Research Article

Clinical study of myoclonic epileptic syndromes

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ABSTRACT

Background: Incidence of different myoclonic epileptic syndromes is variable in different regions. Here in as there is very few literature available internationally being inclusive of all myoclonic epilepsies together. Very few studies are available which describe all characteristics in a given study population. The aim of the study was to find incidence of different types of myoclonic epilepsies among patients presenting with myoclonic seizures their characteristics and to study all myoclonic epilepsies and juvenile myoclonic epilepsy in the study population.

Methods: In this study conducted in neurological unit at Ruby hall clinic, a total of 188 case of epileptic disorder were enrolled irrespective of age and sex, among 136 were new case of epileptic disorder were classified based on seizure pattern, 23 were new cases of myoclonic epilepsy, these 23 new case of myoclonic epilepsy along with 52 old cases of myoclonic epilepsy attending to neurological unit were clubbed, a total of 75 cases myoclonic epilepsy were studied. All cases of myoclonic epilepsy and juvenile myoclonic epilepsy were studied with respect to age of onset different seizures, relation with family history, response to treatment, EEG findings.

Results: Out of 136 cases 23 were new cases of myoclonic epilepsy, these 23 newly diagnosed cases of myoclonic epilepsies along with 52 already diagnosed myoclonic epilepsy are clubbed together, total of 75 cases were further studied. Incidence of myoclonic epilepsy among epileptic patients found to be 16.9%. Incidence of JME among myoclonic epilepsies is 75-80%, in all myoclonic epilepsies and JME association with GTCS, family history, EEG abnormalities were common finding, valproate and leviteracetam are good therapeutic options, carbamazepine aggravated myoclonus.

Conclusions: For diagnosis of myoclonic epilepsy proper clinical history stress laid to ask history of myoclonic jerk in case of all seizure disorder, diagnosis basically depends on proper knowledge of myoclonic epileptic syndrome, eliciting history, EEG as an ancillary testing when in doubt always expert opinion is required as misdiagnosis of the myoclonus as partial seizure leads to wrong prescription of carbamazepine which exacerbates the myoclonus.

Keywords: Clinical study, Myoclonic, Syndrome

INTRODUCTION

Hammond in 1867 described three patients whose condition came close to the entity of myoclonus as it is known today.[1] His patients had typical jerky movements with movement of joint though pathophysiology not clearly described. He reported a head shook violently the muscles of his face were convulsed his arms and hands trembeled, gluteal muscles contracted so powerfully so as to move convulsively up and down on his chair. Other

patient had episodes in which he was seized as much suddenness as he though he were struck with an epileptic fit. Hammond suggested these symptoms were secondary to cerebellar disease.

In 1902, Clark et al stated that the milder types of essential myoclonus (without epilepsy) and the severest and fatal form of myoclonus (myoclonus epilepsy) should be considered as affections similar in pathogenesis and course to epilepsy.[2] They gave an excellent review of this disorder they thought that origin was in cortical elements. They stated that epileptic seizures antedated myoclonus in half of the patients by a period ranging from few weeks to several years, whereas myoclonus occurred first in one-third of patients and two conditions occurred simultaneously in rest of the cases, the myoclonus was itself atypical in the sense it was like a lightening contraction, they occasionally had fibrillary character involving certain parts of muscle producing son called live flesh. In myoclonus with epilepsy, the clonic contractions of myoclonus impercetably in tonic stage of epileptic paroxysm. As a rule poor mental and physical development was present. The prognosis was poor longevity was curtailed.

Hodskins et al studied 300 cases of epilepsy and found myoclonus in 10% to 15%.[3] The family history in these cases was frequently positive; symptoms of involvement of the pyramidal tract were seen more frequently than they were in nonselected instances of epilepsy, whereas extrapyramidal symptoms were found less frequently. One-third of the patients with myoclonus had cerebellar symptoms, as compared with a 10% incidence in the entire group of epileptics. They made necropsy studies on 18 myoclonic patients encountered from 1911 to 1928 and found three types of lesions, namely:

- Primary atrophic lesions.
- Degenerative cellular changes, sometimes identical with those found in amaurotic familial idiocy.
- Abnormal inclusion bodies both extracellular and intracellular, amyloid bodies, lipoid inclusions, and fatty degeneration.

