Original Article

Clinical profile of patients with nascent alcohol related seizures

P. Sandeep, Ajith Cherian, Thomas Iype, P. Chitra, M. K. Suresh[1], K. C. Ajitha[1]

Departments of Neurology, and [1]Internal Medicine, Government Medical College, Trivandrum, Kerala, India

Abstract

Aim: The aim of this study is to characterize the clinical profile of patients with alcohol related seizures (ARS) and to identify the prevalence of idiopathic generalized epilepsy (IGE) in the same. **Materials and Methods:** 100 consecutive male patients presenting to a tertiary care center in South India with new onset ARS were analyzed with alcohol use disorders identification test (AUDIT) score. All underwent 19 channel digital scalp electroencephalography (EEG) and at least computed tomography (CT) scan. **Results:** A total of 27 patients (27%) who had cortical atrophy on CT had a mean duration of alcohol intake of 23.62 years compared with 14.55 years in patients with no cortical atrophy ($P < 0.001$). Twenty-two patients (22%) had clustering in the current episode of whom 18 had cortical atrophy. Nearly, 88% patients had generalized tonic clonic seizures while 12% who had partial seizures underwent magnetic resonance imaging (MRI), which identified frontal focal cortical dysplasia in one. Mean lifetime duration of alcohol intake in patients presenting with seizures within 6 hours (6H-gp) of intake of alcohol was significantly lower ($P = 0.029$). One patient in the 6H-gp with no withdrawal symptoms had EEG evidence for IGE and had a lower AUDIT score compared with the rest. **Conclusion:** CT evidence of cortical atrophy is related to the duration of alcohol intake and portends an increased risk for clustering. Partial seizures can be a presenting feature of ARS and those patients may benefit from MRI to identify underlying symptomatic localization related epilepsy (8.3% of partial seizures). IGE is more likely in patients presenting with ARS within first 6 hours especially if they do not have alcohol withdrawal symptoms and scalp EEG is helpful to identify this small subgroup (~1%) who may require long-term anti-epileptic medication.

Key Words

Alcohol use disorders identification test, anti-epileptic drugs, convulsions, electroencephalography, ethanol, magnetic resonance imaging

For correspondence:
Dr. Ajith Cherian, Department of Neurology, Government Medical College, Trivandrum, Kerala, India.
E-mail: drajithcherian@yahoo.com

Ann Indian Acad Neurol 2013;16:530-3

Introduction

Alcohol related seizures (ARS) are defined as adult-onset seizures that occur in the setting of chronic alcohol dependence.[1] Many studies have examined the complex relationship between alcohol consumption and epilepsy, with the main focus on alcohol-induced seizures due to withdrawal. Victor and Brausch stated that seizures during alcohol withdrawal in the absence of other epileptogenic factors are not symptoms of a latent disorder activated by the alcoholism, but rather a transient disturbance of cerebral functioning during withdrawal.[2] Available evidence shows a strong and consistent association between alcohol consumption and epilepsy, although this association and its strength is not clear. The basis of our current study was to interrogate this relation.

Access this article online	
Quick Response Code:	Website: www.annalsofian.org
	DOI: 10.4103/0972-2327.120454

Excessive alcohol use is a well-known precipitant of idiopathic generalized epilepsy (IGE). Some proportion of late onset IGE may present as ARS. We hypothesized that at least a small proportion of new onset ARS could be unmasking of IGE. Aim was to characterize the clinical profile of patients with new onset ARS and to identify the prevalence of IGE in the same.

Materials and Methods

A total of 100 consecutive patients without a prior diagnosis of epilepsy presenting with seizures related to alcohol intake to either emergency room (ER) or out-patient tertiary care neurology clinic at Government Medical College, Trivandrum, Kerala, South India from December 2010 to December 2012 were studied. All subjects gave informed written consent to participate in the study and approval of the Institutional Ethics committee was obtained. We collected details of alcohol use and seizures from patient and a reliable informant in case the patient was in delirium. The drinking history consisted of total duration of alcohol intake, type of alcohol used, amount consumed per day, recent change in drinking habits, amount of alcohol consumed in the bout preceding the seizure and time interval between last bout and seizure. Blood alcohol levels were not performed. Withdrawal symptoms and its temporal

relationship with seizure were also assessed. Alcohol use disorders identification test (AUDIT) was performed in each patient and "AUDIT" scores were calculated to identify persons with hazardous and harmful patterns of alcohol consumption.[3] Family history of alcohol dependence and epilepsy in the first degree relatives were also collected. All patients who had a proximate well-known provoking cause of seizure (e.g., subdural hematoma, dyselectrolytemia and hypoglycemia) other than alcoholism were excluded from the study. Though smokers were included patients with other substance abuse were excluded.

