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Common Errors in Diagnosis and Treatment of Pediatric Epilepsy

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ABSTRACT

Background: epilepsy affects people in all nations and of all races. Its incidence is greater in African American and socially disadvantaged populations. Epilepsy is the most commonly encountered neurologic conditions in children.

Aim of the Work: learning from one's mistakes is the best learning tool in medicine and this applies as well to epilepsy, so the aim of our work is to review some of the most frequently identified mistakes and errors in the diagnosis and treatment of pediatric epilepsy and how to avoid their occurrence.

Patients and Methods: the study included fifty children with epilepsy and condition mimic epilepsy, aged less than fifteen years (35 males and 15 females). The children participating in the present study were selected randomly from patients attending the pediatric neurology outpatient clinic of Al-Azhar University Hospital. The present work was conducted from January 2018 till the end of September 2018.

Results: in the present study it was found that 70 % of the studied patients are males and 30 % females. 76% of our patients were coming from rural areas, and only 24% living in urban. In this study we found that 34 % of our patients are wrongly diagnosed as Epilepsy. The study showed that 27% of epileptic cases are not controlled mostly due to improper selection of drug in 55.6 % and 44.4 % due to improper dose.

Conclusion: In fact, in patients with epilepsy, a detailed history is likely to lead to an accurate diagnosis in up to 90% of patients.

Keywords: Diagnosis, Treatment of Pediatric Epilepsy.

INTRODUCTION

Epilepsy affects people in all nations and all races. The incidence rate is greater in African Americans and socially disadvantaged populations [(1)].

Epilepsy is the most common neurological condition in children. Incidence rates among children under the age of 11 years are about seven to eight cases per 1000 cases per year [(2)]. The prevalence rate in childhood is estimated at 0.05-1% [(3)].

Shawki in the study reported a prevalence rate of 3.5/1000 among primary school children while ***Shawki*** [(4)] reported a prevalence of 20/1000 in the age group 6-12 years in Assiut Governorate. The prevalence of epilepsy in primary school children in El-Minia City in Egypt was 7.2/1000 in conventional schools and 133.3/1000 in school for subnormal. Male: Female ratio was 2:1. Prevalence was significantly higher among lower socioeconomic class. Neonatal insult, febrile convulsions, consanguineous marriage in parents and family history of epilepsy were the commonest perinatal risk factors [(5)]. Nonepileptic paroxysmal events (NEPEs) that have been misdiagnosed as epileptic seizures affect as many as 20–30% of patients diagnosed with epilepsy; these patients have often received treatment for epilepsy for many years or have been admitted to tertiary care epilepsy units [(6)]. The problem is complicated by the fact that approximately 30% of patients with genuine epileptic seizures also suffer from non-epileptic, mainly psychogenic seizures. In one study, the mean time lapse between the first attack and the correct diagnosis of non-epileptic seizures was over 9 years [(7)].

NEPEs are common and are numerous episodic clinical manifestations of diverse etiologies that mimic or look like, but are not, epileptic seizures [(8)].

Failure to get a good and detailed history is the most frequent cause of diagnostic errors in any of the medical fields, and epilepsy is not an exception. In fact, in patients with epilepsy, a detailed history is likely to lead to an accurate diagnosis in up to 90% of patients. In such cases, auxiliary studies help to confirm the clinically based diagnostic formulation. In the evaluation of patients with a presumed diagnosis of epilepsy, the first task is to establish whether the paroxysmal episode under investigation is, in fact, epileptic or nonepileptic. If the clinical characteristics of the event are suggestive of an epileptic seizure, the next step is to establish the type of seizure and epileptic syndrome, and whether the seizure in question was the first epileptic seizure ever, including seizures of other types that have gone unrecognized by the patient or family [(9)].

