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To identify the risk factors of refractory childhood epilepsy.

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Abstract

Background & Methods: The aim of the study is to identify the risk factors of refractory childhood epilepsy. Early identification and the risk factor analysis and dynamics of the disease helps the physician in initiating the appropriate treatment, thereby avoiding the wrong therapy, low dose therapy and infrequent therapy.

Results: Perinatal injury (64), multiple risk factors (57) neonatal seizures (53) were identified as predominant risk factor. P value also shows the significant association of risk factor. 23 children had CP due to the perinatal injury, 07 had congenital CNS abnormalities like Tuberous Sclerosis, Neuronal Migration disorder, and infection with TORCH (08) was also identified as a risk factor. Inborn errors of metabolism and Neuro Degenerative disorder (19) like mitochondrial disorders also were important risk factors.

Conclusion: The following risk factors are identified as associated with refractoriness. Male sex, infantile onset of seizures in , generalized seizures, multiple seizure types, myoclonic seizures, Infantile spasms, developmental delay, were the bad prognosticating factor Perinatal injury, neonatal seizures, multiple risk factors ,congenital anomalies Tubers sclerosis, Struge weber syndrome, IEM, etc. were the main cause of structural and metabolic seizures associated with refractoriness. High seizure score (increased frequency) prior to the treatment or clusters of seizures carry the bad prognosis.

Keywords: risk, refractory, childhood & epilepsy.

Study Design: Observational Study.

Introduction

“A failure of adequate trials of two tolerated, appropriately chosen and used AED schedule [as monotherapies or combination] to achieve sustained seizure freedom.” ILAE latest definition encompasses two hierarchical levels[1]. This provides a scheme to categorize outcome of the treatment. Level 1 as ‘seizure freedom’ (defined as freedom from seizures for minimum three times, the longest pre-intervention or inter seizure interval of 12 months.) Level 2 as ‘treatment failure’ (defined as recurrent seizure after intervention has been adequately applied) or ‘undetermined’ (defined as whether has not been applied adequately for a valid assessment of outcome or adequate information is lacking to make the assessment). Level 1 forms a basis for level 28. This defines the Refractory epilepsy[2].

‘EPILEPTOGENESIS’ is an operational term referring to the time period between the brain insult and the appearance of the first seizures[3]. It refers to the dynamic process that

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progressively alters neuronal excitability and establishes critical interconnections and structural changes before clinical signs appears.

Cognitive and Behavioral disturbance are the most common comorbid conditions of the patients with RE which is usually associated with early onset seizures, severity of seizures, lower socioeconomic class, longer duration etc[4-5].

Material and Methods

Children with idiopathic or symptomatic epilepsy who are on two or more AEDs and who were in follow up. Study was conducted for 01 Year on 100 Paediatric cases. The study was done in the outpatient department of neurology and on in-patients, with refractory seizures, from age group of 6 months to 12 years after obtaining written consent and after counseling. Age of onset, type of seizure, number of seizures at baseline before starting treatment (per day/week/month/year, response to antiepileptic drug(s), longest seizure free interval, any history of status epilepticus (SE) before or as a part of presentation, hospital admissions and treatment, perinatal history, birth history, neonatal history, diet history, development history, associated symptoms (febrile convulsions, head trauma etc) and CNS infection were taken into account. Family history of seizure disorder and history of poor scholastic performance, behavioral abnormality and focal motor deficits were also considered.

INCLUSION CRITERIA

Patients on adequate treatment with two AEDs either alone or in combination , with proper compliance and dosage.

EXCLUSION CRITERIA

Patients with poor compliance in the form of irregular medication or inadequate dosing were excluded.

Result

Table No. 1: AGE OF ONSET

S. No.	Age	No.	Percentage	P Value
1	Less than 01 Year	54	54	.448019
2	01-05 Years	29	29	
3	More than 05 Years	18	17	

Age less than 1year - (54%), 1-5 years-(29%), >5years-(17%) age less than 1 year of onset has the significance. The chi-square statistic is 0.5757. The *p*-value is .448019. The result is *not* significant at $p < .05$.

