A STUDY ON AETIOLOGICAL PROFILE OF SEIZURES IN A TERTIARY CARE CENTRE

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ABSTRACT

BACKGROUND

This study was taken up to study the distribution of type of seizures and to evaluate the aetiological profile among patients presenting with seizures in a tertiary care centre

METHODS

This was an observational prospective study done from April 2014 - March 2015 in Government Stanley Hospital. The study included 150 patients above 12 years of age presenting with acute symptomatic seizures. Detailed history to ascertain the type of seizure and clinical examination was done. Routine investigations, EEG and imaging of the brain was done for all patients. Data recorded and analysed.

RESULTS

Among 150 patients included in the study generalised seizures accounted for the majority of seizures of around 92% followed by focal seizures 6% and others 2%. Among generalised, generalised tonic clonic seizure was the most common subtype. Alcohol related seizures was the most common cause followed by CNS infection.

CONCLUSIONS

Our study concluded that generalised seizure is the predominant type of seizure and alcohol related seizures was the most common cause among patients presenting in Govt. Stanley Medical Hospital.

KEYWORDS

Seizures, Generalized, Focal, Aetiology.

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INTRODUCTION

A seizure is a paroxysmal event due to abnormal, excessive or synchronous neuronal activity in the brain. Depending on the distribution of discharges, this abnormal brain activity can have various manifestations ranging from dramatic convulsive activity to experiential phenomena not readily discernible by an observer.^[1]

Determining the type of seizure that has occurred is essential for focusing the diagnostic approach on particular aetiologies, selecting the appropriate therapy and providing potentially vital information regarding prognosis. Hence, our study focused on determining the distribution of type of seizures among study population.

OBJECTIVE

To study the distribution of type of seizures and to evaluate the aetiological profile among patients presenting with seizures in a tertiary care centre.

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METHODOLOGY

Ethical Committee approval and informed consent was obtained from study subjects. This was an observational prospective study done from April 2014 - March 2015 in Government Stanley Hospital. The study included 150 patients above 12 years of age presenting with acute symptomatic seizures. Our study included both new onset and also known epileptics presenting with seizures. Detailed history to confirm occurrence of seizures and to ascertain the type of seizure was obtained. The type of seizure was assigned based on standard definitions and criteria. Complete general and neurological examination was done. Apart from routine investigations, EEG and imaging of the brain was done for all patients. Data recorded and analysed with the help of Epi Info Software and Microsoft Excel.

Criteria for Alcoholic

Presence of 2 out of 11 symptoms according to DSM-5 criteria.

RESULTS

Based on the statistical analysis done at the end of the data collection, the following results were obtained.

- 79% of cases were of new onset, 21% were recurrent.
- Generalised seizures were the most common type of seizure accounting for 92%, followed by focal in 6% and

others 3%. Among the generalized seizures, generalized tonic-clonic seizure was the most predominant subtype.

- Out of all the seizure cases, 63% of cases were alcohol related followed by CNS infection (9%) and CVA (7%).
- Generalised Seizures (GTCS) was the predominant type of seizure in alcoholics - 96% of the seizures were of generalised type.
- Alcohol related seizures were most common in age group >35 years - 69% followed by CVA - 9.4%. Among age group 18-35 years, Alcohol related seizure was most common - 50% followed by CNS infection - 9.3%. Among age group 12-18 years, CNS infection was the most common cause of seizure - 40%.
- Of all the cases, 20% of them had imaging abnormalities, maximum was accounted for by CVA (7%) followed by tuberculoma (4%).
- Imaging abnormalities were present in 10% of alcoholics.
- EEG abnormalities present in 9% of patients.

Fig. 1: Distribution of Type of Seizures among Study Population

			Alcoholic		Total
			No	Yes	
Type	GTCS	Count	24	114	138
		% Within Alcoholic	75.0%	96.6%	92.0%
	Others	Count	2	1	3
		% Within Alcoholic	6.3%	.8%	2.0%
	Partial	Count	6	3	9
		% Within Alcoholic	18.8%	2.5%	6.0%
Total		Count	32	118	150
		% Within Alcoholic	100.0%	100.0%	100.0%
Table 1: Distribution of Type of Seizures among Alcoholics					

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	Value	df	Asymp. Sig. (2-Sided)
Pearson Chi-Square	15.973 ^a	2	.000
Likelihood Ratio	12.703	2	.002
No. of Valid Cases	150		

Aetiology	Number of Cases
Alcohol	95 (63%)
CNS Infection	14 (9%)
CVA	11 (7%)
SOL (Brain Tumour)	2 (1%)
Metabolic	6 (4%)
Head Injury	3 (2%)
Break Through	10 (7%)

