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Early electroencephalography in patients with Emergency Room diagnoses of suspected new-onset seizures: Diagnostic yield and impact on clinical decision-making

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ABSTRACT

Purpose: To assess the utility of acute electroencephalography (EEG) performed in the emergency room (ER) and its impact on subsequent management of patients with new-onset seizures. Adults who recover fully in the ER following suspected isolated new-onset seizures are usually discharged to the neurology clinic for further review. An EEG at that stage may be normal. We sought to assess the feasibility and yield of early EEG in the ER setting, its impact on management.

Methods: A prospective study from January 2008 to January 2011 of patients diagnosed by ER physicians with uncomplicated suspected first episodes of unprovoked convulsive seizures. All patients underwent routine 30-min EEG in the ER prior to discharge and specialist review was arranged in the epilepsy clinic within 2 weeks of presentation. Management decisions were at the discretion of the treating neurologist. Seizure recurrence was assessed during a follow up period between 9 months and 3 years.

Results: 136 patients were included in the study (92 males). Mean age was 32 years (range 16–73). Forty had abnormal EEGs: 16 focal epileptiform discharges, 12 focal slowing, 10 generalized spike-wave discharges and 2 generalized slowing. Using multivariate analysis, those with abnormal EEG (51% vs 11%, $p = 0.003$) and abnormal MRI (53% vs 28%, $p < 0.001$) were more likely to be commenced on anticonvulsant therapy. Abnormal MRI ($p = 0.001$) was independently associated with a higher risk of recurrence.

Conclusions: Following an ER diagnosis of new-onset uncomplicated seizure, early EEG had a high diagnostic yield. Abnormal EEG and abnormal MRI significantly contributed to decision-making regarding treatment at specialist review. Abnormal MRI was associated with significantly higher risks of subsequent seizures.

1. Introduction

Approximately 8–10% of the general population will have a single non-febrile seizure during their lifetime [1]. While a first seizure caused by an acute disturbance of brain function (acute symptomatic or provoked) is considered to have low risk of recurrence in the range of 3–10%, unprovoked seizures tend to recur in the range from 23% to 71% dependent on study design [2–6]. A meta-analysis suggests that 30–50% will be a realistic measure for seizure recurrence (SR) in these patients [7]. Patients who present with new-onset unprovoked seizures are referred in our practice to the neurology clinic either via the Emergency Room (ER) or their general practitioners [8]. Most of them will be seen in a first seizure clinic run by epileptologists.

Most patients who make a full neurological recovery and have no seizure recurrence in the ER can be safely discharged with

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follow-up arrangements [8]. The interval between presentation and outpatient review varies considerably amongst healthcare institutions. When indicated, neuroimaging and EEG are arranged after a specialist review [9]. EEG is often normal when assessed in follow-up. The aim of our study was to evaluate the feasibility and utility of early EEG, its impact on outpatient management decisions, differential diagnosis with regards to syncope, and correlation with seizure recurrence rates in patients with a confirmed unprovoked first seizure.

2. Methods

We collected prospectively data of 136 patients who attended the ER at our tertiary level teaching hospital from January 2008 to January 2011 with first episodes of suspected unprovoked convulsive seizures and referred to subsequent first seizure clinic. The study was approved by the hospital Institutional Review Board.

Those over the age of 18 years were included in the study. Patients were included if the diagnosis of suspected seizure was made by ER specialists (national board certified), based on a high clinical index of suspicion or eyewitness accounts that described jerking movements of limbs and loss of consciousness and patient was given follow up at first seizure clinic on discharge from ER. Only those who had made a complete neurological recovery prior to the EEG were included in the study. Those with a history of alcohol and/or substance abuse which may have contributed to the seizure were excluded from the study. Patients were also excluded from the study if seizures was considered to be provoked as a result of acute stroke, encephalitis, or metabolic derangements. Based on institutional protocols, patients were observed in the ER for up to 24 h prior to being discharged home. Decisions regarding acute neuroimaging using computerized tomography (CT) were left to the discretion of the ER physician, based on clinical indication: patients with clearly focal onset of seizure, focal abnormality on neurological examination, age >65 years, seizure activity lasting for more than 15 min, signs of head injury and persistent altered mentation at time of presentation.

A routine 30 min digital EEG using 16 channels with hyperventilation and photic stimulation was performed by trained EEG technologists during their stay in the ER. The recording was interpreted by a neurologist with EEG certification who was blinded to the results of neuroimaging, if performed. The ER physician was in turn blinded to the EEG results so as not to influence the ER clinical diagnoses.