Patients underwent physical examination, routine hematological and biochemical investigations for liver and renal functions. Serum electrolytes, sodium, potassium, calcium and magnesium were carried out in all patients at the time of presentation. A computed tomography (CT) of the brain was done in all patients to rule out head injury and any other provoking cause for seizure like subdural hematoma. 1.5 tesla magnetic resonance imaging (MRI [Avanto-SQ Engine, Siemens Medical Systems, Erlanger, Germany]) of the brain was done in 12 patients with semiology suggestive of partial seizures.

Once the acute withdrawal symptoms settled as assessed by revised Clinical Institute Withdrawal Assessment for alcohol scale (CIWA-Ar),[4] a video electro-encephalography was performed in all cases. All recordings were carried out on a 19-channel digital electroencephalography (EEG) acquisition system (NicVue, Nicolet-Viking, USA) with the scalp electrodes placed according to the international 10-20 system. The scalp-EEG was recorded for 40 min (20 min awake and 20 min sleep record) and included 3 min of hyperventilation and photic stimulation in wakefulness. A partial sleep deprivation protocol was used.[5] Signatures of IGE in the form of frontally dominant generalized spike-wave discharges, Grade III photo-paroxysmal response and other EEG abnormalities in the form of slowing either focal or generalized, interictal epileptiform discharges or excessive generalized fast activity were looked for during interpretation of EEGs. All EEGs were reported systematically and classified according to Mayo clinic system.[6] Statistical analyses were performed using the statistical package for the social sciences 16.0 (SPSS Inc, Chicago). Continuous variables were analyzed by independent Student's *t*-test and categorical variables were analyzed by Chi-square test and Fisher's exact test. A $P < 0.05$ was considered to indicate statistical significance.

Results

All 100 consecutive patients enrolled for the study were males. The clinical characteristics of patients are given in Table 1.

The average age of patients was 43.7 years (median age was 45 years and the range was 25-67 years). The mean duration of alcohol intake was 17 years. The mean AUDIT score was 21.9 indicating a severe degree of alcohol related problem amounting to alcohol dependence. Mean duration of alcohol use was 17.16 years with 24% patients using alcohol for more than 20 years. Nearly, 76% patients were in the habit of consuming rum. Mean daily intake in the month prior to seizure was 140.36 g, roughly six drinks per day. The mean alcohol intake in the bout before seizure was 199.2 g, i.e., roughly 8 drinks (60 ml of 40% alcohol in each drink). 68% patients were smokers. Mean number of seizures per patient during the current episode was 2.26. 54% patients had just one seizure. Clustering defined as three or more seizures at presentation occurred in 22 patients (22%). Mean time interval between prior alcohol intakes to the first seizure was 19.35 h. 88% patients had generalized tonic clonic seizures (GTCS) while 12% patients had semiology suggestive of partial seizures. None of them presented with status epilepticus. 8 (8%) patients reported epilepsy in a first degree relative while 3 (3%) had a history of febrile seizures. 65% patients had withdrawal symptoms at the time of first seizure while 20% noticed the same after onset of seizures. 15 patients had just one seizure and none had any withdrawal symptoms even after their sole seizure.

