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An Assessment of 24-Hour Ambulatory Electroencephalography [EEG] Monitoring in New Onset Idiopathic Generalized Epilepsy [IGE]

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Abstract: ***The 24-hour ambulatory electroencephalography [EEG] monitoring in new onset idiopathic generalized epilepsy [IGE] provided a better yield of diagnostic information compared with conventional EEG recording in 28% of patients (total patients were 50) who were admitted or attented neurology OPD in SMS hospital, Jaipur during December 2017 to December 2019.***

Keywords: Idiopathic generalised epilepsy, 24-hour ambulatory electroencephalogram.

1. Introduction

The idiopathic generalized epilepsies [IGE] constitute approximately 20-40 % of all epilepsies. The term "idiopathic" comes from the Greek word "Idios" which means oneself.[1, 2, 3] By definition, patients with idiopathic generalized epilepsy have no structural brain lesions on MRI and a lack of symptoms and signs interictally.[4, 5] Approximately 50 million people worldwide have epilepsy. Worldwide the point prevalence of active epilepsy is 6.38 per 1000 persons and life time prevalence is 7.6 per 1000 persons. The prevalence of epilepsy does not differ between sex or by age group.[6, 7] Generalized seizures and epilepsies of unknown etiology have highest prevalence.[8]

IGE is clinically characterised by absence, myoclonus seizure and tonic-clonic seizures with electroencephalographic (EEG) pattern of bilateral, synchronous and symmetrical spike and wave or polyspike and wave discharges. On the basis of predominant seizure type and age of onset , the international classification recognises four main IGE subsyndromes, childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME) and IGE with tonic-clonic seizure alone (GTCA).[9, 10]

The electroencephalogram (EEG) is one of the most important diagnostic tools for evaluating seizures and spells in patients. Epileptiform abnormalities on EEG can help differentiate epileptic from nonepileptic events, as well as assess risk of recurrent seizures following a first unprovoked seizure. According to the American Academy of Neurology practice parameter for evaluation of a first unprovoked seizure in adults, epileptiform abnormalities on EEG were associated with a greater risk of seizure recurrence, 49.5% with epileptiform discharges versus 27.4% without epileptiform discharges.[11] only 29–55% of epilepsy patients have been reported to show epileptiform discharges on a single routine EEG. Thus sensitivity of routine eeg is low but specificity is better, but again variable at 78–98%.

The American Clinical Neurophysiology Society (ACNS) guidelines for performing EEG recommends at least 20 minutes of satisfactory, artifact-free recording during wakefulness at minimum, with additional recording time for photic stimulation, hyperventilation, and sleep when possible.[12] European guidelines recommend at least 30 minutes of artifact-free recording.[13] To improve the diagnostic yield of EEG—in addition to using hyperventilation, photic stimulation, and sleep deprivation—there are two basic approaches: Increase the number of recordings or increase the duration of a single recording. While the yield of epileptiform abnormalities on first EEG is only 29–55%, a population-based study demonstrated that a second routine EEG would identify epileptiform abnormalities in an additional 10% of patients following a single unprovoked seizure.[14] Therefore, repeating studies at different points in time in patients in whom the first EEG is negative may increase the yield. The ILAE recommends long term EEG monitoring where there is diagnostic uncertainty as to the diagnosis of epilepsy. Video EEG monitoring is unavailable to many patients under investigation due to limited provision and high cost. The alternate investigation of prolonged outpatient ambulatory EEG is a relatively recent inception as the technology to allow for portable devices only became commercially available in 1979 enabling patients to be investigated at home with exposure to their typical seizure provoking factors, make outpatient ambulatory EEG an attractive option. Prolonged interictal sampling using EEG monitoring increases yield by about 20%, and is now more widely available through 24 hour ambulatory multichannel digital EEG.

Aims & Objectives

An assessment of 24-hour ambulatory electroencephalography [EEG] monitoring in new onset

idiopathic generalized epilepsy [IGE] so to determine whether the routine use of ambulatory 24-hour EEG monitoring provide a better yield of diagnostic information compared with conventional EEG recording.

2. Material & Methods

This is a hospital based observational study of patients with IGE.

Inclusion criteria
A total of 50 patients were recruited from December 2017 to December 2019 (New onset idiopathic generalised epilepsy) admitted or attending OPD in Department of Neurology, SMS hospital, Jaipur. They were referred because of episodes of loss of consciousness or impaired awareness which were felt by the referring physician possibly to be due to epilepsy. All patients fulfilled the diagnostic criteria on recruitment as idiopathic generalized epilepsy have no structural brain lesions on MRI and a lack of symptoms and signs interictally with normal routine EEG.

