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PHOTOSENSITIVITY IN EPILEPTIC SYNDROMES OF CHILDHOOD AND ADOLESCENTS IN NORTH INDIA

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ABSTRACT

Purpose behind the work was to study the prevalence of photosensitivity in epileptic syndromes of childhood and adolescents in a tertiary care center in North India. Cross-sectional study on 89 epileptic patients selected by random sampling. All patients were subjected to standard Intermittent Photoc Stimulation Test (IPS test). Photosensitivity is an abnormal electroencephalographic or clinical response to light. Of 89 patients included in the study 13(14.6%) were showing a Photo-Paroxysmal Response (PPR) to IPS on EEG. The mean age of patients showing photosensitivity was 6.65 ± 3.79 yrs with a male preponderance (16.12% vs 11.11%). Prevalence of photosensitivity in generalized and focal epilepsy groups was 12.5% and 23.52% respectively. The observed prevalence of photosensitivity in various syndromes was 33.33% in idiopathic rolandic epilepsy, 25% in lennox-gastaut syndrome, 18.18% in Complex focal epilepsy and 13.33% in grandmal epilepsy. None of the patients with West syndrome, childhood absence epilepsy, juvenile myoclonic epilepsy and myoclonic-astatic epilepsy were showing PPR. Generalized grades of PPR were more prevalent in generalized epilepsy ($p= 0.05$) and non-generalized grades were more prevalent in focal epilepsy ($p= 0.05$). None of the patients with generalized epileptic syndromes who were on sodium valproate were showing PPR in contrast to those who were on some other or no antiepileptic medicine in which 18% were showing a PPR on IPS ($p < 0.05$). Prevalence of photosensitivity in North Indian epileptic children is 14.6%. Photosensitivity is more prevalent in focal epilepsies however, further studies on a larger sample is required to analyze the association. Our study might have underestimated the prevalence of photosensitivity as patients of generalized epileptic syndromes who were on sodium valproate were not showing PPR as compared to those who were not on sodium valproate.

Key Words: *Children, Epileptic Syndromes, Photosensitivity, Grades of Photosensitivity*

INTRODUCTION

It has long been recognized that in some individuals a wide variety of external stimuli can precipitate epileptic seizures. These kinds of epilepsies are known as reflex epilepsies (Masoud, 2008). Triggering stimuli may be light in photosensitive epilepsy, reading in reading epilepsy, listening music in musicogenic epilepsy, extensive thinking in noogenic epilepsy etc. Visual stimuli are the most common triggers of reflex epilepsies, particularly in this era when children are more often exposed to television and video-games. Individuals with reflex epilepsy may have seizures exclusively in response to specific stimuli and do not suffer spontaneous seizures (Pure photosensitive epilepsy); alternatively, reflex seizures may coexist with spontaneously occurring seizures. Photosensitivity is defined as an abnormal electroencephalographic or clinical response to light (Shashi, 2005). The electroencephalographic pattern can show a wide range of expression from solely occipital to generalized irregular spikes and waves (Grade 1 to Grade 4 Photoparoxysmal Response = PPR) (Doose, 1993). In photosensitive patients electroencephalography usually shows a photoparoxysmal response (PPR) with intermittent photic stimulation (IPS) typically between 10 and 30 flashes /second (Kesteleijn-Nolst Trenite, 1998). Many studies on photosensitivity have been performed in children and adolescents, the periods during which the

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prevalence of photosensitivity is highest. In India there are very few studies showing relation between photosensitivity and epileptic syndromes in children. The purpose of our study was to study prevalence of photosensitivity and its grades in epilepsy and various epileptic syndromes in northern India.

MATERIALS AND METHODS

Patients

This cross-sectional study was performed in the department of Pediatrics in collaboration with dept of Neurology, S.P. Medical College & A.G. Hospitals, Bikaner from April 2009 to January 2010. Eighty nine patients between one and fifteen years of age who were diagnosed to have epilepsy were recruited by random sampling but cases of neonatal seizures, febrile seizures, seizures due to metabolic disturbances (e.g. hypocalcemic seizures etc.) and those with established neuropathology (e.g. meningitis, tuberculoma, neurocysticercosis, tubercular meningitis etc.) were excluded from the study.

Patients were subjected to detailed history, thorough clinical examination and relevant investigations like electroencephalography (EEG), skiagram skull, computerized tomography scan (CT scan) of head etc. Patients included in the study were categorized into various epileptic syndromes and the definition of epileptic syndrome was consistent with the revised classification of epilepsy, epileptic syndrome, proposed by the International League against Epilepsy (1989). EEG with IPS was performed in all patients. The study was approved by the institutional review board.

