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Research Article

Attention-Deficit Hyperactivity Disorder in Childhood Epilepsy

Abstract

Introduction: Attention-Deficit Hyperactivity Disorder (ADHD) is a recognized cause of learning impairment in children. Several studies have shown that there is an increased prevalence of ADHD in children with epilepsy.

Objectives: To determine the prevalence of ADHD and its associations in children with epilepsy in a secondary care referral centre.

To analyze the clinical characteristics of epileptic patients in the study group.

Methods: A cross-sectional analytical study was conducted at the General Hospital, Chilaw, Sri Lanka in September 2012. All patients aged over 3 years with a confirmed diagnosis of epilepsy for at least 1 year were recruited into the study until a sample size of 100 was achieved. Data were collected using a pre-tested interviewer administered questionnaire. ADHD was defined using Diagnostic and Statistical Manual (DSM-IV) diagnostic criteria. Chi-square test and multiple logistic regressions were used in the analysis.

Results: Sixty-one percent of the study populations were males. Seventy-four patients had generalized epileptic seizures and 26 patients had partial epileptic seizures. Twenty-nine (29%) of patients had ADHD. Male sex, partial epileptic seizure type, duration of epilepsy over 5 years and use of more than one anti-epileptic drug were significantly associated with increased risk of having ADHD. Having partial epileptic seizures and use of more than one antiepileptic agent were independent predictors for the development of ADHD in multiple logistic regression.

Conclusions: More than one-fourth of epileptic children in this study had associated ADHD. Male sex, partial epileptic seizure type, duration of epilepsy over 5 years and use of more than one anti-epileptic drug were significantly associated with ADHD.

Introduction

Attention-Deficit / Hyperactivity Disorder (ADHD) is a neuro-behavioural and developmental disorder [1]. It is a condition that becomes apparent in some children in the pre-school and early school years. It is hard for these children to control their behaviour and/or pay attention. The prevalence of ADHD is given as 3 to 5% of school-aged children by DSM IV [2].

ADHD is recognized cause of learning impairment in children. It is characterized by hyperactivity, impulsivity and inattention and diagnosed according to the DSM- IV criterion which requires the presence of six of nine criteria for the inattentive type and six of nine criteria for the hyperactivity- impulsivity type. In addition, these symptoms must be present for at least 6 months before 7 years of age, and cause significant distress or impairment. The diagnosis of ADHD is subdivided into ADHD predominantly inattentive type if only inattention criteria are met; ADHD predominantly hyperactivity-impulsivity type if only hyperactive and impulsive criteria are met; and ADHD combined type when both criteria are met.

Several studies have shown the increased prevalence of ADHD (8 - 77%) in children with epilepsy [3,4]. Many factors may contribute to this co-morbidity including the underlying brain pathology, chronic effects of seizures, epileptiform EEG discharges and the effects of antiepileptic drugs [4-6]. By conducting this study we aimed to further delineate the nature of ADHD in epilepsy.

Objective

1. To determine the prevalence of ADHD and its associations in children with epilepsy in a secondary care referral centre.
2. To analyze the clinical characteristics of epileptic patients in the study group.

Method

A cross-sectional analytical study was conducted in the pediatric epilepsy clinic in General Hospital – Chilaw, Sri Lanka during September 2012 after obtaining the permission from the Head of the Institution. The ethical clearance was taken from the ethical review committee, Faculty of Medicine, University of Colombo. Our study center is a secondary care referral centre with all main specialties and a number of sub-specialties. The Paediatric Epilepsy Clinic is conducted weekly by a Consultant Paediatrician and care is provided for about 130 epileptic patients aged below 16 years.

During the month of September 2012, consecutive patients were recruited in to the study until a sample size of 100 is achieved. All patients aged over 3 years with a confirmed diagnosis of epilepsy for at least 1 year were recruited into the study. Lower cut off age of 3 years was used, as it was difficult to diagnose ADHD before this age. Patients with cerebral palsy and global developmental delay were excluded from the study as, they were well known confounding factors associated with ADHD [4,7]. Parents/caretakers were informed

about the details of the study and verbal consent was obtained before recruiting their children into the study.

Following recruitment the principal investigator interviewed the parent or caretaker and went through the child's clinical records to gather relevant informations for the study (e.g. confirmed diagnosis, EEG findings, Drug treatment and response etc). Data were collected using pre-tested interviewer-administered questionnaire. Questionnaire contained questions on age & sex of children, duration and type of epilepsy, EEG abnormalities, current treatment and questions to assess ADHD.

ADHD was defined using DSM-IV diagnostic criteria [2]. Seizures were classified using international classification of epileptic seizures [7].

