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EXECUTIVE DYSFUNCTION IN PATIENTS WITH IDIOPATHIC EPILEPSY

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ABSTRACT **Background**: Idiopathic epilepsy is defined as disorder in which there is no underlying cause or structural pathology other than a possible hereditary predisposition for generating seizures which can be generalised or focal in nature.Several epilepsy variables including ,age at seizure onset, seizure type ,seizure severity ,disease duration and antiepileptic drug therapy seem to have an impact on cognition, behavior and academic skills.[2]

Objectives: To study the occurrence of Executive Dysfunction in patients with idiopathic epilepsy.To study the association of antiepileptic drug therapy (mono therapy vs poly therapy) with executive dysfunction in patients with idiopathic epilepsy.

Methods: The study is a Observational Cross sectional study. All patients with idiopathic epilepsy were evaluated by taking a detailed history and conducting a clinical examination, neuro imaging and interictal EEG recording .Details of the history ,examination and the investigations were recorded on a pre-designed proforma All patients will be subjected toDetailed history in relation to the duration of epilepsy,age at seizure onset, seizure type, frequency and control. Frontal assessment battery was used to assess executive dysfunction in the patients.The correlation of executive dysfunction with antiepileptic drug therapy (mono therapy vs poly therapy) was assessed using Chi square test.The level of significance was set at p value < 0.05

KEYWORDS :

INTRODUCTION:

Epilepsy is a multifaceted disorder that affects people of all ages and both gender.International league against epilepsy (ILAE) defines Epilepsy as a disease characterized by an enduring predisposition to generate epileptic seizures or recurrent unprovoked seizures with neurobiological ,cognitive,psychological and social consequences .It can be idiopathic or symptomatic in nature.Idiopathic epilepsy is defined as disorder in which there is no underlying cause or structural pathology other than a possible hereditary predisposition for generating seizures which can be generalised or focal in nature .Idiopathic epilepsies can be classified on the basis of age at seizure onset,clinical and electroencephalographic characteristics.[1]

An increased frequency of learning disoders and attention deficit-hyperactivity disorder (ADHD) has be-n observed in patients with idiopathic epilepsy.Several epilepsy variables including ,age at seizure onset,seizure type ,seizure severity ,disease duration and antiepileptic drug therapy seem to have an impact on cognition,behavior and academic skills.[2]

Executive functions (EF) are a set of cognitive skills that enable an individual to perform goal oriented voluntary actions in cognitive,emotional and social areas[2].They are responsible for focusing .guiding ,managing and integrating cognitive functions,emotions and behaviours necessary to the active solution of new problems resulting in effective and adaptive behaviours Executive dysfunction reduces the capacity of an individual to successfully engage in important activities of daily life, including academic and occupational pursuits,social activities and self care.The contribution of the frontal lobes in executive control remains significant and can be easily assessed by well defined and tested frontal assessment batteries.There is scant and inconclusive data regarding the occurrence of frontal executive dysfunction in patients with idiopathic epilepsy,especially in the Indian literature.It is important to study the impact of epilepsy on frontal executive functions,not only for diagnostic ,prognostic and therapeutic implications but also for devising strategies to improve and enhance the quality of life in patients with idiopathic epilepsy

MATERIALS AND METHODS:

STUDY POPULATION-50 patients of epilepsy ≥ 18 years of age ,attending Neurology OPD or admitted in the ward ,were screened and epileptic patients with normal CT Scan brain /MRI brain were included in the study for analysis.Written informed consent was taken form the patients for inclusion in the study

CASES:

Inclusion criteria:

- Cases of generalized or focal idiopathic epilepsy with normal CT scan Brain/MRI Brain
- Age ≥ 18 years

Exclusion criteria:

- Mental retardation
- Patients with dementia /psychosis
- Patients with chronic medical illness
- Patients with recent(< 6 weeks) traumatic brain injury
- Patients with stroke or neurological deficit.
- Patients with meningo-encephalitis
- History of alcohol and drug abuse.

