Journal of Clinical Neuroscience xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

Behavioral comorbidity in children and adolescents with epilepsy

Anita Choudhary [a,c], Sheffali Gulati [a,*], Rajesh Sagar [b], Madhulika Kabra [a], Savita Sapra [a]

[a] Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar East, Gautam Nagar, New Delhi 110029, India
[b] Department of Psychiatry, All India Institute of Medical Sciences, New Delhi, India
[c] Department of Pediatrics, SMS Medical College, Jaipur, Rajasthan, India

ARTICLE INFO

Article history:
Received 5 November 2012
Accepted 10 November 2013
Available online xxxx

Keywords:
Antiepileptic drugs
Behavioral comorbidity
Child behavior checklist
Epilepsy

ABSTRACT

This cross sectional study assessed the prevalence of behavioral comorbidity and its association with epilepsy-related factors in children and adolescents with epilepsy. One hundred consecutive patients with active epilepsy, aged 6–16 years, were screened for behavioral comorbidity using the Child Behavior Checklist and those who qualified as having behavioral comorbidity were compared with those who did not have it. Behavioral comorbidity was found in 43 of 100 participants. Being treated with antiepileptic drug polytherapy (odds ratio 6.3, 95% confidence interval 1.4–17.3, $p = 0.01$) independently predicted behavioral comorbidity in the patients studied. The demonstrated high frequency of behavioral comorbidity in children with epilepsy suggests that pediatricians and pediatric neurologists should be sensitive to this fact in order to identify and manage behavioral comorbidity in children with epilepsy.

1. Introduction

Epilepsy is one of the most prevalent chronic neurological disorders affecting children. The burden of epilepsy is greater in developing countries compared to developed countries [1]. The estimated prevalence of epilepsy in India is 5.59 cases per 1000 people [2]. It has been observed that children with epilepsy (CWE) are at an increased risk of behavioral and emotional problems. In the landmark pediatric psychiatric epidemiological Isle of Wight study, Rutter et al. observed that the prevalence of behavioral problems was 28.6% in children with uncomplicated epilepsy and 58.3% in children with seizures and structural brain abnormality, as compared to 6.6% in the general child population [3]. Prevalence of behavioral and emotional problems in CWE in developed countries is greater than in those with other chronic illnesses not involving the central nervous system, such as diabetes mellitus or bronchial asthma [4,5]. Reported prevalence of behavioral and emotional problems in CWE ranges from 24% to 66% [6–10].

Theoretical models of psychopathology propose that psychopathology in epilepsy can stem from a complex interplay of multiple etiological variables [11]. Risk factors may be biological (seizure-related and treatment-related) or psychosocial. Some studies from developed countries have observed that behavioral and psychiatric problems are associated with frequent and severe seizures [12–14], early onset of seizures [12], antiepileptic drug (AED) polytherapy and symptomatic epilepsy [15], whereas other studies demonstrated no association of age at seizure onset, seizure frequency, seizure type, or lateralization of seizure focus with psychopathology in CWE [16,17].

There are limited data on the prevalence and association of epilepsy-related variables with behavioral comorbidity in children and adolescents with epilepsy from developing countries [9,10]. Therefore the present study's primary objective was to determine the prevalence of behavioral comorbidity in children and adolescents aged 6 to 16 years with active epilepsy using the Child Behavior Checklist (CBCL) [18]. The secondary objective was to explore the potential epilepsy-related risk factors for behavioral comorbidity in the same study population.

2. Material and methods

2.1. Procedure

This cross sectional, observational study was conducted between October 2008 and August 2009. All children and adolescents diagnosed with active epilepsy attending the outpatient services of the Division of Pediatric Neurology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi were screened for eligibility for this study. The International League Against Epilepsy (ILAE) definitions were used to define active epilepsy as two or more unprovoked seizures occurring 24 hours apart, with at least one epileptic seizure in the previous 5 years, regardless of AED treatment [19]. The inclusion criteria were (1) children aged from

* Corresponding author. Tel.: +91 11 2659 4679; fax: +91 11 2658 8663.
E-mail address: sheffaligulati@gmail.com (S. Gulati).

http://dx.doi.org/10.1016/j.jocn.2013.11.023
0967-5868/

6–16 years and (2) duration of epilepsy for at least 6 months. Patients were excluded if they had an intellectual disability or comorbid chronic systemic disease. Intellectual disability was defined as a verbal intelligence quotient of 70 or less. Malin's Intelligence Scale for Indian Children was used to screen children for intellectual disability [20].