If the event is suspected to be nonepileptic, it is necessary to establish if it may be organic (i.e., syncope, sleep disorder, movement disorder, etc.) or psychogenic. The misdiagnosis of nonepileptic events as epileptic seizures is a relatively frequent occurrence. Indeed, 1 of 4 to 5 patients admitted to a video-electroencephalogram (EEG) monitoring unit with a diagnosis of pharmacoresistant epilepsy

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is found to have nonepileptic events, the majority of which are of psychogenic origin [9].

Learning from one's mistakes is the best learning tool in medicine and this applies as well to epilepsy. It encompasses errors in the clinical diagnosis that result in the choice of the erroneous antiepileptic drug (AED), errors in the way auxiliary tests like the electroencephalogram and magnetic resonance imaging studies are ordered, mistakes in the recognition of subclinical status epilepticus, errors in the selection of AEDs, consequences of the failure to factor in the pharmacokinetic and pharmacodynamic properties of AEDs in the choice and dosification of medication, misconceptions on the expectations of therapeutic effect of AEDs, and mistakes in the recognition and management of comorbid psychiatric disorders[9].

AIM OF THE WORK

Aim of our work is to review some of the most frequently identified mistakes and errors in the diagnosis and treatment of pediatric epilepsy and how to avoid their occurrence.

SUBJECTS AND METHODS

The study included fifty children with epilepsy and condition mimic epilepsy, aged less than fifteen years (35 males and 15 females). The children participating in the present study were selected randomly from patients attending the pediatric neurology outpatient clinic of Al-Azhar University Hospital.

The present work was conducted from January 2018 till the end of September 2018.

Ethical approval

The parents of all patients gave a written consent form for agreeing their children to participate in the study. The work has been approved by Al-Azhar Assiut University Ethical Committee.

Inclusion criteria

1. Children diagnosed as epilepsy or NEPE according to the International League against Epilepsy classification.
2. Children aged less than 15 years.

All patients and controls were subjected to the following:

1. Full and careful history was obtained from patients and their parents including age, sex, feeding pattern, detailed history of seizures including history of the first fit, frequency of fits, time of fit, prodroma, aura, ictus, post ictus, precipitating factors, history of associated neurological complaint, past history of other system affection, family history of similar condition, history of drug intake and if the seizures were recurrent or first attack. Complete clinical and full neurological examination was done.
2. Routine investigations including full blood count, blood glucose, serum calcium, potassium and sodium and serum drug level.

3. Electroencephalogram (EEG):

EEG records were done for all patients to detect abnormalities and to confirm diagnosis using 10 channel EEG machine (Nihon Khoden) with two marker channels and adhesive cup electrodes placed according to 10-20 international system. The paper speed was 30 mm/sec.

Four standard montages were done for every patients, two unipolar and two bipolar montages were done.

EEG recording was carried out under sedative effect of chloral hydrate (50 mg / kg / dose orally) in young patients and uncooperative older children and the record was carried out within less than twenty minutes after the onset of sleep, while the record was in the awake state with provocation through hyperventilation for three minutes or photic stimulation in older cooperative patients. EEG recording was carried out at least 48 hours after the last fit to exclude post ictal slowing.

4. **Brain computerized tomography (CT) and magnetic resonance imaging (MRI):** Owing to their high coast and poor financial support they were done only for selected patients with intractable epilepsy to exclude suspected structural abnormalities.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
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- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
  - Probability (P-value)
  - P-value <0.05 was considered significant.
  - P-value <0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

RESULTS

Table 1: Demographic data of fifty (50) studied patients with epilepsy and NEPE.

	No. (n=50)	%
Sex		
Male	35	70.0
Female	15	30.0
Age		
Mean±SD	6.88±3.16	
Residence		
Rural	38	76.0
Urban	12	24.0

-70 % of the studied patients are males and 30 % females, their mean ±SD of age was 6.88±3.16, and 76 % of them were coming from rural areas and only 24% were living in urban areas (Table 1).

Table 2: Percentage of epileptic to NEPE cases according to clinical presentation.