Drug Withdrawal	4 (3%)
Drug Induced	1 (1%)
Others	4 (3%)

Table 2: Aetiology of Seizures

			Alcoholic		Total
			No	Yes	
Aetiology	ALC	Count	0	95	95
		% Within Alcoholic	0.0%	80.5%	63.3%
	Break	Count	8	2	10
		% Within Alcoholic	25.0%	1.7%	6.7%
	BT	Count	1	1	2
		% Within Alcoholic	3.1%	.8%	1.3%
	CVA	Count	4	7	11
		% Within Alcoholic	12.5%	5.9%	7.3%
	DI	Count	1	0	1
		% Within Alcoholic	3.1%	0.0%	.7%
	DW	Count	4	0	4
		% Within Alcoholic	12.5%	0.0%	2.7%
	Head Inj.	Count	0	3	3
		% Within Alcoholic	0.0%	2.5%	2.0%
	Infection	Count	7	7	14
		% Within Alcoholic	21.9%	5.9%	9.3%
	MET	Count	3	3	6
		% Within Alcoholic	9.4%	2.5%	4.0%
	Others	Count	4	0	4
		% Within Alcoholic	12.5%	0.0%	2.7%
Total		Count	32	118	150
		% Within Alcoholic	100.0%	100.0%	100.0%
Table 3: Aetiological Profile among Alcoholics					

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	Value	df	Asymp. Sig. (2-Sided)
Pearson Chi-Square	92.526 ^a	9	.000
Likelihood Ratio	100.575	9	.000
No. of Valid Cases	150

Fig. 2: Age Distribution Chart

Imaging Abnormalities	Number of Patients	Number of Alcoholics
Neurocysticercosis	4	2
Tuberculoma	6	3
Toxoplasma	1	1
Brain Tumour	2	0
Infarct	9	5
Intracerebral Haemorrhage	2	1
Haematoma	3	3
Mesial Temporal Sclerosis	1	0
Chronic Myelinolysis	1	0
Cerebral Palsy	1	0

Table 4: Imaging Abnormalities

			Alcoholic		Total
			No	Yes	
Image	No	Count	18	102	120
		% of Total	12.0%	68.0%	80.0%
	Yes	Count	14	16	30
		% of Total	9.3%	10.7%	20.0%
Total		Count	32	118	150
		% of Total	21.3%	78.7%	100.0%
Table 5: Imaging Abnormalities among Alcoholics					

DISCUSSION

A seizure is a paroxysmal event due to abnormal excessive or synchronous neuronal activity in the brain. Determining the type of seizure that has occurred is essential for focusing the diagnostic approach on particular aetiologies, selecting the appropriate therapy and providing potentially vital information regarding prognosis. The International League Against Epilepsy (ILAE) Commission on Classification and Terminology, 2005–2009 has provided an updated approach to classification of seizures. This system is based on the clinical features of seizures and associated electroencephalographic findings.[1]

1. Focal seizures (Can be further described as having motor, sensory, autonomic, cognitive, or other features)
2. Generalized seizures
a. Absence
Typical
Atypical
b. Tonic clonic
c. Clonic
d. Tonic
e. Atonic
f. Myoclonic
3. May be focal, generalized, or unclear
Epileptic spasms

Fig. 3: Classification of Seizures

A fundamental principle is that seizures may be either focal or generalized. Focal seizures originate within networks limited to one cerebral hemisphere. Generalized seizures arise within and rapidly engage networks distributed across both cerebral hemispheres. Focal seizures are usually associated with structural abnormalities of the brain. In contrast, generalized seizures may result from cellular, biochemical or structural abnormalities that have a more widespread distribution. There are clear exceptions in both cases, however. Focal seizures can spread to involve both

cerebral hemispheres and produce a generalized seizure. Focal seizures in turn sub-classified into simple focal and complex focal based on cognitive function.