Mandatory exclusion criteria
Patients who had structural brain lesion and history suggestive of CNS infection and provoked seizures were excluded.

Tests used:
All patients had one or more routine computerized 16-channel EEG records with 10-20 system of electrode placement carried out using longitudinal bipolar (double banana) montage, a period of hyperventilation and photic stimulation as routine procedures. The average duration of recording was 45 min. The EEG records were read by a clinical neurophysiologist. Ambulatory EEG/ECG 24-hour monitoring was carried out using computerized 16-channel with 10-20 system of electrode placement with using longitudinal bipolar (double banana) montage.

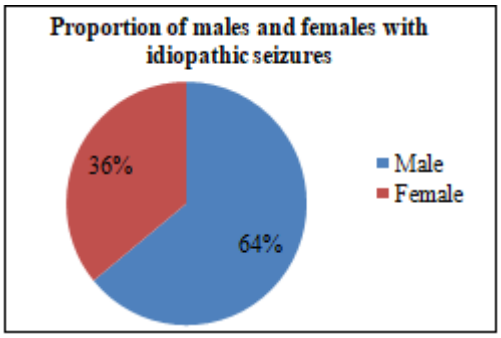
Ethics
A prior informed consent was taken from the patients recruited in the study.

Statistical analysis
Data generated from the study will be analysed according to standard statistical methods. Results were analysed using students 't' test and the level of significance was determined as its p value with $p<0.05$ taken as statistically significant and $p<0.001$ taken as highly significant. $P>0.05$ was taken as statistically not significant.

3. Results and Observations

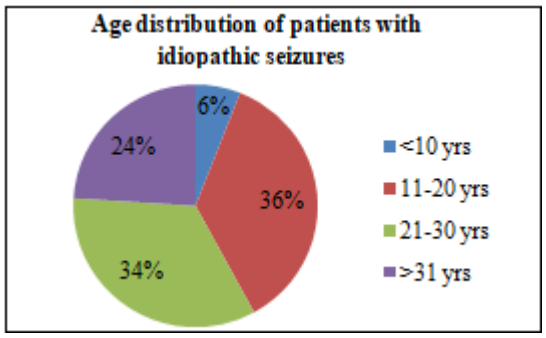
About 50 patients with idiopathic seizures were followed up with Magnetic resonance imaging (MRI), Routine Electro Encephalogram (EEG) and ambulatory EEG. The results are as shown below.

Sociodemographic characteristics



Graph 1.1: Sex distribution of study participants (n=50)

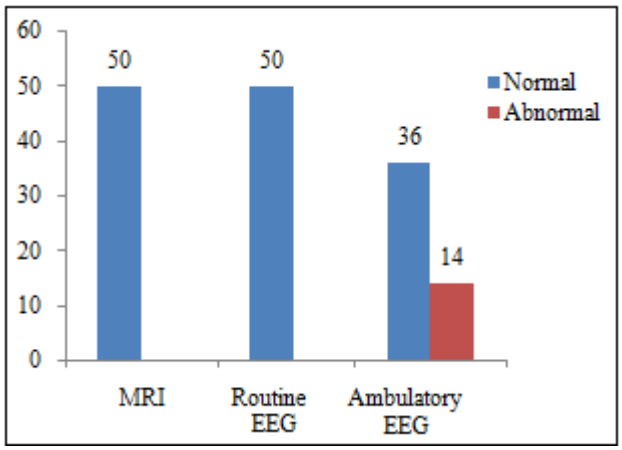
More than three fifths of the patients were males (64%) and 18 (36%) were females. Male to female ratio was almost 2:1.



Graph 1.2: Age distribution of study participants (n=50)