Table 1: Clinical characteristics of patients with alcohol related seizures

Mean age (SD)	43.7 years (10.77)
Median age	45 years (range 25-67)
Drinking pattern	
Mean duration of alcohol intake (SD*)	17 years (9.13)
Mean AUDIT score (SD)	21.9 (4.86)
Mean daily intake in past 1 month (SD)	280.72 g (151.44)
Mean intake in the bout before seizure (SD)	398.40 g (217.46)
Seizure characteristics	
Average number of seizures (SD)	2.26 (4.74)
Mean time interval between alcohol intake to seizure (SD)	19.35 h (35.94)
Clustering in the current episode (%)	22 (22)
Withdrawal symptoms before the onset of seizure (%)	65 (65)
Epilepsy in first degree relative (%)	8 (8)
History of Febrile seizures (%)	3 (3)

*SD=Standard deviation, AUDIT=Alcohol use disorders identification test

78 patients had their first seizure between 6 and 48 h of alcohol use and can be considered as having withdrawal seizures. 14 patients had seizures within 6 h of alcohol intake (6H-gp). The mean duration of alcohol intake in years was significantly lower in this 6H-gp compared with those who had seizures after 6 h of alcohol intake ($P = 0.029$) [Table 2]. Eight patients out of the 14 had no withdrawal symptoms at all. The mean duration of alcohol intake in this subgroup of eight was significantly lower than those who had withdrawal symptoms ($P = 0.013$) [Table 3]. One young male in this subset had EEG abnormalities suggestive of IGE.

27 patients (27%) had non-specific generalized cortical atrophy on CT scan of the brain. The mean duration of alcohol intake in patients with cortical atrophy was 23.62 years compared to 14.55 years in patients with normal imaging, which was statistically significant ($P < 0.001$). Eighteen patients who had cortical atrophy presented with clustering of seizures. MRI of the brain was done in 12 patients with semiology suggestive of partial seizures. Only one patient had imaging evidence suggestive of focal cortical dysplasia in the left frontal lobe.

Scalp EEG recording was done in all patients. The mean background frequency in posterior head region was 10.365 Hz (standard deviation - 1.88). 67% patients had

Table 2: Relationship between mean lifetime duration of alcohol intake and time interval between alcohol intake and seizure (*P*=0.029)

Relation of first seizure with alcohol intake	Number of patients	Mean life time duration of alcohol intake in years (SD)
Less than 6 h	14	12.28 (9.96)
More than 6 h	86	17.95 (8.74)

SD=Standard deviation

Table 3: Relationship between withdrawal symptoms and duration of alcohol intake in patients with seizures <6 h of intake of alcohol (*P*=0.013)

Withdrawal symptoms	Number of patients	Mean duration of alcohol intake in years (SD)
Present	6	20.66 (9.87)
Absent	8	6.2 (2.91)

SD=Standard deviation

increased generalized fast beta activity with low amplitude. 15 patients (15%) had intermittent bursts of theta slowing with a normal background coming under the category of dysrhythmia I according to Mayo Clinic classification of EEG abnormalities. Specific epileptiform abnormalities in the form of spike and wave discharges were noticed only in 2 patients. 1 patient (95% confidence interval: 0-3%) had normal background rhythm with frontally dominant generalized spike and wave discharges. Intermittent photic stimulation revealed activation of generalized spike and wave discharges at 18, 20, 22, 24 and 28 Hz stimulation suggestive of IGE. He had an AUDIT score of 15, had no withdrawal symptoms and had just one seizure within 6 h of alcohol intake. Another patient had independent left frontal and bifrontal spike and wave discharges with focal fast frontal polyspikes over a slow background of 7-7.5 Hz possibly suggesting a localization related epilepsy of frontal origin, which turned out to be a focal cortical dysplasia in the left frontal lobe.

Discussion

The link between alcohol and seizures dates back to the time of hippocrates. Alcohol consumption, one of five most important risk factors for the global burden of disease and disability has been shown to be associated with epilepsy.[7] 20 to 40% of patients with seizures who present to an ER have seizures related to alcohol abuse.[8] Alcohol may act in several ways to produce seizures in patients with or without underlying foci. Partial or absolute withdrawal of alcohol after a period of chronic intake may lead to glutamatergic over activity. Binge drinking can cause an acute alcohol-related metabolic disorder (e.g., hypoglycemia, hyponatremia) leading to acute symptomatic seizures. It can create a situation leading to cerebral trauma or can precipitate seizures in patients with idiopathic or posttraumatic epilepsy. Persistent heavy intake of alcohol without alcohol withdrawal can also cause seizures.[9]