EEG findings were classified in 5 classes as either (1) Normal, (2) focal epileptiform, (3) generalized epileptiform, (4) focal slowing or (5) generalized slowing. Most of the earlier studies classified EEG findings into 3–5 subtypes [10]. Recordings that had more than one finding were categorized according to the abnormality that was felt to have the greatest diagnostic impact. For example, focal abnormalities were given greater credence than generalized changes, if both were seen at different time points in the same recording.

At the point of discharge, arrangements were made for patients to be reviewed within 2 weeks at a specially designated 'first seizure' clinic run by trained epileptologists. Clinical decisions were made according to the clinician's analysis and management recommendation for first seizure, and was considered particularly in patients who had structural brain abnormalities and EEG abnormalities, those who were susceptible to significant injury from subsequent seizures, or those who were at risk of economic hardship such as loss of employment [11,12] Patients were started on anti epileptic medication at first seizure clinic as per analysis of treating neurologist and were not started on medications at ER.

Follow-up clinic data was obtained by review of patient's electronic chart review. The clinical impression, neuroimaging findings, commencement of antiepileptic drugs (AED) and seizure recurrences were recorded. Patients were also asked if they presented to other hospitals with seizures and this data was included.

Those who were not scanned in the ER (100 patients) underwent outpatient neuroimaging if the neurologist concurred with the diagnosis of seizure and/or focal abnormalities were present on EEG. The choice of modality (CT or MRI) was left to the discretion of the neurologist dependent on the likelihood of a focal (structural) versus generalized epilepsy syndrome and after discussion with the patient in view of the costs involved. In some instances, a patient may have undergone CT in the ER and MRI as outpatient.

The rate of diagnostic agreement between ER physicians and the epileptologist was analysed for all patients who were referred to and seen in the clinic. Subsequent follow-up was arranged for patients who were thought to have truly had seizures by the epileptologist. All analyses about factors determining initiation of treatment and seizure recurrence were done on this subgroup of patients

3. Statistical analysis

We present the numerical variables as means and standard deviations, or medians and ranges. Categorical variables are presented as percentages. Numerical predictors were tested by using 2-sample t test or Mann–Whitney U test where applicable. Categorical predictors were evaluated using x^2 test or Fisher exact test where applicable. Univariate analysis of potential predictors was first performed. Multivariate analysis was performed with logistic regression to identify factors that independently influence the decision to initiate AED and variables that might predict seizure recurrence. Each factor was examined in a simple logistic regression model, and a selection of those with a p-value <0.10 were included as candidates into a multivariable logistic regression model with backward stepwise selection. Predictor variables that were significant at p-value <0.05 were retained in the multivariate model. Associations are presented as odds ratios (OR) with corresponding 95% confidence intervals. Statistical analysis was performed using SPSS version 20.

4. Results

136 patients were included in the study, 92(67.6%) of whom were male. The mean age was 32.5 years (range 16.5–73.6). EEG was abnormal in 40 patients (29.4%) out of 136 patients included in study (see Table 1). Focal epileptiform abnormalities were seen in 16 patients; isolated focal slowing was observed in 12 patients. Generalized epileptiform discharges were seen in 10 patients and 2 had generalized slowing. In cases where both ER physicians and the study epileptologist agreed on the clinical diagnosis of seizure, the rate of EEG abnormality was 48.6%. Three of the 28 patients diagnosed in the clinic with syncope had abnormal EEG (2 diffuse slowing, one focal slowing).

95 patients underwent neuroimaging with either computed tomography (CT) and/or Magnetic Resonance Imaging (MRI) of the

Table 1
EEG abnormalities in 40 of 136 patients with suspected first unprovoked seizure.

EEG abnormality	Number (%)
Focal epileptiform	16 (40.0%)
Generalised epileptiform	10 (25.0%)
Focal slowing	12 (28.0%)
Diffuse slowing	2 (5.0%)

Table 2
Neuroimaging abnormalities in 14 out 136 patients with suspected first unprovoked seizure.

