

Profile of intractable epilepsy in a tertiary referral center in upper Assam

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Introduction: Epilepsy is a common and diverse disorder with many different causes. Outcomes are varied with 60-70% of newly diagnosed people rapidly entering remission after starting treatment, and 20–30% developing a drug-resistant epilepsy with consequent clinical and psychosocial distress. **Methods:** It is a Descriptive Cross-sectional study which was conducted in Assam Medical College and Hospital, Dibrugarh from April 2014 to April 2016. A total of 42 patients of IE attending the neurology, paediatrics and medicine department were included in the study. **Results:** Forty-two patients (males 24, females 18) with intractable epilepsy were included for the study. Maximum patients were in between 20-40 years of age (42.9%) and their mean duration of epilepsy was 13.2 ± 7.13 years. The seizure frequency varied from once every month to more than 200 per (mean 26.2 ± 24.17) month. Twenty-six patients (61.9%) had partial seizures, 8 (19.1%) patients had generalized seizures and 8(19.1%) had multiple seizure semiology. Thirty-six patients had risk factors of intractable epilepsy. Seven (16.6%) patients were having family history of epilepsy and 4(9.5%) patients had history of febrile seizures. Mesial temporal lobe sclerosis (MTLS) and birth hypoxia are the two major risk factors for intractable epilepsy. EEG was abnormal in 66.7% cases, with generalized background slowing in 19.1%, focal slowing in 14.2%, generalized epileptiform discharges in 9.5% and focal epileptiform discharges in 23.8%. CT brain was abnormal in 18(42.9%) patients. MRI brains were abnormal in 25 out-off 36 patients (69.4%). Carbamazepine was the most commonly used drug (57.1%) followed by clobazam (47.6%). Phenytoin, levetiracetum, Phenobarbitone, oxcarbazepine, zonisemide, lacosemide are the other AEDs used in combination. **Conclusion:** This study showed, patients with partial seizures, birth hypoxia, history of febrile seizures, family history of seizures, structural brain abnormalities and background EEG abnormalities were the most common risk factors for development of intractable epilepsy.

Keywords: Epilepsy, Intractable epilepsy, Seizures, MTLS, Birth hypoxia

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Introduction

Epilepsy is a common and diverse disorder with many different causes. Outcomes are varied with 60–70% of newly diagnosed people rapidly entering remission after starting treatment, and 20–30% developing a drug-resistant epilepsy with consequent clinical and psychosocial distress [1]. About one third of patients with a first unprovoked seizure will have further seizures within five years, and about three quarters of those with two or three unprovoked seizures have further seizures within four years [2]. There are a number of factors which are predictors of poor seizures control and leading to medically refractory epilepsy [3,4].

These include organic brain lesions, partial seizures, multiple seizure types, high seizure frequency and abnormal background EEG activity. Till date, studies on intractable epilepsy (IE) are limited in India. The present study has been undertaken in Assam Medical College and Hospital, Dibrugarh, Assam to find out the profile of intractable epilepsy in Upper Assam.

Material and Methods

It is a Descriptive Cross-sectional study which was conducted in Assam Medical College and Hospital, Dibrugarh from April 2014 to April 2016. A total of 42 patients of IE attending the neurology, paediatrics and medicine department were included in the study. While selecting the study subjects, only those patients who had uncontrolled seizures despite two appropriate first line drugs for two years, were included. All included cases were underwent detail history of seizure semiology, duration of seizures, perinatal brain injury in the form of birth hypoxia, forceps delivery, history suggestive of CNS infections, history of head trauma, family history of seizure were recorded in proforma.

Details regarding antiepileptic drugs (AED) were recorded i.e. number of drugs, duration of therapy, dosage, and compliance. Seizures were classified according to International League Against Epilepsy Classification. All patients were examined in detail with special emphasis on presence or absence of any neurocutaneous markers, subcutaneous nodules, behavioural disorders, mental retardation and neurological deficits. All the patients were subjected to EEG and CT examination. MRI examinations were done in 36 patients.

Results

A total of 42 patients (males 24, females 18) of IE were registered over 2 year period. The age of the patients ranged from 8-66 (mean 32.6) years. Maximum patients (42.9%) were in the age group of 20-40 years. The duration of epilepsy varied from 4-52 years (mean+SD = 13.2± 7.13 years). The seizure frequency varied from once every month to more than 200 per (mean+SD = 26.2 ± 24.17) month. Fourteen patients (33.3%) had seizure frequency more than one seizure per day, 23.8% had more than one seizure per week and only 23.8% had seizure frequency more than one seizure per month. Twenty-six patients (61.9%) had partial seizures, 8 (19.1%) patients had generalised seizures and 8(19.1%) had multiple seizure semiology. Amongst patients with partial seizures, 2(4.7%) had simple partial seizures and 8(19.1%) had complex partial seizures and 16 (38.0%) had partial seizures with secondary generalization (Table 1).

