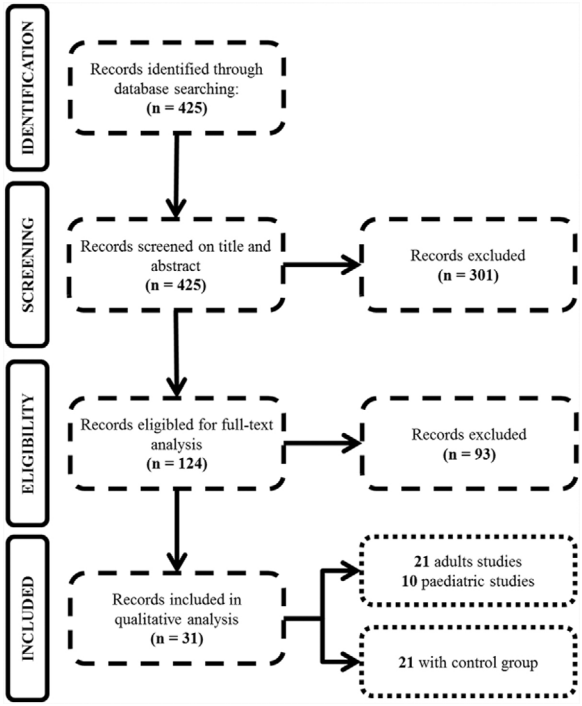

Fig. 1. Study assessment diagram.

3. Results

Of 425 studies screened for inclusion, 31 (21 adult, 10 paediatric) fulfilled the inclusion criteria (Tables 1 and 2). Twenty articles compared outcomes between PWE and controls (Babu et al., 2009; Batista and Nunes, 2007; Chan et al., 2011; Chen et al., 2011; de Weerd et al., 2004; Gutter et al., 2013; Hoeppner et al., 1984; Im et al., 2016; Ismayilova et al., 2015; Khatami et al., 2006; Krishnan et al., 2012; Larson et al., 2012; Ng and Bianchi, 2014; Ong et al., 2010; Pizzatto et al., 2013; Samaitiene et al., 2013; Stores et al., 1998; Wirrell et al., 2005; Yazdi et al., 2013; Zhou et al., 2012), whilst one compared individuals with refractory and non-refractory epilepsy (Garcia-Morales et al., 2014). Most studies were hospital-based and cross-sectional, applied sleep questionnaires and evaluated highly selected convenience populations, such as those without other sleep symptoms/disorders, including excessive daytime sleepiness (EDS) (Chan et al., 2011; Ismayilova et al., 2015; Khatami et al., 2006; Vendrame et al., 2013; Yang et al., 2016), with higher rates of psychiatric disorders (military veterans) (Lopez et al., 2013) and with different patterns of seizure control or antiepileptic drug (AED) therapy (Chan et al., 2011; Cobabe et al., 2015; de Weerd et al., 2004; Gutter et al., 2013; Hoeppner et al., 1984; Im et al., 2016; Krishnan et al., 2012; Zhou et al., 2012).

In this review, it was noted that studies regarding epilepsy and sleep disturbances frequently lack descriptive and statistical analysis for specific sleep disorders (such as insomnia, parasomnia and sleep apnea) and rather focus on sleep complaints and sleep quality more generally. Only five out of the 31 studies focused on insomnia as a primary endpoint/objective, none in paediatric populations (Im et al., 2016; Lopez et al., 2013; Quigg et al., 2016; Vendrame et al., 2013; Yang et al., 2016). Of the 26 remaining studies, two evaluated the presence of insomnia disorder (Ismayilova et al., 2015; Jain et al., 2013), five applied an insomnia inventory (Cobabe et al., 2015; Garcia-Morales et al., 2014; Piperidou et al., 2008; Yazdi et al., 2013; Zhou et al., 2012), nine assessed an insomnia subscale of a sleep questionnaire (Batista and Nunes, 2007; Chan et al., 2011; de Weerd et al., 2004; Gutter et al., 2013; Krishnan et al., 2012; Larson et al., 2012; Ong et al., 2010; Samaitiene et al., 2013; Wirrell et al., 2005) and the rest remarked on the presence of at least one insomnia symptom (Babu et al., 2009; Chen et al., 2011; Conant et al., 2009; de Almeida et al., 2003; Hoeppner et al., 1984; Khatami et al., 2006; Komolafe et al., 2015; Pizzatto et al., 2013; Stores et al., 1998).

3.1. Insomnia classification

1. This review found that the term “insomnia” has been used to refer to both insomnia symptoms and classifiable disorders, with few including both and differentiating the two (Cobabe et al., 2015; Ismayilova et al., 2015; Quigg et al., 2016; Yang et al., 2016; Yazdi et al., 2013). Sleep questionnaires were used to assess insomnia symptoms in both adult and paediatric population and studies commonly explored sleep onset insomnia and sleep maintenance insomnia. Early morning awakening was directly evaluated in only two studies (Stores et al., 1998; Yazdi et al., 2013). In adult population studies, insomnia symptoms were commonly evaluated by the ISI or AIS (Cobabe et al., 2015; Garcia-Morales et al., 2014; Im et al., 2016; Piperidou et al., 2008; Quigg et al., 2016; Stores et al., 1998; Vendrame