DATA COLLECTION:

All patients with idiopathic epilepsy will be evaluated by taking a detailed history and conducting a clinical examination,neuroimaging and interictal EEG recording .Details of the history ,examination and the investigations were recorded on a pre-designed proforma

All patients will be subjected to:

- Detailed history in relation to the duration of epilepsy,age at seizure onset,seizuretype,frequency and control
- History of any systemic illnesses e.g .diabetes mellitus, hypertension and any associated co-morbid psychiatric illnesses e.g. anxiety,depression or other mood disorders
- Family history of seizures
- Detailed record of antiepileptic drug therapy with regards to the number of drugs prescribed.theirdose.compliance and duration of therapy

Controlled and uncontrolled epilepsy are defined as follows

Controlled epilepsy:Patients who have been seizure free for a minimum period of 6 months

Uncontrolled epilepsy:Patients having one or more seizures in last 6 months

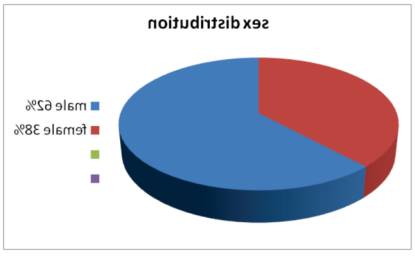
Compliance is defined as:
Poor-missing medications one or more times per month
Fair-missing medication < once a month
Good-never missed a dose

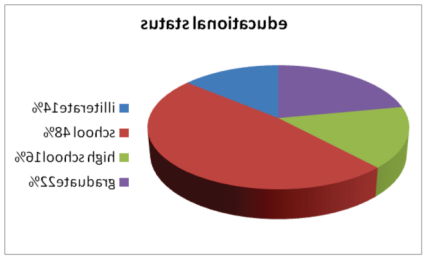
Detailed Clinical examination
- General examination
- Systemic examination
- Neurological examination

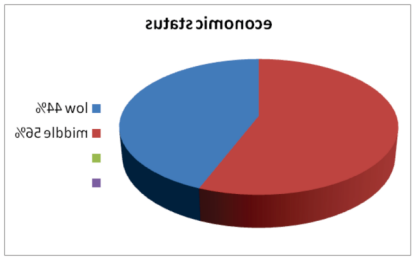
Investigations:
All patients will be subjected to MRI Brain or CT Brain and an interictal EEG recording
Executive Function Testing :
The following was used to assess executive dysfunction:
.Frontal Assessment Battery
The Frontal Assessment Battery has 6 sutests (Score:0-3) including testing for Similarities (conceptualization),Lexical fluency (mental flexibility),Motor series
'Luria"test (programming),Conflicting instructions(sensitivity to interference).G0-N0-G0 (inhibitory control),Prehension behavior (environmental autonomy).The total score is from a maximum of 18,higher scores indicating better performance

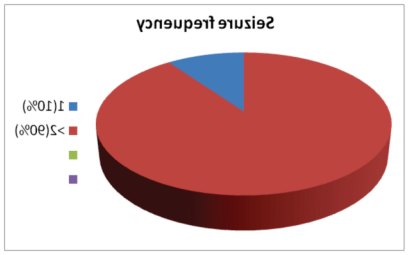
Scoring:
16-18 : Normal or non-significant
13-15: Mild impairment
7-12: Moderate impairment
0-6: Severe impairment.

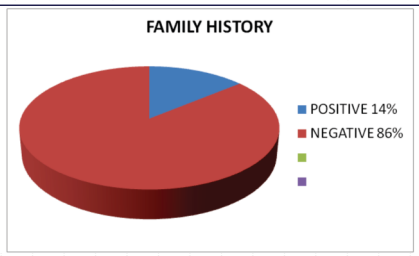
RESULTS:
PATIENT CHARACTERISTICS

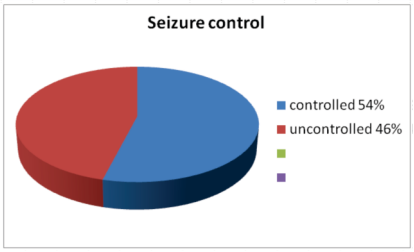


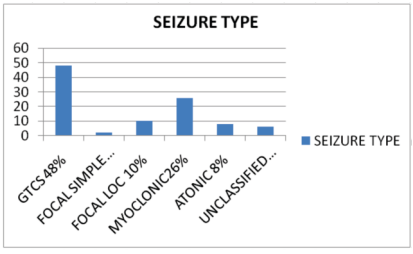


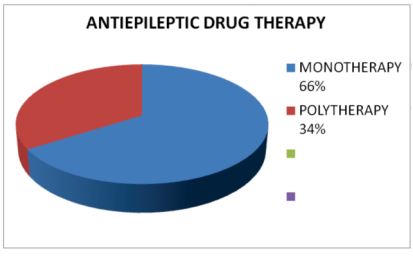


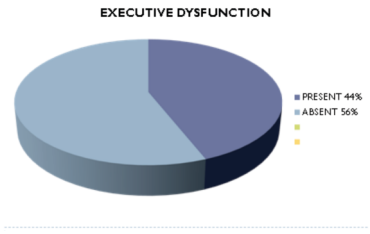












Correlation Between Executive Dysfunction And Polytherapy With Aed		FAB Ab N	N	TOTAL	Pearson Chi Square Value	P val
ANTIEPILEPTIC DRUGS	MONOTHERAPY	8	25	33	6.629	0.021
	POLYTHERAPY	14	3	17		
TOTAL		22	28	50		