Lafora et al discussed the physiologic and pathologic considerations of the disorder and presented an excellent cure.[4] Robert et al first classified myoclonus in detail. They classified myoclonus as [5]

Type 1: Myoclonus, seizures, objective evidence of neurological disorders or mental disorders or both.

Type 2: Myoclonus and seizure without objective evidence of neurologic mental deficits or both.

Type 3: Myoclonus alone, without evidence of seizures and neurologic or mental deficits or both.

Type 4: Myoclonus and neurologic or mental deficit no seizure.

Incidence of different myoclonic epileptic syndromes is variable in different regions. Here in as there is very few literature available internationally being inclusive of all myoclonic epilepsies together.[6] Very few studies are available which describe all characteristics in a given study population. So this study was taken up to find incidence of different types of myoclonic epilepsies among patients presenting with myoclonic seizures their characteristics. The objective was to study all myoclonic epilepsies and juvenile myoclonic epilepsy in the study population.

METHODS

Study was conducted at one neurological unit of Ruby Hall Clinic, a tertiary care hospital in Pune, India. Patients coming with epileptic disorder to neurologic unit were selected as study population. Retrospective and prospective observational study was done from December 1, 2014 to April 1, 2016.

Sample size

Sample size calculation was based on the results (effect sizes) from the previously published studies.[5,7] Thus a sample of size 73 cases (minimum) satisfying the inclusion criteria would produce 80.0% statistical power (type II error=0.20) and 5% type I error probability (alpha=0.05) to be able to detect the incidence and prevalence of myoclonic epilepsies. To calculate incidence of myoclonic epilepsy a total of 136 new cases were enrolled and classified. A total of 75 cases of myoclonic were studied. Study was done from November 1, 2012 to November 1, 2014.

Inclusion criteria

- All new cases of epileptic disorder arriving to one neurological unit of Ruby hall Clinic irrespective of age, sex are included.
- In case of myoclonic epilepsy both old and new cases arriving to neurological unit were studied.

Exclusion criterion

Physiologic and metabolic myoclonus were excluded.

Statistical methods

The comparison of distribution of qualitative characteristics was done using chi-square test or Fisher's exact probability test. P-value less than 0.05 considered to be statistically significant.

Methodology

This study experience of myoclonic epilepsy in tertiary care hospital has been carried out at Ruby hall clinic, Pune, India. Study has been conducted for a period of two years from November 1, 2012 to November 1, 2014.

All new cases of epileptic disorder both inpatient and outpatient attending to one neurological unit irrespective of age and sex were classified based on their seizure pattern incidence of myoclonic epilepsy has been calculated. Among the diagnosed case of myoclonic epilepsy incidence of juvenile myoclonic epilepsy has been calculated. Along with newly diagnosed cases of myoclonic epilepsy already diagnosed cases of myoclonic epilepsy attending to the neurological unit were clubbed and analysed.

Each case was further studied in detail after taking an informed consent. All myoclonic and juvenile myoclonic epilepsies were studied with respect to age of onset of myoclonus, age of onset of GTCS, absence and association of myoclonic jerk with other seizures, developmental history, and family history.

EEGs were analysed and different EEG patterns were tabulated, imaging data if available was recorded. Response to various to drugs as subjective perception of decreased frequency of jerks and GTCS episode were observed. Adverse events if any were recorded. Mean effective dose of valproate calculated. Associations between family history and abnormal EEG findings, family history and response to drug therapy were compared with those who have no family history, $P < 0.05$ considered significant. Patients with myoclonic jerks and GTCS and abnormal EEG findings and rest with abnormal EEG findings were compared $P < 0.05$ considered significant.