Table-1: Baseline characteristics of the study population (n=42).

Men	24 (57.1%)
Women	18 (42.9%)
Age of patients in years	
0-20 yrs	10 (23.8%)
20-40yrs	18 (42.9%)
40-60yrs	10 (23.8%)
>60yrs	4 (9.5%)
Mean	32.6±27.3
Duration of epilepsy in yrs	
< 5yrs	6 (14.2%)
5-10yrs	8 (19.1%)
10-20 yrs	12 (28.6%)
20-30yrs	10(23.8%)
>30yrs	6 (14.2%)
Mean duration of epilepsy	13.2 ±7.13 yr
Seizure Frequency at inclusion	
>1 seizure per day	14 (33.3%)
>1 seizure per week	16 (38.0%)
>1 seizure per month	10 (23.8%)
Mean seizure frequency per month	26.2±24.17
Family history of seizure	7 (16.6%)
Febrile seizure in childhood	4 (9.5%)
Seizure types	
Primary generalized seizure: GTCS	8 (19.1%)
Partial seizure	26 (61.9%)
Simple partial	2 (4.7%)
Complex partial	8 (19.1%)

Partial with secondary generalisation	16 (38.0%)
Multiple seizure semiology	8 (19.1%)

Table-2: Risk factors of intractable epilepsy in study population.

MTLS	11 (26.1%)
Birth hypoxia	9 (21.4%)
CNS infections	6 (14.2%)
Head trauma	4 (9.5%)
Vascular malformation	2 (4.7%)
Tuberous sclerosis	1 (2.3%)
Focal cortical dysplasia	1 (2.3%)
Arachnoid cyst	1(2.3%)
stroke	2 (4.7%)
Unknown	5 (11.9%)

We found various risk factors of intractable epilepsy in 36 patients. Family histories of epilepsies were found in 7(16.6%) patients and histories of febrile seizures were found in 4(9.5%) patients.

Table-3: EEG, CT and MRI abnormalities in study population.

n	
EEG(n=42)	
Generalized background slowing	8 (19.1%)
Focal slowing	6 (14.2%)
Generalized epileptiform discharges	4 (9.5%)
Focal epileptiform discharges	10 (23.8%)
Normal	14 (33.3%)
CT and MRI findings	
Abnormal CT (n=42)	18 (42.9%)
Abnormal MRI(n=36)	25 (69.4%)
MTLS	11(26.6%)
Periventricular ischaemic lesions	9(21.4%)
Gliotic lesions	6(16.7%)
NCC/calified granuloma	4(9.5%)
Sub-ependymal calcification	1(2.3%)
Focal cortical dysplasia	1(2.3%)
AVM	2(4.7%)
Arachnoid cyst	1(2.3%)

EEG was done in all cases and abnormality in EEG was found in 28 (66.7%) patients. CT brain was done in all 42 patients and abnormalities were detected in 18(42.9%) patients. MRI brain was done in 36 patients and abnormalities were detected in 25(69.4%) patients.

All patients who had normal brain CT were undergone MRI study and additional brain abnormalities were detected in these include medial temporal sclerosis (MTLS), arachnoid cyst, focal cortical dysplasia (FCD), gliotic lesions.

Table2 showing various EEG, CT and MRI abnormalities in the study.

Table-4: Antiepileptic drug profiles.

Two AEDs	6 (14.2%)
Three AEDs	22 (52.4%)
Four AEDs	14 (33.3%)
Carbamazepine	24 (57.1%)
Phenytoin	12 (28.6%)
Sod.Valproate	8 (19.1%)
Phenobarbitone	4 (9.5%)
Levetiracetum	18 (42.9%)
Lacosemide	6 (14.2%)
Zonisemide	4 (9.5%)
Oxcarbazepine	7 (16.7%)
Lamotrigine	2 (4.7%)
Clobazam	20 (47.6%)

Among the 42 patents, 6(14.2%) patients were receiving a combination of 2 antiepileptic drugs (AED), 22(52.4%) patients were receiving combination of 3 AEDs and remaining 14(33.3%) patients were receiving combination of 4 or more AEDs. Carbamazepine was the most commonly used drug (57.1%) followed by clobazam (47.6%). Phenytoin, levetiracetum, Phenobarbitone, oxcarbazepine, zonisemide, lacosemide are the other AEDs received by the patients (Table 4).