DISCUSSION
Epilepsy is a common neurological disorder ,more so in the developing world and accounts for around 1% of the global disease burden.According to an estimate,at any given time,50 million individuals worldwide have a diagnosis of epilepsy [3].It is estimated that there are 55,00,000 persons with epilepsy in India.[4] Epilepsy is not a single disease ,but a syndrome of varied etiology (genetic, vascular,metabolic,structural or traumatic) and can either be idiopathic or symptomatic in nature and do not have a detectable neuroanatomical or neuropathological abnormality.[4]

Epilepsy is often associated with a wide range of cognitive abnormalities,such as attention deficit,memoryimpairment,language problems and executive functions that have negative effects on social

life,work,orschool.Cognitive impairment in epilepsy can be multifactorial and relate to underlying etiology,age at seizure onset,seizuretype,duration and severity of epilepsy, interictalepileptiformdischarges,drugtreatment,hereditary and psychosocial factors.It has been suggested that seizures can modify,slow down ,or accelerate a wide range of unique processes that take place during development and that are essential for the correct formation and function of brain circuitry.Patients with different types of epilepsy have different kinds of cognitive impairments.In symptomatic epilepsy,cognitive impairments usually occur in the affected lobe,typically driven by the primary injury or neurological disease.However,because idiopathic epilepsy does not have any apparent cause or detectable brain lesions,the neurological basis for its associated cognitive impairment remains unknown.In idiopathic epilepsy cognitive dysfunction may arise from more subtle abnormalities in cellular physiology and also directly from seizures.Because they lack obvious structural lesions,these patients tend to have less severe cognitive dysfunctions than those with symptomatic epilepsy.

This study was undertaken to find out the occurrence of executive dysfunction in patients with idiopathic epilepsy.50 cases of idiopathic epilepsy,≥ 18 years of age with normal CT Scan brain/MRI Brain,were included in the study for evaluation of executive dysfunction.We also evaluated the association of antiepileptic drug therapy with executive dysfunction in patients with idiopathic epilepsy.Idiopathic epilepsies are characterized by generalised or partial seizures in otherwise normal infants,children,adolescents and young adults with normal brain imaging.The various syndromes of idiopathic epilepsies differ in age of onset.In our study ,age of the patients with idiopathic epilepsy ranged from 19-48 years(mean age 27.92 years).The majority of the cases fell in the 21-30 years age group.According to a study by G.A.Shehata et al,[22] mean age of patients with idiopathic epilepsy was 28.92 ±8.70 years,similar to that observed in our study.In another study by GiedreGelziniene et al,[20] mean age of idiopathic epilepsy was 15.5 years.

Our study showed a slight male preponderance(31 males and 19 females),male female ratio being(1:1.63) It was also observed by Tian et al,[25] in their study in idiopathic epilepsy patients,there was almost equal proportion of males and females(21 boys and 22 girls).Another study by GiedreGelziniene et al, [20] showed female preponderance(24 males and 35 females,M:F ratio – 1: 1.45.

Idiopathic epilepsy can interfere with learning and have an overall negative impact on education.Although many patients with idiopathic epilepsy perform well academically and occupationally,they are at far higher risk for learning problems.[39].Sturniolo et al ,[40] in their study of 41 children of idiopathic epilepsy ,found that school underachievement occurred in 25 children(61%).Another study by Davidson et al [41] observed that 23.8% of idiopathic generalised epilepsy patients had at some time received learning support.A large proportion of parents (42.9%) reported some degree of concern about their child's progress in school.In our study also,a similar trend ws observed .Majority (62%) of the cases were either illiterate or school dropouts In our study,around 56% cases belonged to the middle and 44% cases to the low socioeconomic strata.None of the cases belonged to the high socioeconomic strata.Sturniolo et al,40 found that out of 41 children of idiopathic epilepsy,11 belonged to the middle class and 30 to the lower class.These figures reflect the overall poor socioeconomic status of the population attending a government tertiary care hospital for free healthcare.