RESULTS

To study the incidence of myoclonic epilepsy among epileptic patients attending to neurological unit were classified and incidence of myoclonic epilepsy calculated which is found to be 16.9%. A total of 23 cases among 136 new epileptic cases. For the purpose of the study these 23 cases of myoclonic epilepsy which were clubbed with the cases attending regularly to the neurological unit. 52 already diagnosed cases of myoclonic epilepsy were included. Total of 75 cases were studied (Table 1).

Table 1: Distribution of type of epilepsy among new cases.

Type of epilepsy	New Cases	
	No. of cases	% of cases
GTCS	75	55.2
Simple partial	19	14.0
Complex partial	15	11.0
Absence seizure	4	2.9
Myoclonic	23	16.9
Total	**136**	**100.0**

Table 2 distributes all myoclonic epilepsies into final epileptic syndrome among new and old cases showing a predominance of juvenile myoclonic epilepsy. With

73.9% incidence in newly diagnosed and 84.6% in old cases.

Table 2: Distribution of type of myoclonic epilepsy among new and old cases.

Myoclonic epilepsy	New cases		Old cases	
	No. of cases	% of cases	No. of cases	% of cases
Juvenile myoclonic epilepsy	17	73.9	44	84.6
Infantile myoclonic epilepsy	2	8.7	3	5.8
Progressive myoclonic epilepsy	0	0.0	3	5.8
Other epileptic myoclonus	4	17.4	2	3.8
Total	23	100.0	52	100.0

Table 3 describes relation of response to therapy and positivity of family history. The distribution of Response to therapy did not differ significantly between cases having family history and the case shaving no family history in the entire group of myoclonic cases (P-value >0.05) and in JME (P-value >0.05).

Table 3: Distribution of response to therapy.

Response (later therapy)	All myoclonic epilepsy		Juvenile myoclonic epilepsy	
	With family history	Without family history	With family history	Without family history
Good	16 (84.2)	50 (89.3)	16 (100.0)	44 (97.8)
Poor	3 (15.8)	6 (10.7)	0	1 (2.2)
Total	19 (100.0)	56 (100.0)	16 (100.0)	45 (100.0)
P-values	P-value=0.556 (Non-significant)		P-value=0.548 (Non-significant)	

P-value by Chi-Square test.

Table 4: Distribution of imaging status.

Imaging status	All myoclonic cases	Juvenile myoclonic cases
Normal	48 (64.0)	41 (67.2)
Abnormal	5 (6.7)	0
N/A	22 (29.3)	20 (32.8)
Total	**75 (100.0)**	**61 (100.0)**

Imaging in case of juvenile myoclonic epilepsies were obtained in 41 patients almost all had normal imaging. Indicating JME has essentially normal imaging findings. In case of all myoclonic epilepsies imaging was available in 53 patients only 5 had abnormal imaging (Table 4).

Table 5 describes abnormalities in EEG in patients with myoclonic+GTCS and myoclonic. The distribution of EEG findings did not differ significantly between Myoclonic+GTCS cases and myoclonic cases in the entire group of myoclonic cases (P-value>0.05) and JME (P-value>0.05).

Table 5: Distribution of EEG findings.

EEG findings	All myoclonic epilepsy		Juvenile myoclonic epilepsy	
	Myoclonic+GTCS	Others myoclonus	Myoclonic+GTCS	Other myoclonus
Normal EEG	14 (31.1)	6 (30.0)	14 (35.0)	6 (37.5)
Abnormal EEG	31 (68.9)	14 (70.0)	26 (65.0)	10 (62.5)
Total	45 (100.0)	20 (100.0)	40 (100.0)	16 (100.0)
P-values	P-value=0.929 (Non-significant)		P-value=0.860 (Non-significant)	

