Assessment of EEG as a Diagnostic and Prognostic Indicator Tool in the Febrile Seizures

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Abstract

Objective: To assess the sensitivity, specificity, and predictive value of EEG as a diagnostic and prognostic tool in the febrile seizures.

Method: This study was conducted on 50 consecutive children with febrile seizures attending the pediatric OPD of a tertiary care hospital. The children were prospectively identified and EEG was carried out on two occasions. First EEG was done within one week of febrile seizure episode and second EEG was done after 03 months of first EEG. EEG records were obtained with the standard international protocols for duration of 35 minutes which included 25 minutes of sleep record in all the children. Photic stimulation, hyperventilation and sleep deprivation were used as activation procedures. Descriptive analysis of EEG tracings was done in terms of background activity and presence of abnormal waveforms.

Result: Paroxysmal EEG abnormalities were present in 54% of children. Most common epileptiform discharges were of generalized epileptic discharge followed by focal polyspikes. Sleep deprivation was the most effective activation procedure in evaluating febrile seizure with abnormal epileptiform discharge patterns. Validity measures of EEG in febrile seizure were found to have 90% sensitivity, 70% specificity, 72% positive predictive value and 88% negative predictive value within 95% confidence interval.

Conclusion: EEG is a sensitive method for identifying and quantifying electrical activity in febrile seizures. EEG is useful as a diagnostic and prognostic tool in febrile seizures and can provide information regarding presence of abnormalities, degree of encephalopathy and electrographic features but like all diagnostic tool it is not fully infallible and requires further alternative diagnostic and clinical support.

Key words: EEG, Febrile seizure, Epileptiform discharges, Diagnostic and prognostic indicators.

Introduction

Febrile seizure is a very common age related acute seizure disorder in children provoked by a febrile illness. Febrile seizures affect 3% of all children under six years of age and are the most frequent seizure disorder in childhood (1). Seizures are the most common cause for referral to pediatric neurology and important cause of pediatric morbidity (2). Seizure is a paroxysmal event due to abnormal excessive hypersynchronous neuronal discharge originating from the brain. In nature, rhythm is inherent; and dysrhythmia means disease; in
Though there are limited data regarding electroencephalographic changes in febrile seizure and its role in predicting outcome in western literature, Indian population have no data in this regard. Thus present study has been done to assess the utility of EEG to identify the abnormal discharge pattern in febrile seizure and its outcome. The present study is an attempt to understand the various forms of epileptic changes present in children with febrile seizure and to assess its further future progression. The importance of such an understanding of various changes and its outcome measures is vital to assess the children at risk and to prevent the morbidity and mortality, by taking primordial steps of prevention.

Material & Method

Study design:
A selective population based descriptive study.

Study population and sample:
Fifty children of age group 05-72 months with febrile seizure, reporting to pediatric OPD of a tertiary care hospital within the period of 2008-2010 were taken up for the study. The selections of cases of febrile seizure were done according to the guideline definition given by The National Institute of Health Consensus (NIH) and The International League Against Epilepsy.

EEG machine and electrode:
24 channel software based computerized digital EEG (RMS, Superspec) was used. The electrodes were placed according to the international 10-20 system of electrode placement. The impedance values were kept below 10 kilo ohms.

EEG recording protocol:
Two sets of EEG were recorded in each patient. First EEG was done within 07 days of seizure and second EEG was done after 03 months of 1st EEG. Intermittent photic stimulation, hyperventilation and sleep deprivation were used as activation procedures. The protocol included an initial recording with eyes
open (including two activation procedure photic stimulation and hyperventilation of 2 minutes each) for 10 minutes followed by the 25 minutes sleep recording. In those younger children where achieving natural sleep was difficult, Pedicoryl (chloral hydrate) was used for sleep induction as and when required. Artifacts were identified visually and noted down. Children were also observed throughout the record to note any clinical seizure.

Analysis of EEG:

Different stages of the EEG record were analyzed offline to estimate amplitude, frequency, morphology and spatial distribution. EEG was reported in terms of background activity, wave form, right and left symmetry and abnormal discharge patterns.

Statistical analysis:

Validity of EEG as a diagnostic test in febrile seizure was evaluated (11) using Statistical tests by 2*2 contingency table using “Java Stat”. All the variables were evaluated within 95% confidence interval.

Result

Age and gender Distribution:

58% children (n=29) with febrile seizures were in the age range of 05 months to 24 months and only 20% children (n=10) were older than 4 year. Median age of sample varies from 17 to 22 months (Table I). 54% of sample population (n=27) comprises of the male gender (Fig. 1).

Degree of rise in temperature and febrile seizure:

84% children (n=42) with febrile seizure had temperature more than 39 degree centigrade and 16%

<table>
<thead>
<tr>
<th>Age (month)</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>05–24</td>
<td>29</td>
</tr>
<tr>
<td>25–48</td>
<td>11</td>
</tr>
<tr>
<td>49–72</td>
<td>10</td>
</tr>
</tbody>
</table>

Fig. 1: Pie graph of gender distribution in febrile seizure.
Activation procedure in febrile seizure:

Photic stimulation:

In 84% children (n=42) photic stimulation was carried out. In 16% children (n=8) photic stimulation could not be done (due to sleep induction by the chloral hydrate). Responses to photic stimulation in all the patients were physiological (76% photic driving and 8% photomyoclonic) (Fig. 2).