Generalized Seizures

The most common and dramatic, and therefore the most well-known, is the generalized convulsion, also called the grand-mal seizure. Generalized tonic-clonic seizures are common in 10% of persons with epilepsy. The seizure usually begins abruptly without warning, although vague premonitory symptoms proceed seizure. The initial phase of the seizure is tonic contraction of muscles of expiration and larynx producing a loud moan or "ictal cry." Respirations are impaired, secretions pool in the oropharynx and cyanosis develops. Contraction of the jaw muscles causes biting of the tongue. A marked enhancement of sympathetic tone leads to increases in heart rate, blood pressure and pupillary size. After 10-20 sec the tonic phase of the seizure typically evolves into the clonic phase produced by the superimposition of periods of muscle relaxation (<1 mt) on the tonic muscle contraction. Postictal phase is characterized by unresponsiveness, muscular flaccidity and excessive salivation that can cause stridorous breathing. Bladder or bowel incontinence may occur. Patients gradually regain consciousness over minutes to hours with postictal confusion. The EEG during the tonic phase of the seizure shows a progressive increase in generalized low-voltage fast activity followed by high-amplitude, polyspike discharges. In the clonic phase, the high-amplitude activity is typically interrupted by slow waves to create a spike-and-wave pattern. The postictal EEG shows diffuse slowing that gradually recovers as the patient awakens. Atonic seizures are characterized by sudden loss of postural muscle tone lasting 1-2 seconds. Consciousness is briefly impaired without postictal confusion. The EEG shows brief, generalized spike-and-wave discharges followed immediately by diffuse slow waves that correlate with the loss of muscle tone.[2]

Absence seizures cause a short loss of consciousness (Just a few seconds) with few or no symptoms. The patient, most often a child, typically interrupts an activity and stares blankly. These seizures begin and end abruptly and may occur several times a day. Patients are usually not aware that they are having a seizure, except that they may be aware of "losing time." Typical absence seizures are characterized by sudden, brief lapses of consciousness without loss of postural control which lasts for only seconds with consciousness returning as suddenly as it was lost and there is no postictal confusion. Absence seizures are usually accompanied by subtle bilateral motor signs such as rapid blinking of the eyelids, chewing movements and clonic movements of the hands. The electrophysiologic hallmark of typical absence seizures is a generalized, symmetric, 3-Hz spike and wave discharge that begins and ends suddenly superimposed on a normal EEG.[2]

Myoclonic seizures consist of sporadic jerks, usually on both sides of the body. Patients sometimes describe the jerks as brief electrical shocks. When violent, these seizures may result in dropping or involuntarily throwing objects. Myoclonus is a sudden and brief muscle contraction that may involve one part of the body or the entire body. A normal physiologic form of myoclonus is the sudden jerking movement observed during sleep, while pathologic myoclonus is most commonly seen with metabolic disorders,

degenerative CNS diseases or anoxic brain injury. The EEG shows bilaterally synchronous spike-and-wave discharges synchronized with the myoclonus.

Clonic seizures are repetitive, rhythmic jerks that involve both sides of the body at the same time.

Tonic seizures are characterized by stiffening of the muscles.

Atonic seizures consist of a sudden and general loss of muscle tone, particularly in the arms and legs, which often results in a fall.

Depending on the presence of cognitive impairment, partial seizures can be simple and complex. Partial seizure activity begins in a very discrete region of cortex and spread to neighbouring regions, i.e. seizure initiation and a propagation phase. Sufficient activation and recruitment of neurons leads to loss of surrounding inhibition and propagation of seizure activity into contiguous areas. Partial seizures cause motor, sensory, autonomic or psychic symptoms without impairment of cognition. The phenomenon described by Hughlings Jackson and known as "Jacksonian March," represents the spread of seizure activity over a progressively larger region of motor cortex. Post epileptic paresis (Todd's paralysis) evolves in minutes to hours. Partial seizures manifest as auras like paraesthesias, flashing lights, flushing, sweating and piloerection. Partial seizures arising from the temporal or frontal cortex may cause alterations in hearing, olfaction like unusual odours or psychic symptoms like sense of impending change, detachment, depersonalization, *déjà vu* or illusions like micropsia or macropsia. Complex partial seizures are accompanied by a transient impairment of consciousness and recovery occurs within seconds to an hour. Focal seizures can spread to involve both cerebral hemispheres and produce a generalized seizure. *Epilepsia partialis continua* consists of repetitive focal muscle contractions of the fingers and corner of the mouth, persisting for days or weeks without loss of consciousness and is often refractory to medical therapy. Generalized seizures arise at some point in the brain and rapidly engage neuronal networks in both cerebral hemispheres. Status epilepticus is defined as a seizure that is repeated frequently and recovery of consciousness between attacks does not occur.^[2]