Diagnosis	No. (n=50)	%
NEPE	17	34.0
Epilepsy	33	66.0

-As in table (2) 34 % of our patients were wrongly diagnosed as epilepsy .

Investigation which done to studied cases.

Table 3: A-EEG

EEG	No. (n=50)	%
Done	50	100.0
Reported	20	40.0
Not reported	30	60.0
Not done	0	0.0

This table (3) showed that EEG was done to all patients (epileptic and NEPE) and only 40 % of them had full report.

Table 4: B – Serum level of AED.

Serum level	No. (n=50)	%
No	29	87.9
Yes	4	12.1

This table (4) showed that serum level of the AED was done to only 12.1 % of epileptic cases**,** in spite of its importance in judgment of efficacy of treatment.

Table 5: C- MRI brain.

MRI brain	No. (n=33)	%
Done	4	12.1
Not done	29	87.9

This table (5) showed that MRI brain was done to 12.1 % of epileptic cases.

Table 6: Percentage of uncontrolled epileptic cases received AED and the cause.

Treatment	No. (n=33)	%
Improper	9	27.3
Selection of drug	5	55.6
Dose of drug	4	44.4
Proper	24	72.7

This table (6) showed that 27% of epileptic cases are not controlled mostly due to improper selection of drug in 55.6 % and 44.4 % due to improper dose.

Table 7: Frequency of EEG done as a follow up investigation.

Follow up EEG	No. (n=33)	%
Done	13	39.4
<6 months	3	23.1
6 months	7	53.8
> 6 months	3	23.1
Not done	20	60.6

This table (7) showed that EEG was done as a follow up investigation in 39.4 % of epileptic cases .

Table 8: Duration of treatment of epileptic cases.

Duration of treatment	No. (n=33)	%
Less than 2 years	4	12.1
2-3 years	25	75.8
More than 3 years	4	12.1

The majority of epileptic cases in our study (75.8%) received AED for 2-3 years. 12.1% received treatment for less than 2 years and the same for those who received treatment more than 3 years (Table 8).

Table 9: Percentage of types of NEPE according to clinical presentation. NEPE cases (n=17)

Types	No. (n=17)	%
ADHD	3	17.6
Autism	2	11.8
Breath holding spells	3	17.6
Developmental language disorder	3	17.6
Headache	2	11.8
Masturbation	2	11.8
Syncopal attack	2	11.8

We found in our study that there were 17 cases, which represents 34 % of patients had nonepileptic paroxysmal events as described in table 9.

Table 10: Percentage of NEPE that received AED as a medical treatment.

Treatment	No. (n=17)	%
Received anti-epileptic drugs	10	58.8
Not received	7	41.2

This table (10) showed that 58.8 % of NEPE received AED as a medical treatment due to errors in diagnosis.

DISCUSSION

Epilepsy is the most commonly encountered neurologic conditions in children. Incidence in children under the age of 11 being around seven to eight cases per 1000 every year [(2)]. Prevalence in childhood is estimated to be 0.05 -1% [(3)]. 10.5 million children worldwide under 15 years old have epilepsy and represent 25% of the global figure of 3.5 million people who develop the condition each year, over 80% of these children are living in developing countries [(10)]. Estimated incidence rates in developing countries are between 61-124 per 100,000 and in developed countries between 41 and 50 per 100,000.

In the present study it was found that 70 % of the studied patients are males and 30 % females.

The mean ±SD of age was 6.88±3.16 in our patients. 76% of our patients were coming from rural areas, and only 24% living in urban.

In this study we found that 34 % of our patients were wrongly diagnosed as epileptics. This is in agreement with **NICE** [(6)] which showed that nonepileptic paroxysmal events (NEPEs), that were misdiagnosed as epileptic seizures, affected as many as 20–30% of patients diagnosed with epilepsy; these patients received treatment for epilepsy for many years or were admitted to tertiary care epilepsy units.