Hyperventilation:

Hyperventilation as an activation procedure requires co-operation of the patient. 62% children (n=31) could do the hyperventilation. In 38% of children (n=19) it could not be done due to age less than 24 months. In all the children response to hyperventilation was within physiological limits (42% hypersynchronous slowing and 20% no response) (Fig. 3).
Sleep deprivation:

Partial sleep deprivation was used in all the children to induce sleep. It was observed that most of the epileptiform discharge pattern was present in sleep EEG. Sleep deprivation was found to be very useful in obtaining the epileptic discharge as an outcome.

Descriptive result of abnormal sleep EEG discharge:

Results of the descriptive analysis of EEG were of 3 types; Normal, Borderline and Abnormal cases (Fig. 4). Cases with normal EEG had no sign of epileptiform activity and cases of abnormal EEG had predominant epileptic activity. Borderline EEG cases were showing abnormal EEG changes but were not epileptiform type. Borderline cases of EEG, where clinical situation was not supportive, following the wisdom of under reporting an EEG, were reported to be normal, but for research purposes they were kept in borderline category as per recommendations given by American epilepsy society (9). In the first EEG (postictal) analysis of all the cases, 54% children (n=27) were found to have epileptiform discharge, 12% children (n=6) with query epileptiform discharge and 34% children (n=17) had no epileptic discharge.

Among 27 cases with epileptic discharge, 09 had polysharps, 08 had bizarre wave complexes, 06 had spikes, 02 had sharps followed by slow waves, 01 had periodic lateralized epileptic activity and 01 had spike and wave pattern (Fig. 5-9). Among these patients one with periodic lateralized epileptic activity and other with bizarre wave complexes died within three months of follow up due to generalized epilepsy. Out of 6 patients of borderline category 03 had frontal and central spikes, 02 had occipital spikes, and 01 had centrotemporal spikes.

Second visit follow up EEG Result:

Out of 50 cases in first visit, 43 cases were available for follow up study. Out of 27 cases with epileptic discharge in first EEG, 25 cases (2 died) who were available for follow up second EEG, 21 cases were again had epileptic discharge while 04 cases were in borderline category. And out of 6 borderline EEG case in first EEG 04 cases were found to have
epileptic discharge in second EEG recording (Table: II-III). Both the false positive and negative were from the borderline category from postictal EEG.

**Clinical Outcome Measurement result:**

In the interval of 03 months, among 25 cases that were electroencephalographically epileptic, 18 had seizure clinically. 2 cases that were electroencephalographically negative also had seizure. On evaluating symptomatology 18 cases were found to have bilateral tonic clonic features and 2 cases had unilateral tonic activity. Kappa coefficient
TABLE II: EEG abnormality in febrile seizure patients from two visits.

<table>
<thead>
<tr>
<th>Follow up EEG</th>
<th>Epileptic activity present</th>
<th>No. Epileptic activity</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postictal EEG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epileptic activity present</td>
<td>21</td>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>No Epileptic activity</td>
<td>3</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>19</td>
<td>43</td>
</tr>
</tbody>
</table>

TABLE III: Outcome measures of postictal EEG.

<table>
<thead>
<tr>
<th>Outcome occurred</th>
<th>Outcome did not occur</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factor present</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td>Risk factor absent</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>23</td>
</tr>
</tbody>
</table>

TABLE IV: Variable indicators of EEG as a diagnostic tool.

<table>
<thead>
<tr>
<th>Quantities derived from 2 by 2 contingency table</th>
<th>Value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kappa</td>
<td>0.586</td>
<td>0.316 0.715</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.791</td>
<td>0.654 0.856</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.900</td>
<td>0.753 0.970</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.696</td>
<td>0.568 0.757</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.720</td>
<td>0.603 0.776</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>0.889</td>
<td>0.726 0.967</td>
</tr>
<tr>
<td>Positive likelihood ration</td>
<td>2.957</td>
<td>1.744 3.985</td>
</tr>
</tbody>
</table>

Assessment of EEG in predicting clinical outcome of febrile seizure was found to have Sensitivity of 0.90, Specificity of 0.70, Positive predictive value was found 0.586 and shows good agreement between EEG and epileptic outcome i.e. a clinical seizure. Polyspikes present in all the electrodes on the background of delta.

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Fig. 7: EEG showing, Polyspike, case of 50 months old child presenting with focal features.

Fig. 8: EEG showing, Single sharpwave, case of 15 months old child. Child died due to status.
0.72, negative predictive value 0.90 and Accuracy or overall fraction correct of 0.79 within 95% confidence interval. Positive likelihood ratio was 2.957 within 95% confidence interval. All these values are pointing toward the high sensitivity of the EEG in predicting the outcome.