In our study,Seizure frequency ranged from around 1 per week to 1 seizure every 3 years or so.Majority (86%) had a seizure frequency of 1 to 12 per year(mean seizure frequency:3.85 ±7.51 per year).In a study by G.A.Shehata et al.[22] mean seizure frequency was 1/year in 50.9%, 1/month in 23.6%,1/week in 21.8% and daily in 3.6%.Davidson et al,[41] in their study of patients with idiopathic generalisedepilepsy,observed seizure frequency less than 1 per month in 33.3%, 1 or 2 per month in 9.5%,1 or 2 per week in 19% and daily in 14.3% cases.

In our study,family history of seizures was positive in 14% cases only.Almost similar trend was observed in a study by Paolo Piccinelli et al,[6] who showed positive family history in 11.6% cases of idiopathic epilepsy.Another study by G.A.Shehata at al [22] showed family history in 18.2% cases of idiopathic generalisedepilepsy.According to a study by Andrea Bandeira et al [2] family history of epilepsy was positive in 25.8% cases Idiopathic epilepsy can be generalised or partial or there can be more than one seizure types.In our study seizure type was GTCS in 48%,simple partial in 2%,complex partial in 10% and partial seizures with secondary generalization in around 14% cases.Around 26% cases with ME had both GTCS and myoclonic seizures.In our study major seizure type was generalisedseizure.A study by Paolo Piccinelli et al[6] showed generalised seizures in 53.5%,partial seizure in 18.6% and partial with secondary generalization in 27.9%.Another study by Andrea Bandeira et al [2] showed that 71% patients had generalized epilepsy and 25.8% had focal epilepsy.G.AShehata et al [22] in their study,observed generalized seizures in 77.46% and focal seizures in 22.53% cases.A similar observation was made in our study also,the most common seizure type being generalized seizure.

Majority of the cases of idiopathic generalized epilepsy show good response to antiepileptic drug therapy.In our study seizures were well controlled in 56% of the cases and uncontrolled in 46% of cases.Majority of our patients 66% were on monotherapy and only 34 % were on polytherapy.In a study by Andrea Bandeira et al ,[2]67.7 % patients were on monotherapy ,19.4% were on polytherapy.In another study of patients with idiopathic generalised epilepsy ,by GiedreGelziniene et al ,[20]and in another study by Davidson et al,[41]majority of subjects received monotherapy.A similar pattern was observed in our study also Antiepleptic drugs have long been known to have a negative effect on cognitive function,although this effect is generally considered to be small when recommended dosages and therapeutic blood levels are not exceeded and polypharmacy is avoided.In our study,we observed significantly more executive dysfunction in patients receiving polytherapy .FAB score was abnormal in 82.35 % cases on polytherapy compared to 24.24% cases onmonotherapy and this difference was statiscallysignificant.On the contrary ,a study by Andrea Bandeira et al[2]didn't find any correlation between number of antiepileptic drugs and executive dysfunction Certain antiepileptic drugs can have a more severe or greater negative effect on cognition.Studies involving children with epilepsy have linked phenobarbitone to lower Iq[44] In a study by GiedreGelziniene et al,[20]AED's were found to have no significant effects on cognition in idiopathic epilepsy patients In conclusion a significant proportion of patients with idiopathic epilepsy have Executive Dysfunction.Several epilepsy associated variables like age,educational and socioeconomic status,seizure frequency and antiepileptic drugs can impact executive function In our study executive dysfunction was more in patients on polytherapy compared to monotherapy.

Executive dysfunction can significantly impact the quality of life in all domains and further add to the seizure burden by reducing the capacity of an individual to successfully engage in self care,social,academic and occupational pursuits.To improve and enhance the quality of life in patients with idiopathic epilepsy,cognitive behavioral therapy and other strategies for improving Executive dysfunction are as important as a good seizure control and should be included as a part of the therapeutic intervention protocol

CONCLUSION

FAB score was abnormal in 82.35 % cases on polytherapy compared to 24.24% cases on monotherapy signifying more Executive dysfunction in the polytherapygroup.The difference was statistically significant with a(P value =0.021).In conclusion ,a significant proportion of patients with idiopathic epilepsy have executive dysfunction which adds to the seizure burden by reducing the capacity of an individual to successfully engage in self care,social,academic and occupational pursuits .To improve and enhance the quality of life in patients with idiopathic epilepsy ,cognitive behavioural therapy and other strategies for improving ED are as important as a good seizure control and should be included as a part of the therapeutic intervention protocol

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