Neuroimaging abnormalities	Number of patients ($n = 14$)
Encephalomalacia	3 (2 post-traumatic, 1 post-stroke)
Developmental	6 (3 arterio-venous malformation, 2 focal cortical dysplasia, 1 gyral atrophy)
Neoplastic	3
Mesial temporal sclerosis	2

brain. Thirty two had MRI, 69 patients underwent CT. 6 patients had both CT scan and MRI of the brain. Abnormalities in MRI and CT were 32.2%(10/32) and 5.8%(4/69) respectively (Table 2). Thirty six patients were scanned in the ER, of which only one was abnormal, revealing a temporal arachnoid cyst. Of 10 patients with abnormal MRI, 5 had focal epileptiform activity on EEG that corresponded topographically to the abnormality on MRIs (see Fig. 1).

From the included patients in study, 104 patients attended follow-up. The epileptologist concurred with the ER diagnosis of seizure in 74 (71.1%) patients. A diagnosis of syncope was made in 28 (26.9%) patients and in 2 patients (2%), no firm diagnosis was made.

Using univariate analysis, abnormal EEG and abnormal MRI findings were found to be statistically significant variables in patients who were initiated on AEDs. On multivariate analysis, patients with abnormal EEG ($p = 0.003$, OR 4.09, CI 1.61–10.36) and abnormal MRI ($p = 0.001$, OR 5.78, CI 2.23–14.97) were more likely to be commenced on medication.

27 of 104 patients (25.9%) developed seizure recurrences during the follow up period. On univariate analysis, abnormal EEG (p value 0.005), abnormal MRI (0.002) and the initiation of treatment (0.019) were statistically significant in this group. After multivariate analysis, abnormal MRI ($p = 0.001$, OR 9.38, CI 3.09–28.44) remained an independent predictor of recurrence. Patients who were commenced on anticonvulsant medication also had higher risks of recurrence although this did not reach statistical significance on multivariate analysis.

5. Discussion

This prospective study reports the utility of early EEG to supplement the clinical assessment of patients who are diagnosed by ER physicians with possible new-onset suspected seizures. We found that performing 'acute' EEGs in a non-emergent clinical setting was logistically feasible with minor adjustments to the work-flow of the EEG technicians.

Results from the study suggest that early EEG in the ER has a higher sensitivity than routine outpatient recordings, in keeping with the literature [10,13], particularly in patients whose diagnosis is supported following an epileptologist review. Abnormalities on EEG and neuroimaging may have influenced the decision to treat patients early with AEDs despite this being their first seizure. The revised diagnostic criteria highlight that patients with first unprovoked seizure and supportive data predicting higher recurrence risks, can already be diagnosed with epilepsy [14]. It is conceivable that the higher yield of early EEGs led to a higher proportion of patients who were diagnosed and treated.

The study was performed in a routine and 'real-time' clinical setting with little in the way of external controls. Diagnostic and treatment decisions were left to the discretion of the clinicians involved. The diagnostic rate of agreement for seizures between ER physicians and epileptologists was 71.1%. In this group of patients, the sensitivity of acute EEG approached 50%, confirming other studies that demonstrate higher rates of interictal abnormalities when the EEG is performed in close temporal relationship to the seizure [9,13,15–17]. AAN guidelines recommend that EEG should be considered a part of the diagnostic evaluation for a patient with first seizure [18]. If performed as soon as possible (preferably within first 24 h of presentation) following the index event, the yield of EEG may increase, aiding in the classification of seizures [19].

In keeping with the literature, neuroimaging abnormalities were seen in 15% of our patients [13]. Our study showed that detection rates for MRI were higher than CT, 32.2% and 5.8% respectively. This is likely due to selection bias as all MRI scans were requested by the neurologist who had specific clinical expertise and access to the EEG data. The MRI in 50% of cases had topographical concordance with focal EEG abnormalities. Two patients with focal electrographical abnormalities on the EEG had normal CT scans. Based on the EEG results, MRI was performed which revealed brain neoplasm that required neurosurgical intervention. Performing MRI in the initial evaluation of all patients with first unprovoked seizures is critical and has become practice in all first seizure clinics [13]. In the ER setting, CT is the procedure of choice because of the relative speed and ease of