Informed written consent was obtained from the primary caregivers of participants before inclusion into the study. The study design was approved by the Institutional Ethics Committee. All participants gave a detailed medical and neurological history and underwent clinical examination. Seizures were analysed by determining age at onset of epilepsy, predominant seizure type, seizure frequency, duration of epilepsy, etiology, and number of AED taken. Participants were placed into one of three categories of seizure frequency, being seizure free, having 1–10 seizures, or having >10 seizures, during the past 6 months. Epilepsy type was classified according to the recommendations of the ILAE [21]. Medical records were checked for confirmation of history. Caregivers were interviewed regarding educational problems of their child, and any repetition of a school grade was noted. If the child was not studying or had dropped out, the cause was evaluated. Socio-economic status was classified into six social classes as per the modified social classification (modification of Prasad's classification) by Agrawal, based on per capita monthly income [22]. Digital electroencephalography (EEG) (Medelec profile; Oxford Instruments, Oxfordshire, UK) was performed using the international 10-20 system of electrode placement. Both awake and sleep recordings were taken. Hyperventilation, photic stimulation and sleep were used for the activation procedure. EEG was reported as normal or showing epileptiform abnormality. The latest available EEG was analysed by a pediatric neurologist if it had been recorded within 3 months of evaluation. In children without such a recent EEG one was recorded on the same day of completing the CBCL.

2.2. Evaluation tools

Caregivers completed the CBCL while waiting in the hospital department. Questions were explained by an investigator if needed. The caregivers were asked to not report behavior which was present just before, during or after seizure. The questionnaire was scored as per manual specification.

The CBCL consists of 118 behavior problem items on which caregivers rate their children using a three point scale, with higher scores reflecting more problems. The CBCL assesses broad band behavior problems (externalizing and internalizing behavior problems) and narrow band behavior problems (attention problems, aggressive behavior, delinquent behavior, withdrawnness, somatic complaints, anxiety/depression, thought problems and social problems). Previous research has shown that CBCL is useful for assessing psychopathology in CWE [23]. The CBCL has been standardized and cut-off scores for significant behavioral comorbidity have been previously established for the Indian population [24]. The score thresholds for having a behavioral problem in children aged 6–11 years are 21 and 16 for males and females, respectively. For children aged 12–16 years the cut-off thresholds are 18 and 13 for males and females, respectively. This checklist has good psychometric properties. For this study, we used total scores only, as other scores have not been validated for Indian children. Children and adolescents were classified as having behavioral comorbidity if they scored above the relevant threshold for their age and sex on CBCL total scores.

2.3. Sample size estimation and statistical analysis

The varied reported prevalence of behavioral comorbidity in CWE has been as high as 42%. We calculated that 97 patients would be required for an expected 50% prevalence of behavioral comorbidity in our study population, with a 95% confidence level and ± 0.10 width of confidence interval (CI). Hence, the present study was planned as an observational study with a sample size of 97 patients.

A Microsoft Excel spreadsheet was used for data entry (Microsoft, Redmond, WA, USA). Data were analysed using Stata software version 9 (StataCorp, College Station, TX, USA). Frequencies were calculated by descriptive analysis. Univariate analysis was done to detect differences between participants with and without behavioral comorbidity. The statistical significance of categorical data was determined using the chi-squared test. The statistical significance of continuous data was determined using Student's *t*-test. The variables that differed significantly in the univariate analysis were used for multivariate analysis, using logistic regression. With the behavioral comorbidity as the dependant variable, odds ratios (OR) for epilepsy-related risk factors were calculated. A p value <0.05 was considered significant.

3. Results

One hundred and seventy two patients fulfilled the inclusion criteria. Seventy two patients were excluded due to intellectual disability (n = 62) and other comorbid chronic systemic illness (n = 10). Caregivers of 100 children gave consent for the study, forming the study population.

3.1. Socio-demographic factors

There were 65 boys and 35 girls in the sample. The mean age of the study population was 9.88 (standard deviation [SD] = 2.7) years. The range of family income (Indian rupee [INR]/capita/month) was very wide, from as low as 375 to 14000 INR/capita/month (median 1000 INR/capita/month). Socio-economic status of the study population comprised of two upper high, 13 high, eight upper middle, 23 lower middle, 52 poor and two patients from the very poor social class. Most families were intact families with two biological parents (96%). Four children lived in a single parent family without co-parenting. Most mothers had achieved a level of education, completing primary education (32%), secondary education (20%), and tertiary study (21%), whereas 27% had not completed primary education. A family history of psychiatric illness was documented in three participants.

3.2. Epilepsy-related variables

The mean duration of epilepsy was 3.66 (SD = 2.7) years. The mean age at onset of epilepsy was 6.46 (SD = 3.0) years. The most commonly prescribed AED was sodium valproate (n = 41), followed by phenytoin (n = 28), carbamazepine (n = 22), clobazam (n = 13), lamotrigine (n = 9), levetiracetam (n = 4), oxcarbazepine (n = 3), topiramate (n = 2), zonisamide (n = 1), and clonazepam (n = 1).

3.3. Behavioral comorbidity

Fifty three mothers, 42 fathers and five grandfathers completed the CBCL questionnaire. Total CBCL scores ranged from 1–84 (median 14). Of the 100 patients included in study, 43 patients qualified as having behavioral comorbidity. Twenty five mothers, 16 fathers and two grandparents reported behavioral comorbidity in their children or grandchildren based on total CBCL scores. There was no statistically significant difference in reported behavioral comorbidity between parent or grandparent reports (p = 0.67).

Please cite this article in press as: Choudhary A et al. Behavioral comorbidity in children and adolescents with epilepsy. J Clin Neurosci (2014), http://dx.doi.org/10.1016/j.jocn.2013.11.023