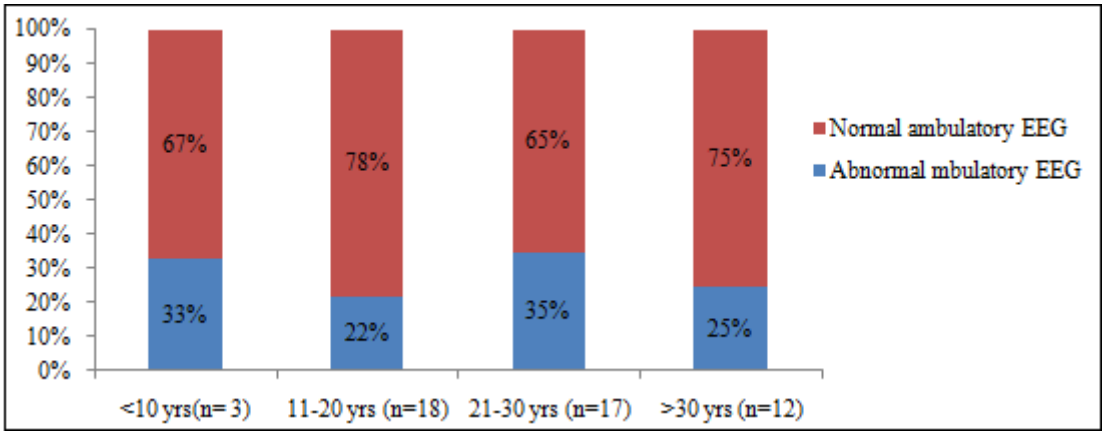
Majority of the patients (70%) belonged to age group of 11-30 years, with 18 (36%) of them between 11-20 years and 17 (34%) of them between 21-30 years. Almost a quarter of them 12 (24%) were aged above 31 years. Only 3 (6%) were less than 10 years of age. Mean age was found to be 23.1 years.

Investigations
All the patients with idiopathic seizures underwent MRI, routine EEG and ambulatory EEG. The MRI and routine EEG of all the patients were normal. Almost three fourth of the patients, 36 (72%) had normal findings on ambulatory EEG. Only 14 (28%) had abnormal ambulatory EEG findings.



Graph 2.1: Investigations done in patients with idiopathic ambulatory seizures (n=50)

The age distribution based on the ambulatory EEG findings is as follows:



Graph 2.2: Age distribution with respect to ambulatory EEG findings

About one third of the patients in age group less than 10 years (33%) and aged between 21-30 years (35%) had abnormal findings in ambulatory EEG. Abnormal ambulatory findings were found in almost a quarter of patients in patients aged between 11-20 years (22%) and above 30 years (25%).

Association between sex, age and ambulatory EEG findings

Table 3.1: Association between sex and ambulatory EEG findings

	Ambulatory EEG abnormal	Ambulatory EEG normal	Total	Chi square value	Degrees of freedom	P value
Female	4	14	18	0.4657	1	0.5230
Male	10	22	32			
Total	14	36	50			

There is no significant association between sex and ambulatory EEG findings (p 0.52; 95% CI).

Table 3.2: Association between age and ambulatory EEG findings

	Ambulatory EEG abnormal	Ambulatory EEG normal	Total	Chi Square value	Degrees of freedom	P value
<20 yrs	5	16	21	0.3154	1	0.5975
>20 yrs	9	20	29			
Total	14	36	50			

There is no significant association between different age groups and ambulatory EEG findings (p 0.5975; 95% CI).

4. Discussion

About 50 patients with idiopathic seizures were followed up with Magnetic resonance imaging (MRI), Routine Electro Encephalogram (EEG) and ambulatory EEG.

Sociodemographic characteristics

More than three fifths of the patients were males (64%) and 18 (36%) were females. Male to female ratio was almost 2:1. Contradictory findings with greater proportion of females among idiopathic seizures were found in studies conducted in Denmark and Iran. In a study conducted to see gender differences in Epilepsy in Denmark, more women (58%) than men (42%) were found to have generalized idiopathic seizures.[15] In the study conducted by Ali A et al in Iran, 57% of the idiopathic seizure patients were females and 43% were males.[16] Data from Epilepsy Phenome Genome Project (EPGP) in USA showed that almost three fifth (58%) of the patients with idiopathic seizures were females.[17] Nirmeen Kish et al documented sex differences in patients with different types of epilepsies in a tertiary care setting in Egypt and found that in idiopathic generalized tonic clonic seizures was more frequent in females.[18] In another study conducted in UK, data collected from epilepsy registry indicated higher proportion of females (58.9%) with idiopathic seizures than males (41.1%) in those with an early age of onset (<20 years) and higher proportion of males (55.6%) than females (44.4%) in those with late onset of seizures.[19] However, though various studies have documented higher proportion of patients of a particular sex having idiopathic seizures, there is no specific predilection of this seizure subtype in a particular sex. Idiopathic seizures occur spontaneously without a known cause and could have a genetic basis.[20] Hence, both the sexes are equally prone to have idiopathic seizures. Few studies have discussed the possibility of women being more prone to idiopathic seizures than men due to role of sex hormones in development of idiopathic seizures. But this difference has not been established yet.[15] The possible reasons for higher proportion of male patients being documented in our study could be due to differences in health seeking behaviour patterns in Indian settings or could be differences in population demographics (sex ratio) owing to a slightly higher male population.