There are very few studies, which focused on the distribution of type of seizure. A study published by the Department of Neurology, University of Kuopio, Finland investigated the type of seizure in an epidemiological survey of 1,220 patients over 15 years of age. The results were as follows: Classification of clinically dominant seizure type according to the International Classification of Epileptic Seizures (ICES) was possible in 1,005 cases (82.5%). Fifty-six percent of patients had partial seizures and 26.5% had generalized seizures. Subclassification of partial seizures revealed Simple Partial Seizures (SPS) in 7.5% of the cases, Complex Partial Seizures (CPS) in 23% and Partial Secondly Generalized Seizures (PSGS) in 25.5% of the cases. Simple partial onset was seen in 56% of the patients with CPS and impairment of consciousness at the onset occurred in the remaining 44%. PSGS started with simple partial onset in 92% of the cases and the remaining 8%

started with a complex partial phase. Tonic-clonic seizures were the most common type of generalized seizures accounting for 23% of all and 88% of generalized seizures. Absence seizures were seen in 1% of the cases. The term partial is no longer used and is replaced by focal seizure.^{[3][4]}

In contrast, our study concluded that generalized seizure was the most predominant type and generalised tonic clonic was the most common subtype. Determining the correct type of seizure is most appropriate, since it guides towards aetiology, alters the treatment strategy and affects prognosis.

The relationship between alcohol and seizures is complex and multifaceted. The prevalence of epilepsy in alcohol-dependent patients of western industrialised countries may be at least triple that in the general population, whereas the prevalence of alcoholism is only slightly higher in patients with epilepsy than in the general population. The seizure threshold is raised by alcohol drinking and declines on cessation of drinking. As a result, during withdrawal from alcohol, usually 6-48 hours after the cessation of drinking, seizures may occur. Alcohol acts on the brain through several mechanisms that influence seizure threshold. These include effects on calcium and chloride flux through the ion-gated glutamate NMDA and GABA receptors. During prolonged intoxication, the CNS adapts to the effects of alcohol resulting in tolerance; however, these adaptive effects seem to be transient, disappearing after alcohol intake is stopped. Although the relationship of seizures to alcohol use is likely to be dose dependent and causal, the available clinical data do not suggest that alcohol use results in seizure genesis. However, a genetic predisposition to alcohol withdrawal seizures is possible. Other seizures in alcohol-dependent individuals may be due to concurrent metabolic, toxic, infectious, traumatic, neoplastic and cerebrovascular diseases and are frequently partial-onset seizures. Alcohol abuse is a major precipitant of status epilepticus (9-25% of cases), which may even be the first-ever seizure type.^[5] Prompt treatment of alcohol withdrawal seizures is recommended to prevent status epilepticus. During the detoxification process, primary and secondary preventative measures can be taken. A meta-analysis of controlled trials for the primary prevention of alcohol withdrawal seizures demonstrated a highly significant risk reduction for seizures with benzodiazepines and antiepileptic drugs and an increased risk with antipsychotics. A meta-analysis of randomised, placebo-controlled trials for the secondary prevention of seizures after alcohol withdrawal showed lorazepam to be effective, whereas phenytoin was ineffective. Because withdrawal seizures do not recur if the patient remains abstinent, long-term administration of antiepileptic drugs is unnecessary in abstinent patients. The first seizure not related to alcohol withdrawal should not result in permanent drug treatment in an alcohol-dependent patient, because of poor compliance and the high likelihood of remission. The treatment of alcohol dependence is more important and should be prioritised before the prevention of further seizures.^{[5][6]}

In small amounts alcohol does not cause seizures. Binge drinking and alcohol withdrawal can lead to seizures. Further alcohol reduces seizure threshold in known epileptics.

Fig. 4: Pathophysiology of Alcohol Withdrawal Seizures

Criteria for Labelling as Alcohol Related Seizures

- History of seizures during heavy alcohol binge termed alcohol induced seizures/rum fits.
- History of seizures from 6 to 48 hours of alcohol intake termed alcohol withdrawal seizures excluding other secondary causes by normal imaging.

European Federation of Neurological Society (EFNS) Guideline was Published in 2005 for the Diagnosis and Management of Alcohol Related Seizures.

The following Recommendations have been Proposed

1. Brief versions of AUDIT (Alcohol Use Disorder Identification Test) are recommended for diagnosis of alcohol overuse.
2. Carbohydrate-Deficient Transferrin (CDT) and Gamma-Glutamyl Transferase (GGT) - Biomarkers to support alcohol overuse.
3. Although obviously alcohol related first known seizure must be evaluated by brain imaging and EEG.
4. The CIWA questionnaire (Clinical Institute Withdrawal Assessment) to grade the severity of withdrawal symptoms.

5. Prophylactic Thiamine is recommended.
6. Benzodiazepines for the treatment and primary prevention of alcohol withdrawal seizures.

CONCLUSION

Our study concluded that generalised seizure was the most common type of seizure and alcohol related seizures were the most common cause of seizures among patients presenting in Govt. Stanley Hospital in contrast to world statistics.

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