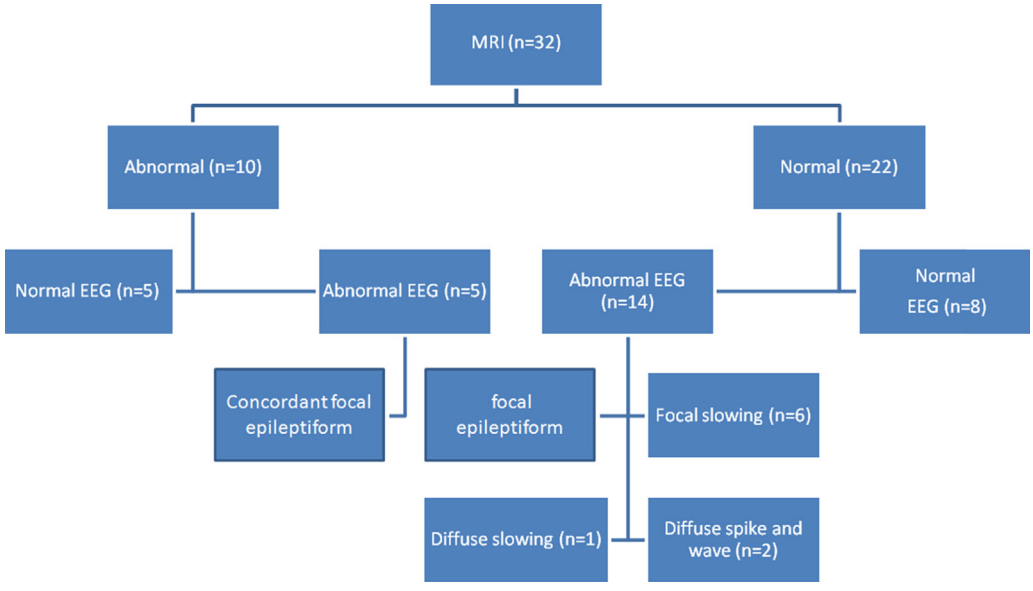

Fig. 1. MRI and EEG correlation.

obtaining the study and its effectiveness in demonstrating gross lesions such as ischemia, neoplasms, bleeding etc. [20,21].

In this study, clinical assessments in conjunction with either abnormal EEG and/or MRI were associated with a higher likelihood of being commenced on AED. An expert consensus by Villanueva et al. found that the presence of generalized spike and wave discharges, abnormal MRI and older age were important factors in initiating treatment with AEDs [22]. Our study concurs that in clinical practice, abnormalities of EEG and/or MRI appear to be significant factors that aid the clinical decision-making process. This likely stems from available data indicating that abnormal EEG is associated with a higher risk of seizure recurrence and that early treatment in this group may be beneficial [1,2,4,22,23].

Population based studies quote recurrence rates of approximately 36–37% at 1 year and 43–45% at 2 years [3,23]. Of the patients who had corroborative diagnoses of seizures made in the ER and at specialist review, the recurrence rate was 36% at 2-year follow up. It is uncertain if the early review and initiation of treatment had an effect on the recurrence rates in this group. Interestingly, on univariate analysis the treated group had more seizures, likely reflective of a high-risk population. However, a longer follow-up duration and a comparison with a 'high-risk' untreated group in an extended study may determine the true effect of early treatment [24–27].

In this study, having an abnormal MRI independently predicted a higher risk of seizure recurrence confirming the critical role of etiology for seizure recurrence [28] In several cases, the abnormal acute EEG prompted the MRI, which had significant consequences for the two patients who were diagnosed with neoplastic lesions. Both EEG and MRI may be useful in evaluating patient with first unprovoked seizure. This merits further investigation on a larger scale and longer follow-up periods.

There are several limitations to our study. Of the 136 patients seen in the ER 104 patients attended the first seizure clinic which limits the interpretation of the follow-up data. MRI was not systematically performed in all patients. The role of MRI for assessing risk of recurrence was not a primary objective in study, therefore only limited conclusions can be drawn on this aspect from our study.

6. Conclusion

In an ER setting of a presumed first seizure, performing 'acute' EEG was logistically feasible and had a higher diagnostic yield than reported sensitivities of routine recordings.

Abnormal EEG and MRI contributed to the decision-making process pertaining to the initiation of treatment.

Abnormal MRI independently predicted higher risks of further seizures.

Author contributions

Drs Paliwal, Wakerley and Yeo were responsible for the data collection, interpretation of data and primary drafting of the manuscript.

Drs Ali and Ibrahim were responsible for the data collection, interpretation of data and manuscript editing.

Professor Wilder-Smith and Dr Sim were responsible for the interpretation of data and critical review of the manuscript for intellectual content.

Professor Bernd Pohlmann-Eden was responsible for editing the manuscript.

Dr Rathakrishnan was responsible for the study concept/design, project oversight, interpretation of data and secondary drafting of the manuscript.

Conflict of interest

The authors have no conflict of interest.

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