Data were entered in to worksheet in Microsoft Excel and were analyzed using computer package SPSS 16.0 for windows. Chi square test and multiple logistic regression were used in the analysis.

Results

Sixty-one percent of the study populations were males. Mean age was 8.6 (SD=3.4) years.

Distribution of age is shown in **Table 1**.

Seventy-four (74%) patients had generalized epileptic seizures of whom 65 (65%) had generalized tonic-clonic seizures and 9 (9%) had absence seizures. Twenty-six (26%) patients had partial epileptic seizures. Clinical characteristics of different seizure types are shown in **Table 2**.

In this study group, twenty nine (29%) patients had ADHD spectrum disorders. Twelve (12%) had ADHD combine type (ADHD-C), 11 (11%) had predominantly inattentive type (ADHD-I) and 6 (6%) had predominantly hyperactive-impulsive type (ADHD-H).

Associations between sub types of ADHD with sex, age category, type of epileptic seizures, duration of epilepsy, current treatment and response to treatment is shown in **Table 3**.

Partial epileptic seizure type [$\chi^2=7.41$, $p<0.01$] and use of more than one anti-epileptic drug [$\chi^2=18.6$, $p<0.001$] were significantly associated with ADHD-C. Age over 10 years [$\chi^2=6.3$, $p<0.05$] and duration of epilepsy over 5 years were significantly associated with ADHD-I. Male sex [$\chi^2=4.08$, $p<0.05$] and partial epileptic seizure type [$\chi^2=5.48$, $p<0.05$] were significantly associated with ADHD-H. Male sex [$\chi^2=5.75$, $p<0.05$], partial epileptic seizure type [$\chi^2=10.5$, $p<0.001$], duration of epilepsy over 5 years [$\chi^2=4.4$, $p<0.05$] and use of more than one anti-epileptic drug [$\chi^2=6.3$, $p<0.01$] were significantly associated with increased risk of having a disorder in the ADHD spectrum (ADHD-C, ADHD-I or ADHD-H).

Multiple logistic regression was carried out to explore the risk factors for ADHD spectrum disorders. Sex, age, type of epileptic seizure, duration of epilepsy and number of drugs used were included in the model. A diagnosis of partial epileptic seizure type [(OR=3.96), (95%CI 1.4-10.7)] and use of more than one antiepileptic agent [(OR=5.14), (95%CI 1.31-20.0)] were independent risk factors for the development of ADHD spectrum disorders in epileptic children.

Discussion

There is high prevalence (29%) of ADHD symptoms in our study sample compared to general population normative values (3-5%). The prevalence of ADHD in our sample is quite similar to that reported by Hempel and coworkers (1995), and Dunn and Austin (2003) [8,9]. But prevalence of ADHD in epileptic children seen at tertiary care centers was much higher (60%) than this [10]. Their sample differs in that it consisted of children referred for neuropsychological assessment to a tertiary care centre. We did our study at secondary care referral center.

We found significant correlation between ADHD (combined and hyperactive-impulsive subtype) and partial epileptic seizure type. This is different to the finding of Hempel and coworkers (1995), who

Table 1: Age distribution of the study population.

	Male (%) [N=61]	Female (%) [N=39]
< 6 years	8 (13.1)	12 (30.8)
6 - 9 years	28 (45.9)	14 (35.9)
10 - 12 years	20 (32.8)	4 (10.3)
>12 years	5 (8.2)	9 (23.1)

Table 2: Clinical characteristics of different epileptic seizure types.

	Generalize tonic clonic seizures [N = 65] (%)	Absence seizures [N = 9] (%)	Partial seizures [N = 26] (%)
Sex			
Male	37 (56.9)	3 (33.3)	21 (80)
Female	28 (43.1)	6 (66.6)	5 (20)
EEG			
Abnormal	49 (75.4)	3 (33.3)	22 (85)
Normal	7 (10.8)	6 (66.6)	3 (11)
Not available	9 (13.8)	0 (-)	1 (4)
Duration of epilepsy			
< 5 years	50 (76.9)	9 (100.0)	20 (77)
> 5 years	15 (23.1)	0 (-)	6 (23)
Family history of epilepsy			
Present	13 (20.0)	0(-)	5 (20)
Absent	52 (80.0)	9 (100.0)	21 (80)
Current treatment			
S	60 (92.3)	8 (88.9)	14 (54)
C	0 (-)	0 (-)	6 (23)
S+Cw	1 (1.5)	1 (11.1)	2 (7.5)
S+L	2 (3.1)	0 (-)	0 (-)
S+Cl	0 (-)	0 (-)	2 (7.5)
S+T	0 (-)	0 (-)	2 (7.5)
S+T+P	2 (3.1)	0 (-)	0 (-)
Response to treatment			
Very good	29 (44.6)	3 (33.3)	14 (54)
Good	32 (49.2)	5 (55.6)	2 (7.5)
Poor	4 (6.2)	1 (11.1)	10 (38.5)