ARS present at varied times after abstaining from drinking. Many patients do not have overt withdrawal symptoms at the time of seizures. There is a general tendency to consider all seizures in alcoholics as withdrawal related. Many studies have shown that not all seizures can be attributed to alcohol withdrawal alone. According to Victor and Brausch in their study, 88% of seizures were related to alcohol withdrawal alone.[2] In studies by Earnest and Yarnell[10] and Hillbom[11] alcohol withdrawal accounted for 59% and 31% of seizures respectively. In a recent study from India only 28% of seizures could be confidently attributed to alcohol withdrawal.[12]

The elicitation of drinking pattern in our patients revealed alarming results. The mean intake of alcohol in the month prior to seizure was around six drinks per day with mean AUDIT scores of 21.9. 73% patients had AUDIT scores more than 20, which required referral to a de-addiction program. The intake of alcohol in the bout before the seizure was significantly higher than the mean for the past 1 month indicating the potential role of alcohol in inducing these seizures.

14 patients in our study had seizures within 6 h of intake of alcohol (6H-gp). When we analyzed this subgroup we found that 8 patients had no significant withdrawal symptoms and the mean lifetime duration of alcohol intake was significantly lower in them compared with the rest. This indicates the potential role of alcohol itself in inducing seizures, rather than the withdrawal state. Hence this group of patients can potentially be considered to have alcohol induced seizures rather than withdrawal seizures. One young male in this subset had EEG abnormalities suggestive of IGE. He had one seizure within 6 h of intake of alcohol and no withdrawal symptoms. He had no history of myoclonic jerks or absence seizures and probably had IGE with GTCS. Considering all alcohol induced seizures as unmasking of late onset IGE would be unwise. IGE is more likely to be detected in this subgroup of patients who have seizures within 6 h of alcohol intake and without any withdrawal symptoms.

A family history of seizure was obtained in 25% of patients with ARS in a study from India.[12] Schaumann *et al*. found an odds ratio of 2.45 in relatives of patients with alcohol induced seizures.[13] Nearly 8% of patients in our series had a history of seizures in their first degree relatives.

Available evidence shows a strong and consistent association between duration of alcohol consumption and epilepsy. Dam *et al*. observed that 74% of long-term heavy alcohol users with epilepsy had cerebral atrophy as a consequence of chronic alcohol intake.[14] 27% of patients in our study had evidence for cortical atrophy in CT scan of the brain. Patients with cortical atrophy had a significantly higher mean duration of alcohol intake compared to those who had no atrophy. In our series, 22% of patients had clustering of seizures in the current episode, out of which eighteen had cortical atrophy on CT scan of the brain. Evidence of cerebral atrophy in patients with ARS portends an increased risk for developing clustering. It is well-known that as the duration of alcohol intake increases the chance of developing epilepsy or unprovoked seizure increases.[9] The kindling hypothesis proposed by Ballenger and Post states that repeated ethanol withdrawal, including natural withdrawal during sleep over the years, in chronic alcoholics lead to the gradual lowering of the epileptogenic threshold.[15,16] It has been observed that cerebral atrophy can potentially cause irreversible central nervous system changes, leading to the onset of spontaneous seizures not immediately

related to alcohol intake. Thus, evidence for cortical atrophy on CT scan of the brain can be used to identify patients with high risk for clustering and having unprovoked seizures.

MRI of the brain done in 12 patients with a partial semiology for their seizure identified one case of focal cortical dysplasia, which was missed in CT scan of the brain. MRI has a higher yield over CT for identifying lesions in patients with alcohol related partial seizures.

Among the IGE syndromes,[17] IGE with GTCS is the one most likely to present to the clinician initially as ARS. Searching for signatures of IGE in patients with ARS with the help of a scalp EEG will still be helpful to identify a very small subgroup (~1%) that may require long-term antiepileptic medication. Patient with findings of IGE in our series was having moderate degree of alcohol related problem. His age was lower compared to mean, had a lower AUDIT score, no withdrawal symptoms and had seizures within the first 6 h following alcohol consumption. No clinical pointers such as recurrent seizure, myoclonus or seizure precipitated by sleep deprivation were present. Short of an EEG, it would have been impossible to identify such a patient in this group. Though our sample is very small, EEG does have a role in identifying this subgroup that requires prolonged treatment.

