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Altered polysomnographic profile in juvenile myoclonic epilepsy

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KEYWORDS
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Summary
Purpose: To study the spectra of sleep profile using PSG in a cohort of patients with JME attending a University hospital.
Methodology: This prospective cross-sectional case—control study involved 25 patients of JME (age: 22.0 ± 6.3 years; M:F = 13:12) on valproic acid (VPA) and 25 matched healthy controls (age: 23.2 ± 3.04 years; M:F = 16:9) were recruited. All patients underwent clinical assessment, electroencephalogram (EEG), and evaluation with sleep questionnaire and PSG.
Results: PSG analysis revealed significant alterations in sleep architecture in the JME group in the form of reduced mean sleep efficiency ($p = <0.035$) and number of patients with reduced sleep efficiency ($p = 0.001$), increased mean sleep onset latency ($p = 0.04$) and number of patients with increased sleep latency ($p = 0.023$), reduced mean N2 sleep percentage ($p = 0.005$) and reduced mean total NREM (non-rapid eye movement) sleep ($p = 0.001$) and increased mean wake percentage ($p = 0.001$). The frequency of arousals, involuntary limb movements, and event related arousals in the JME groups was not different from the controls. Patients >20 years had reduced total sleep time compared to those <20 years ($p = 0.012$). Patients with seizures for >5 years had reduced NREM sleep percentage ($p = 0.042$) and those on VPA therapy >1 year had a longer stage 2 ($p = 0.03$) and N3 latency ($p = 0.03$). Patients on ≤600 mg/day of VPA had a higher prevalence of isolated limb movements ($p = 0.01$).
Conclusions: PSG revealed significant alterations in sleep architecture in JME despite adequate seizure control. There was variable degree of PSG—phenotypic correlation.

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Introduction

Sleep disorders are widely prevalent in the community and are a common accompaniment in patients with epilepsy. In routine clinical practice, symptoms of sleep disorders in epilepsy patients are frequently overlooked, or ascribed to antiepileptic drugs (AEDs), though they may be consequent to uncontrolled seizures, or a concomitant sleep disorder, and often contribute to the intractability of epilepsy (Herman et al., 2001). Sleep disorders in epilepsy patients are less well understood as studies focusing on this aspect are few (Bazil et al., 2000). The effect of seizures on sleep can be studied in terms of changes in the macro and microstructure of sleep, the latter being the focus of most recent studies. Epileptiform discharges (EDs) are part of the internal arousing stimuli that affect the quality of sleep in patients with epilepsy and can do so with or without alterations of sleep macrostructure (Bonakis and Koutroumanidis, 2009; Dhanuka et al., 2001; Ramachandraiah et al., 2012). Significant effects of this nature have been noted in generalized and partial epilepsies. Treatment of sleep disorders and improvement in sleep hygiene may improve seizure control, daytime cognitive functioning, and quality of life (Herman et al., 2001).

Juvenile Myoclonic Epilepsy (JME) is the most common and well-defined idiopathic generalized epilepsy (IGE) and recognized as an epileptic syndrome since 1989 (Janz, 1997; Panayiotopoulos et al., 1994). Pramod et al. (2012) assessed sleep among 50 patients with JME and 50 healthy controls. They found significant sleep disturbances characterized by excessive daytime sleepiness and disturbed night sleep, despite adequate medications and good seizure control. Surprisingly, despite its wide prevalence, strong association with sleep and its potential therapeutic implications, comprehensive studies of sleep in JME using polysomnography (PSG) are far and few. The number of subjects with epilepsy in previous studies has been small; often without controls, but the results have been significant, thereby demanding further scrutiny (Bonakis and Koutroumanidis, 2009; Gigli et al., 1992; Terzano et al., 1991).

The present study aims to study the spectra of sleep profile using PSG in a cohort of patients with JME attending a University hospital.

Materials and methods

This prospective, cross-sectional, hospital based case—control study was conducted at a tertiary Neurology Centre in South India. The study was approved by the Institute Ethical Committee. Twenty-five patients of JME attending the neurological services and fulfilling the inclusion criteria were recruited. The diagnosis of JME was based on the ILAE criteria for JME (Commission ILAE, 1989; Nordli, 2005). Patients were $\geq$12 years old and were recruited for PSG. They were on valproic acid (VPA) as the sole anti-epileptic drug (AED). Twenty-five matched healthy controls consisting of friends/unrelated volunteers ($n = 15$) of the patients from similar educational and socioeconomic status and medical personals (doctors = 5; medical technologists = 5). The medical professionals of the hospital were on routine day duties (9.00 am to 4.30 pm). There was no difference between the 2 subgroups. Controls were not related to the patient and did not have family history of epilepsy. Written informed written consent was obtained from the study subjects. Difficulties were encountered in recruiting appropriate age and sex matched female controls, because of apprehension regarding PSG, reluctance to an overnight study, and other social reasons. Serum VPA levels were not carried out. Subjects with illnesses or medications known to affect sleep, and those with substance abuse of any degree were excluded. All patients underwent a structured evaluation, including a detailed clinical, family and treatment history, neurological examination, 16-channel electroencephalogram (EEG), and other investigations when indicated. Imaging of the brain was normal in all patients. Female patients underwent ultrasound evaluation for polycystic ovarian disease (PCOD). Subjects were administered validated sleep questionnaires: Epworth Sleepiness Scale (ESS) to assess daytime somnolence (Johns, 1991) and Pittsburgh Sleep Quality Index (PSQI) to assess night time sleep (Buysse et al., 1989).

All subjects underwent PSG conducted at the sleep laboratory in the department of Neurology according to the American Association of Sleep Medicine guidelines. AEDs were continued unaltered during the study but non-essential drugs were discontinued a week prior to the sleep study. Since most patients had the EEG done a few days before PSG, there was no delay in commencing PSG on the night of the study. PSG was deferred for a week for subjects with a recent seizure or acute medical illness. PSG was reported according to the AASM 2007 guidelines by a joint sitting of the investigators (Iber et al., 2007).

Statistical analysis employed SPSS version 16 and involved comparison of multiple parameters between the study groups. Chi square test was employed to study qualitative parameters and Independent t test for quantitative parameters. Apart from the comparison between the patient and the control group, patients with and without sleep abnormalities were compared.

Results

Clinical profile

Twenty-five patients (M:F = 13:12) with mean age of 22.0 ± 6.35 years and controls (M:F = 19:6) with mean age of 23.24 ± 3.04 years were recruited. The mean body mass index (BMI = kg/m^2) was 22.62 ± 1.78 in patients and 23.05 ± 1.54 in controls, with a BMI > 25 noted in one patient and 2 controls. No significant differences were noted in these parameters. Majority (48%) of the patients were in their 3rd decade of life, 44% were aged between 12 and 20 years while the oldest was 41 years old. The mean age at seizure onset was 15.7 ± 3.13 years for males and 17.16 ± 7.8 years for females, with myoclonic jerks being the initial seizure type in 18 (72%) patients and generalized tonic—clonic seizures (GTCS) in the remaining 7 patients. All patients had history of myoclonic jerks and GTCS; absence seizures were noted in 4 patients (16%). In 20 (80%) patients, an attack of GTCS was immediately preceded by a single or a series of myoclonic jerks. Most patients (76%) reported seizures on waking from sleep; in 21 (84%) patients there