S = sodium valproate, C=carbamazepine, L= lamotrigine, Cl= clobazam, T= topiramate, P=phenytoin
 Very good - seizure free period of at least one year
 Good - reduced frequency of seizure episodes
 Poor - no response to treatment



noted that children with intractable generalized seizures were more likely to meet diagnostic criteria for ADHD (8). Our sample differs in that we did not have a separate group of intractable epilepsy. Further Elisabeth and coworkers (2007) found that children with ADHD inattention sub type were more likely to have localization related epilepsy than generalized epilepsy [11].

It is known fact that patients with partial epileptic seizure type are having increased incidence of structural brain lesions compared to patients with generalized epilepsy [3]. Furthermore structural brain pathology is a recognized aetiological factor contributing towards the development of ADHD [3].

Our data suggests that the ADHD symptoms are significantly higher in patients who had epilepsy for more than 5 years. This may be due to chronic effects of seizures or prolonged use of antiepileptic drugs. Wei and Kelly (1999), found associations between prolonged use of sodium valproate and ADHD. Further in our study, we found that use of more than one antiepileptic drug was significantly associated with ADHD. This is supported by the finding of Williams and coworkers (1996), who noted that children on polytherapy had significantly lower verbal and visual memory scores than children on monotherapy [12]. Without information on duration of exposure and dosage or blood levels, it is not possible to make any conclusions on antiepileptic drugs and symptoms of ADHD.

In most psychiatric samples, ADHD was more common in males and is most often the combined type. Those results were similar to our findings showing that ADHD is significantly higher in males and is most often the combined type. This raises the question of etiological similarities causing both ADHD and epilepsy.

Several possible explanations can be made for the association between ADHD symptoms and epilepsy. These might be neurological dysfunction, seizure variables, medication effects or psychosocial response to epilepsy. In this cross sectional analytical study we were

able to show an association between epilepsy and ADHD but cannot define causality. We believe neurological dysfunction or seizure variables or effects of medication may contribute to the increase risk for symptoms of ADHD.

This study has significant clinical relevance. Because ADHD is a treatable behavioural syndrome with effective pharmacological and behavioral therapies, a large number of children with epilepsy might potentially benefit from screening and medical intervention. In view of our findings and those of others, systematic screening of children with epilepsy for ADHD may need to be recognized as a routine practice in comprehensive care of such children [10].

Several avenues for future research remain, including research on etiological subtypes in children presenting with ADHD symptoms and epilepsy or research on association between antiepileptic drugs and ADHD.

Conclusions

High prevalence of ADHD is seen among the children with epilepsy. Male sex, partial epileptic seizure type, duration of epilepsy over 5 years and use of more than one anti-epileptic drug were significantly associated with increased risk of having a disorder in the ADHD spectrum. Having partial epileptic seizures and use of more than one antiepileptic agent were independent risk factors for the development of ADHD spectrum disorders in epileptic children.

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Table 3: Associations between ADHD/AD/HD and clinical characteristics of epilepsy patients.

	ADHD-C (N=12)	ADHD-I (N=11)	ADHD-H (N=6)	ADHD (N=29)
Sex				
Male [N=61] (%)	10 (16.4)	7 (11.5)	6 (9.8)	23 (37.7)
Female [N=39] (%)	2 (5.1)	4 (10.3)	0 (-)	6 (15.4)
Age categories				
< 10 years [N=62] (%)	10 (16.1)	3 (4.8)	4 (6.5)	17 (27.4)
>=10 years [N = 38] (%)	2 (5.3)	8 (21.1)	2 (5.3)	12 (31.6)
Type of epileptic seizures				
Generalized [N=74] (%)	5 (6.8)	8 (10.8)	2 (2.7)	15 (20.3)
Partial [N=26] (%)	7 (26.9)	3 (11.5)	4 (15.4)	14 (53.8)
Duration of epilepsy				
< 5 years [N=79] (%)	8 (10.1)	5 (6.3)	6 (7.6)	19 (24.1)
> 5 years [N=21] (%)	4 (19.0)	6 (28.6)	0 (-)	10 (47.6)
Number of drugs				
single drug [N=88] (%)	6 (6.8)	10 (11.4)	5 (5.7)	21 (23.9)
> one drug [N=12] (%)	6 (50.0)	1 (8.3)	1 (8.3)	8 (66.7)

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