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Table No. 2: SEIZURE SEMIOLOGY

S. No.	SEIZURE SEMIOLOGY	No.	Percentage	P Value
1	Multiple seizure types	38	38	< .00001
2	Infantile	11	11	
3	Myoclonic	28	28	
4	Generelized	48	48	
5	Focal	40	40	

On analyzing the detailed history of auras, autonomic symptoms, ictal and postictal events, timing of seizure activity and precipitating factors, generalized seizure type (73) was the most frequent type, followed by focal seizures (68). Multiple seizure was the third most common type followed by myoclonic seizures. The chi-square statistic is 40.95. The *p*-value is < .00001. The result is significant at $p < .05$.

Table No. 3: TIMING OF SEIZURES

S. No.	TIMING OF SEIZURES	No.	Percentage	P Value
1	Nocturnal	16	16	.000483
2	Diurnal	17	17	
3	Any time	67	67	

(67%) patients had seizures irrespective of the time. Diurnal occurrence in (17%) patients and (16%) were nocturnal. The chi-square statistic is 12.179. The *p*-value is .000483. The result is significant at $p < .05$.

Table No. 4: RISK FACTORS

S. No.	RISK FACTORS	No.	Percentage	P Value
1	Perinatal injury	64	64	.000024
2	Multiple risk factors	57	57	
3	Neonatal seizures	53	53	
4	CNS Infection	07	07	
5	TORCH	08	08	
6	Stroke	03	03	
7	NDD & IEM	19	19	
8	Cranial Bleed/ Trauma	06	06	

Perinatal injury (64), multiple risk factors(57) neonatal seizures(53) were identified as predominant risk factor. P value also shows the significant association of risk factor. 23 children had CP due to the perinatal injury, 07 had congenital CNS abnormalities like Tuberous Sclerosis, Neuronal Migration disorder, and infection with TORCH (08) was also identified as a risk factor. Inborn errors of metabolism and Neuro Degenerative disorder (19)

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like mitochondrial disorders also were important risk factors. The chi-square statistic is 24.0484. The *p*-value is .000024. The result is significant at $p < .05$.

Discussion

In a devastating disorder like Refractory Epilepsy, the risk factors for intractability have been evaluated in this study[6-8]. The basic factor that determines the prognosis is the underlying aetiology, identification of the risk factors helps in proper management and prognostication. So it is important to ascertain the type of seizures, localization of the epileptogenic zone, sequence of event, age of onset, sex, perinatal insults, history of status epilepticus etc. Investigations like EEG, MRI, CT scan, TMS, UMS, karyotyping to aid the same. This serves as an important tool in the management of RE.

Myoclonic seizures were present in 43 patients. It had a significant p value of <.01. In 17 patients with Infantile spasms, 15 had TS and 2 had EEG features of hypsarrhythmia without tubers patients. Infantile spasms was associated with RE, p value <.01, as per chi square test. Idiopathic type of seizure was present in 35 patients. Results inferred that seizures due to structural abnormality had the worst prognosis as per Berg et al study which is similar to our study[9].

The fourth risk factor considered was developmental which is also similar to most other studies, including the one by Vrajesh Udhani et al (Mumbai), Muhammad Akbar malik et al and Berg et al . p value in our study was significant <0.01,which proves its association with refractory epilepsy[10-11].

Perinatal insult (64) multiple risk factor (58), neonatal seizures (53) were the major association factors of which; perinatal insult was the predominant independent risk factor followed by neonatal seizures. Multiple Risk factors also contributed to RE, febrile seizures were not considered as the co-existing risk factor. Mohamed Akbar Malik et al found that neonatal seizures were associated with RE[12]. This study was similar to study of “Bebittncourt PR et al, Hauser WA et al”. Whereas studies in India showed perinatal Injury being more predominating risk factor.

Conclusion

The risk factors are identified as associated with refractoriness. Male sex, infantile onset of seizures in , generalized seizures, multiple seizure types, myoclonic seizures, Infantile spasms, developmental delay, were the bad prognosticating factor Perinatal injury, neonatal seizures, multiple risk factors ,congenital anomalies Tubers sclerosis, Struge weber syndrome, IEM, etc. were the main cause of structural and metabolic seizures associated with refractoriness. High seizure score (increased frequency) prior to the treatment or clusters of seizures carry the bad prognosis.

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