The study showed that 27% of epileptic cases were not controlled mostly due to improper selection of drug in 55.6 % and due to improper dose in 44.4 %. This is in agreement of **Brodie *et al.*** [(11)] who noticed that errors in the clinical diagnosis results in the choice of the erroneous antiepileptic drug (AED), errors in the selection of AEDs, consequences of the failure to factor in the pharmacokinetic and pharmacodynamic properties of AEDs in the choice and dosification of medication, misconceptions on the expectations of therapeutic effect of AEDs**.**

The use of AEDs with "broad-spectrum" efficacy may simplify the choice of AED, but it is not an excuse for not having established a correct diagnosis, as it also provides an expectation of response to pharmacotherapy. Indeed, response to pharmacotherapy differs significantly among the various epileptic syndromes. For example, patients with partial seizure disorder of mesial frontal origin have a 50% probability of becoming seizure-free with pharmacotherapy, while patients with childhood absences have up to an 80% probability of becoming seizure-free on the right antiepileptic medications [(12)]**.**

Errors in the way auxiliary tests, like the electroencephalogram and magnetic resonance imaging studies, are ordered is shown in our study as EEG was done to all patients (epileptic and NEPE), which is one of the most common investigation error (misuse and abuse of EEG) and only 40 % of them had full report.

EEG was done as a follow up investigation in 39.4 % of epileptic cases**.**

This is an extremely common error that results in an unnecessary premature discontinuation of AEDs, which could yield a seizure-free state if the dose were to be adjusted to its true potential therapeutic effect, defined as the dose that gives the "best seizure control for this patient" in the *absence* of adverse events. In other words, testing of efficacy and tolerability of an AED must be based on its potential to yield seizure remission (or significant reduction of seizure frequency) at the maximally "tolerated" doses, independent of the serum concentration. Premature discontinuation of AEDs often leads to the false assumption of pharmacoresistance. After all, the concept of therapeutic range is based on a statistical observation, but is not a reflection of the individual's own tolerance to the AED. In fact, it is not unusual to find patients who become seizure-free at serum concentration below the therapeutic range, and conversely patients able to tolerate doses with serum concentrations above the therapeutic range [(12)].

Serum level of the AED was done to only 12.1 % of epileptic cases**; i**n spite of its importance in judgment of efficacy of treatment.

MRI brain was done to 12.1 % of epileptic cases.

The majority of epileptic cases in our study 75.8% received AED for 2-3 years. 12.1% receive2 treatment for less than 2 years and the same for those who received treatment more than 3 years.

We found in our study that there were (n = 17) cases which represented 34 % of patients had non–epileptic paroxysmal events as described.

58.8 % of NEPE received AED as a medical treatment due to errors in diagnosis. This is in agreement with **NICE** [(6)] some patients with NEPE may be treated as epilepsy for many years or were admitted to tertiary care epilepsy units.

CONCLUSION

Failure to get a good and detailed history is the most frequent cause of diagnostic errors in any of the medical fields, and epilepsy is not an exception. In fact, in patients with epilepsy, a

detailed history is likely to lead to an accurate diagnosis in up to 90% of patients.

Careful history must be performed in patients with a first unprovoked GTC seizure with an inquiry of the possibility of other types of seizures. Identification of a family history of epilepsy can often serve as a red flag that may alert the clinician to the possibility of a primary generalized epilepsy.

Common mistakes include failure to use EEG recordings when starting a coma protocol or the use of short EEG studies in the intensive care unit on a daily basis without more prolonged EEG monitoring of the electrical activity, without which it is impossible for clinicians to identify recurrence of epileptic activity.

High-resolution brain MRI studies have facilitated the identification of those structural lesions associated with poor response to pharmacotherapy (i.e., MTS and malformations of cortical development such as focal dysplasias). Unfortunately, these types of lesions go often undetected with "standard" MRI studies.

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