**Discussion**

The febrile seizure predominantly affects the children of the age group of less than 2 year. In present study group 58% children with febrile seizure were less than 25 month of age. Hauser & Anneger (7) and Yelandur (12), had reported similar findings. Although exact mechanism of this increased susceptibility is unclear, insight from animal models suggest that there is enhanced neuronal excitability during the normal brain maturation (1).

The febrile seizure affects male gender more as compare to female gender. In our study 54% children were male. Hauser & Anneger (7) and Millichap (13) had reported the sex ratio between 1.4 to 1 and 1.2 to 1 in children with febrile seizure. The male preponderance may be due to sex ratio imbalance and excess parental concern to male child. In present study 84% children with febrile seizure had the temperature rise of more than 39 degree centigrade. Rise in temperature to more than 38.5 degree centigrade acts as a provocative factor have been reported in literature (1, 14).

**Activation procedures and febrile seizure:**

Photic stimulation, hyperventilation and sleep deprivation were used as activation procedures. The responses to photic stimulation were physiological and are agreement with reported literature (15). The response to hyperventilation was within normal limit. Hyperventilation was also not helpful and this is in agreement reported literature (15). Hyperventilation is more helpful to evaluate patients with absence seizure and absence seizure is uncommon in children less than six years of age.

Sleep deprivation was found to be very useful in enhancing epileptic discharge. Sleep induction in younger children is done by using sedation with Pedicoryl and older children by sleep deprivation (16). Epileptiform discharge in patients with febrile seizures occurred in light sleep, NREM stage 1 & 2. Comparative studies done on patients with awake EEG and sleep EEG reports that the diagnostic yield of sleep deprived EEG in a patient with normal EEG is enhanced to 40% (15, 17, 18).
Abnormal epileptic discharges in febrile seizure:

Based on EEG findings children were categorized into three types: Normal, Borderline, and Abnormal. Sofijanov had reported that the initial EEG of 676 children with febrile convulsions contained paroxysmal abnormalities in 22% (19). Febrile seizures are categorized into simple and complex type. Jeong et al. have reported EEG abnormalities in 31% of patients with febrile seizures and it was more common in children with complex than simple febrile seizures (43% vs. 28%) (20). Kim et al. found complex febrile seizures in 22.6% of all patients with febrile seizures and 12.0% developed subsequent epilepsy (21). In this study, 54% of children showed electroencephalographic epileptic predominance, which is much more than others. It is assumed to the fact that the study is hospital-based, and the likelihood of complex seizure may be higher and the referring physicians were pediatricians.

In this study, among 27 children, 21 (77%) had generalized epilepsy, 06 (23%) had polyspikes, and 01 (3%) children had periodic lateralized epileptic activity. Sharps followed by slow, polysharps, bizarre wave complexes are the three types of presentation of generalized epilepsy. In generalized epilepsy, pattern begins with complexes of shorter duration, a 3/sec spike and wave and progresses to bizarre pattern (18, 22). Sofijanov also reports that in all series patients with generalized epilepsy pattern were most common with focal polyspikes being second about 10% of cases. In the present study, however, cases with polyspikes are slightly more.

In the study, 2 children developed status epilepticus and died due to generalized epilepsy. Kim et al. reported that about 24% of complex febrile seizure patients and 1.2% of simple febrile seizure patients enter to status. Prolonged (>10 min) seizure or the presence of multiple seizures predisposes significantly more frequent subsequent epilepsy in patients (21). In this study, both the children had history of prolonged febrile seizure in postictal EEG recording. Most of the studies state that mortality with febrile seizure is almost nonexistent (1). However, it also has been stated that febrile seizure is a heterogeneous disease. Majority of patients have an excellent outcome; however, the rare cases that could belong to sub syndromes had more severe outcome (22). Aicardi who asserts that although a large majority of simple febrile seizures are brief, bilateral and benign in outcome, some children have a combination of simple febrile seizure and long-lasting unilateral seizure. It also has been reported that periodic discharge pattern, such as periodic epileptic discharges, is associated with status epilepticus prognosis and is not good (23).

Changes in Epileptiform activity in follow up EEG:

In present study, 48.9% cases were true positive and 34.9% were true negative. Frantzen et al. found paroxysmal EEG abnormalities in 35% to 45% with serial EEGs (24). The probable reason for this difference could be two: small sample size and only one follow-up. With each follow-up chances of getting true positives increase to about 25% (23). With the 2nd EEG, 02 children were diagnosed with epileptic activity. This is in agreement with other studies which state that repeat EEG identified an additional 11% positive with previously normal EEG (9). Presence of false positive can be explained with the fact that EEG can be abnormal in about 1% of healthy children and when it is hospital-based chances can be slightly more (9, 22).

EEG in predicting clinical seizure

Validity of a diagnostic tool is evaluated by its sensitivity, specificity, positive predictive value, negative predictive value, and positive likelihood ratio. Sensitivity value of EEG (0.90) in present study is very high; however, specificity is not that significant (0.696). Positive predictive value and negative predictive value is also significant. Validity measurement of EEG as a diagnostic test in assessing outcome with sensitivity, specificity, and predictive value shows that EEG is a highly sensitive test and a very good screening tool (11).
References