Discussion

Epilepsy is one of the most common serious neurological conditions, accounting for 1% of the global burden of disease, based on disability-adjusted life years, the number of person years lost due to disability and premature death [5]. Ten percent of the world’s population will have at least one seizure during their lifetime and one-third of these will develop epilepsy at any given time [6].

In countries where adequate diagnosis and treatment are available, 15-35% of people with epilepsy have seizure that are uncontrolled by medication (IE)[7-9]. The magnitude of the problem of IE in India is unknown. Radhakrishnan et al estimated 20,000–40,000 patients with IE in India [10].

Intractability occurs with equal frequency in both sexes [11]. In our study, 57.1% cases were male and 42.9% were female which could be due to non reporting of female cases due to social stigma or other causes. In our study, partial seizures were the most common type of seizures accounting 61.9% cases.

Mattson et al. observed poor seizure control in patients with partial seizures as compared to generalized seizure after one year of treatment [12]. However there are studies which found that generalized and myoclonic seizures have the worst outcome and also some who did not find seizure type as a predictor of intractability [13-16]. Different risk factors and causes have been associated with intractable epilepsy. Gururaj et al. in their study population reported that developmental delay, neuro-logical deficits, high frequency of seizures at onset and an abnormal brain imaging were associated with intractability [17].

Berg et al. reported a history of status epilepticus, infantile spasms, neonatal seizures, microcephaly to be associated with IE [18]. Kwan and Brodie found patients having many seizures before treatment and inadequate response to initial treatment are likely to have refractory epilepsy [19]. Similarly Kwong et al. observed abnormal neurologic status and early break through attacks after treatment initiation were predictors of IE [20].

An earlier study done in the pediatric population in India by Singhvi et al. found neuroinfections to be a leading cause of intractable epilepsy [21]. In our study, 6(14.2%) cases had CNS infections among which neurocysticercosis (NCC) was predominant. History of febrile seizure is one of the risk factor for IE. Camfield et al observed that prolonged febrile seizures were associated with intractable epilepsy [22]. In our study, 9.5% cases had febrile seizure in childhood which is identical to the previous study.

In our study family history of epilepsy were found in 16.6% cases, signifies role of family history of epilepsy in IE. The seizure remission is less likely in symptomatic epilepsy, caused by either defined acquired brain damage or less well- defined perinatal causes, manifested by gross neuro-logical deficits or MR [23, 24]. Our study shows that presence of a known epileptogenic structural lesion is the most important predictor of intractable epilepsy. MTLE by far the most common risk factor of IE in our series accounting 26.1% cases.

Other important epileptogenic structural lesions found on imaging studies were birth hypoxia, CNS infections, head trauma, neurocutaneous syndrome, vascular malformation, neuronal migration defects and post stroke gliosis. The incidence of cerebral palsy in epilepsy has been reported to be 8% [25]. In our study, we have found more numbers of cerebral palsy as a predictor of IE (21.4%).

The outcome of seizure is poorer if EEG shows background abnormality and focal epileptiform activity [26]. In our study, EEG was abnormal in 66.7% cases, with generalized background slowing in 19.1%, focal slowing in 14.2%, generalized epileptiform discharges in 9.5% and focal epileptiform discharges in 23.8%. In our study CT were abnormal in 42.9% and MRI were abnormal in 69.4% cases, signifying role of structural lesions in development IE.

Many studies have shown that addition of second drug in patients with IE controlled seizures only in additional 10-15% of cases with increased toxicity [27-29]. In our study we have noticed, in spite of combination of drugs used and with proper doses, 14.2% patients on 2 drugs, 52.4% on 3 drugs and 33.3% patients on 4 drugs had uncontrolled seizures.

Conclusion

Intractable epilepsy has diverse risk factors for the development of intractability. Our study showed, patients with partial seizures, birth hypoxia, history of febrile seizures, family history of seizures, structural brain abnormalities and background EEG abnormalities were the predictors of intractable epilepsy.

What this study Adds to existing knowledge?

This study demonstrated that there are different risk factors/predictors of development of intractable epilepsy. Most common risk factors are partial seizures, birth hypoxia, history of febrile seizures in childhood, structural brain lesions, family history of seizures and EEG background abnormalities.

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