DISCUSSION

At 55.2 % of GTCS, 14 % Simple partial, 11.0 % complex partial, 16 % myoclonus, 2.9% Absence. Most of large scale studies showed a predominance of partial seizure with a total of 45-55 %, followed by GTCS of 35-45%, 8-12% of myoclonic epilepsies.[8-10] This variation might be due to study period and centre variability as these studies were with a large population of greater than 1000 and a period of 10 to 12 years or a pooled data of number of studies. Though recently conducted study in Calcutta has some similar incidence profile comparable to this study.[11] Study population of 66. Incidence of myoclonic epilepsy in Hodskins et al was found to be 10 to 15%.[3] Probably time duration of study and inclusion of all neurological units might have given a better analysis comparable to large studies. All neurological units can have a data record of epileptic disorder to know relative incidence of seizure disorders.

The common form of myoclonic epilepsy is juvenile myoclonic epilepsy. At 73.9% for new case of myoclonic epilepsy and 84.6% for old cases of myoclonic epilepsy the incidence of juvenile myoclonic epilepsy is slightly less than seen in with landmark studies which are inclusive of all myoclonus together Minnesota et al study mayo clinic 1999.[7]

At 60.7% incidence of myoclonic among males is comparable to other studies have shown higher incidence in males, few studies showed female preponderance pooled analysis of all studies may yield a good result.[12-14]

Among 75 patients 52 patients were on valproate, 6 on carbamazepine, 3 patients on phenytoin, and 5 were on leviteracetam, 9 requiring multiple anti-epileptic drugs. Among patients on valproate therapy 88.6% had good response which was comparable most of studies on drug response in myoclonic epilepsy.[15]

A total of 57 patients were on valproate 8 on leviteracetam 2 patients were put on intra venous steroids followed by oral as diagnosis of autoimmune encephalitis was made in them. At 98.2% response to valproate was comparable to most of the studies.[16] 100 % response to leviteraxcetam.

Of the 61 cases imaging was available in 41. Among them all had normal imaging findings in accordance with studies on JME.[12,17] Normal brain imaging essentially goes in favour of juvenile myoclonic epilepsy in a patient with myoclonic seizure disorder.

Of the total 75 cases of myoclonic epilepsies EEG was available only for 56 cases out of which 20 were normal. Among those with abnormal EEG, bursts of generalized poly spike wave pattern of 3-6 cycles per second coming recurrently through record, these bursts lasts for 1-3 seconds. Normal record more likely in those on therapy. At 80% of generalised polyspike wave activity among abnormal EEG they were considerably similar to most of previous studies. 11.2 % had focal discharges. 2 patients 4.4% were having Hypssarhythymia were West syndrome.

EEG was available in 56 patients. 20 patients were having normal EEG s rest 36 (64.3%) were abnormal. At 88.9% among available abnormal EEGs generalised poly spike wave pattern on EEG, EEG abnormalities were comparable to Indian and Asian studies.[14,19]

Among 36 patients of JME with abnormal EEG, 11 had a positive family history. The distribution of EEG findings did not differ significantly between cases having with and without family history in the group of Juvenile myoclonic cases (P-value>0.05). This is in contrast previous study which showed significant association study was conducted on a large study population of 266.[19]

Among 45 with abnormal EEG 11 had a positive family history. The distribution of EEG findings did not differ significantly between cases having with and without family history in the group of Juvenile myoclonic cases (P-value >0.05). This is in contrast previous study which showed significant association study was conducted on a large study population of 266.[19]

CONCLUSIONS

For diagnosis of myoclonic epilepsy proper clinical history stress laid to ask history of myoclonic jerk in case of all seizure disorder, diagnosis basically depends on proper knowledge of myoclonic epileptic syndrome, eliciting history, EEG as an ancillary testing when in doubt always expert opinion is required as misdiagnosis of the myoclonus as partial seizure leads to wrong prescription of carbamazepine which exacerbates the myoclonus.

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