Conclusion

Partial seizures can be an occasional presenting feature of ARS and they may benefit from MRI to identify underlying symptomatic localization related epilepsy (8.3% of partial seizures). CT evidence of cortical atrophy is related to the duration of alcohol intake and portends an increased risk for clustering. IGE is more likely in patients presenting with ARS within first 6 h especially if they do not have alcohol withdrawal symptoms and scalp EEG is helpful to identify this small subgroup (~1%) who may require long-term anti-epileptic medication.

References

1. Rathlev NK, Ulrich AS, Delanty N, D'Onofrio G. Alcohol-related seizures. J Emerg Med 2006;31:157-63.
2. Victor M, Brausch C. The role of abstinence in the genesis of alcoholic epilepsy. Epilepsia 1967;8:1-20.
3. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption – II. Addiction 1993;88:791-804.
4. Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: The revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). Br J Addict 1989;84:1353-7.
5. Liamsuwan S, Grattan-Smith P, Fagan E, Bleasel A, Antony J. The value of partial sleep deprivation as a routine measure in pediatric electroencephalography. J Child Neurol 2000;15:26-9.
6. Mayo Clinic and Mayo Foundation. Clinical Examination in Neurology. 6th ed. Baltimore: Mosby; 1991. p. 354-451.
7. Samokhvalov AV, Irving H, Mohapatra S, Rehm J. Alcohol consumption, unprovoked seizures, and epilepsy: A systematic review and meta-analysis. Epilepsia 2010;51:1177-84.
8. Rathlev NK, D'Onofrio G, Fish SS, Harrison PM, Bernstein E, Hossack RW, *et al*. The lack of efficacy of phenytoin in the prevention of recurrent alcohol-related seizures. Ann Emerg Med 1994;23:513-8.
9. Brust JC. Acute neurologic complications of drug and alcohol abuse. Neurol Clin 1998;16:503-19.
10. Earnest MP, Yarnell PR. Seizure admissions to a city hospital: The role of alcohol. Epilepsia 1976;17:387-93.
11. Hillbom ME. Occurrence of cerebral seizures provoked by alcohol abuse. Epilepsia 1980;21:459-66.
12. Murthy P, Taly AB, Jayakumar PN. Seizures in patients with alcohol dependence. Ger J Psychiatry 2007;10:54-7.
13. Schaumann BA, Annegers JF, Johnson SB, Moore KJ, Lubozynski MF, Salinsky MC. Family history of seizures in posttraumatic and alcohol-associated seizure disorders. Epilepsia 1994;35:48-52.
14. Dam AM, Fuglsang-Frederiksen A, Svarre-Olsen U, Dam M. Late-onset epilepsy: Etiologies, types of seizure, and value of clinical investigation, EEG, and computerized tomography scan. Epilepsia 1985;26:227-31.
15. Ballenger JC, Post RM. Kindling as a model for alcohol withdrawal syndromes. Br J Psychiatry 1978;133:1-14.
16. Kokka N, Sapp DW, Taylor AM, Olsen RW. The kindling model of alcohol dependence: Similar persistent reduction in seizure threshold to pentylenetetrazol in animals receiving chronic ethanol or chronic pentylenetetrazol. Alcohol Clin Exp Res 1993;17:525-31.
17. Fisher RS, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, *et al*. Epileptic seizures and epilepsy: Definitions proposed by the international league against epilepsy (ILAE) and the international bureau for epilepsy (IBE). Epilepsia 2005;46:470-2.

How to cite this article: Sandeep P, Cherian A, Iype T, Chitra P, Suresh MK, Ajitha KC. Clinical profile of patients with nascent alcohol related seizures. Ann Indian Acad Neurol 2013;16:530-3.
Received: 17-04-13, **Revised:** 07-07-13, **Accepted:** 16-08-13

Source of Support: Nil, **Conflict of Interest:** Nil