Majority of the patients (70%) belonged to age group of 11-30 years, with 18 (36%) of them between 11-20 years and 17 (34%) of them between 21-30 years. Almost a quarter of them 12 (24%) were aged above 31 years. Only 3 (6%) were less than 10 years of age. Mean age was found to be 23 years. In studies conducted by Ali et al and Nicolson et al, majority of the study participants belonged to 30 years.[16, 19] Similar findings of mean age at presentation (26 years) also was documented in study conducted in Egypt.[18] The findings in the study are similar to literature as most of the idiopathic

seizures are age dependant and typically occur within the first two decades of life.[16]

Investigations

All the patients with idiopathic seizures underwent MRI, routine EEG and ambulatory EEG. The MRI and routine EEG of all the patients were normal. Almost three fourth of the patients, 36 (72%) had normal findings on ambulatory EEG. Only 14 (28%) had abnormal ambulatory EEG findings. In a study conducted in children with seizures, MRI revealed abnormal imaging findings in children with idiopathic partial and generalized seizures.[21] In studies conducted by Ponnatapura et al and Betting et al, almost a quarter of patients with idiopathic seizures had abnormal MRI findings, however these were non specific.[22, 23] Few other studies including a meta analysis documented that increase in gray matter volume in the MRIs of patients with idiopathic seizures.[24-26] One of the study mentioned this as a subtle structural abnormality.[24] Appropriate use of MRI can enhance detection of epileptogenic focus and detect structural abnormalities in up to 80% of the cases thereby aiding in evaluation of common and unusual etiologies.[27, 28] Findings of the present study and other studies indicate that MRI does not reveal anything in diagnosis of patients with idiopathic seizures. Quantitative and functional MRIs reveal subtle changes which could help in the management. Focal EEG abnormalities were documented in patients with idiopathic seizures by Jerzy P. et al.[29]

In a study conducted in Brazil, 45% of idiopathic seizure patients had normal EEG findings and among the 55% with abnormal findings, only 33% showed typical findings. The study reiterated already known recommendations that diagnosis should be made on clinical history and EEG can provide only strong supportive evidence.[30] Generalised idiopathic seizures on awakening have no distinct EEG patterns.[31] A review article on EEG patterns in idiopathic seizures has highlighted that several confounding factors affect EEG features in idiopathic seizures.[32] EEG has low sensitivity (25-26%) and variable specificity (78-98%) in diagnosis of epilepsies and thereby normal EEG would not exclude epilepsies.[31] The diagnostic yield of different types of EEGs was discussed in another review article by Seneviratne et al. The diagnostic yield of an outpatient EEG was found to be around 28%. It has been found that 24 hour ambulatory EEGs have 2.23 times higher diagnostic sensitivity than routine EEGs in detecting idiopathic seizures.[33] In the present study, none of the patients had findings on routine EEG and this could be possibly due to small sample size keeping in mind the low diagnostic yield of a single EEG. In the same study population in the present study, almost one third of the patients had abnormal findings on ambulatory EEG. This indicates the increase in sensitivity of ambulatory EEG in detecting abnormalities in idiopathic seizures, but its significance cannot be determined accurately due to lesser sample size in the current study.

Association between sex, age and ambulatory EEG findings

There is no significant association between sex and ambulatory EEG findings (p 0.52; 95% CI).There is no significant association between different age groups and ambulatory EEG findings (p 0.5975; 95% CI). There was no significant association between gender and EEG findings in a study conducted in a tertiary hospital in Egypt (p 0.94).[18] In a study conducted by Jerzy P. Et al, no significant findings were found between EEG findings and gender (p 0.069) and age at enrolment (p 0.729).[29] As no significant differences have been established between sex and gender with idiopathic seizures in literature as discussed above, it is unlikely to find a significant association between these variables. A study with larger sample size and inclusion of other variables with respect to age of onset, hormonal parameters, different subtypes of idiopathic seizures etc. might be able to draw more inferences regarding the association between different variables.

5. Conclusion

In our study, the 24-hour ambulatory electroencephalography [EEG] monitoring in new onset idiopathic generalized epilepsy [IGE] provided a better yield of diagnostic information compared with conventional EEG recording in 28% of patients. Hence we recommend routine use of ambulatory EEG in such patients as it will help in the better management of such patients.

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