Procedure

The standard IPS test was done according to the protocol given by the European Expert Panel (Kesteleijn-Nolst Trenite, 1999). Intermittent photic stimulation was provided with Nicolet one photic stimulator in a dim room. Lamp distance was 25 cms. Flash frequencies of 1,2,4,6,8,10,12,14,16,18,20 and 30 flash/s. were tried for 10 seconds each at intervals of 10 seconds between stimulus train. During 10 sec of stimulation, the eyes were open for first 5 sec, closed for another 5 sec. Those patients who were taking antiepileptic medications were advised not to omit the same if it was scheduled to be taken before the time when EEG with IPS was performed. Higher flash frequencies were not used in this study.

Interpretation of Results

A diagnosis of photosensitivity required precipitation of interictal epileptiform EEG-discharges to intermittent photic stimulation *de novo* or in the situation where epileptiform discharges were already present during rest, photosensitivity was assumed if two fold or more increase during photic stimulation was observed (Wolf, 1986 and Demirkaya, 2009).

The quantitative expression of photoparoxysmal response (PPR) was graded on a scale of 1 to 4, ranging from solely occipital alpha rhythm (grade 1), parieto-occipital spikes followed by biphasic slow waves (grade 2), parieto-occipital spikes followed by biphasic slow waves spreading to the frontal region (grade 3) to generalized spikes and waves and polyspike waves discharges (grade 4) (Waltz, 1992).

For statistical analysis Chi-squared test was implemented using MSTAT software. A p-value of less than 0.05 was considered as significant.

RESULTS

Eighty nine patients were recruited for the study and categorized into various epileptic syndromes as per ILAE classification (1989). These patients were subjected to standard IPS test and the EEGs were analyzed for photoparoxysmal response and its grades. The distribution and clinical data of patients in both groups are shown in Table 1.

Age and Sex Distribution of Photosensitivity

Of eighty nine patients included in the study 13 (14.60%) were showing a photoparoxysmal response to intermittent photic stimulation (IPS). The mean age of patients showing photosensitivity was 6.65 years \pm 3.79 years. In children 1 to 5 years, 5 to 10 years and 10 to 15 years the prevalence of photosensitivity was 16.21%, 15.15% and 10.52% respectively. It was more common in younger age group but the

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Table 1: The Distribution and Clinical Data of Patients in Generalized and Focal Epilepsy

Epileptic syndromes	Gender		Age of onset	
	Male n(%)	Female n(%)	Mean	Range
Generalized Epileptic syndromes				
(a)Symptomatic/Cryptogenic				
1.West syndrome (n=2)	2(100)	0	9 months	7 months to 11 months
2.Lennox-Gastaut syndrome (n= 4)	0	4(100)	1.7 yrs	11 months to 3 yrs
(b) Idiopathic				
1.Grandmal epilepsy(n=60)	44(73.33)	16(26.66)	4.5 yrs	3 days to 15 yrs
2.Childhood absence epilepsy (n=2)	1(50)	1(50)	4 yrs	1 yr to 7 yrs
3.Juvenile myoclonic epilepsy (n=3)	2(66.66)	1(33.33)	11.5 yrs	7.5 yrs to 14 yrs
4.Juvenile absence epilepsy (n=0)	-	-	-	-
5.Myoclonic astatic epilepsy (n=1)	1(100)	0	1 yr	1 yr
Focal Epileptic syndromes				
(a)Symptomatic/cryptogenic				
Complex focal epilepsy (n=11)	7(63.63)	4(36.36)	3.5 yrs	15 days to 11 yrs
(b)Idiopathic				
Rolandic epilepsy (n=6)	5(83.33)	1(16.66)	5.1 yrs	2 yrs to 7 yrs

Table 2: Prevalence of Photosensitivity in Various Epileptic Syndromes

Epileptic syndromes	No. of Patients n	Patients with PPR n (%)
Generalized Epileptic syndromes		
(a)Symptomatic/Cryptogenic		
1.West syndrome	2	0
2.Lennox-Gastaut Syndrome	4	1(25%)
(b) Idiopathic		
1.Grandmal epilepsy	60	8(13.33)
2.Childhood absence epilepsy	2	0
3.Juvenile myoclonic epilepsy	3	0
4.Juvenile absence epilepsy	-	-
5.Myoclonic astatic epilepsy	1	0
Focal Epileptic syndromes		
(a)Symptomatic/cryptogenic		
Complex focal epilepsy	11	2(18.18)
(b)Idiopathic		
Rolandic epilepsy	6	2(33.33)

association was not statistically significant (p value 0.56). Photosensitivity was more prevalent in males as compared to females (16.12 % vs 11.11%) in this study (p value 0.54).

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Photosensitivity in Various Epileptic Syndromes

The prevalence of photosensitivity in generalized and focal epilepsy was 12.5% and 23.52% respectively. Photosensitivity was more prevalent in idiopathic rolandic epilepsy (33.33%) than idiopathic generalized epilepsy (12.12%) ($p=0.19$). It was comparable in generalized and focal epileptic syndromes of symptomatic/cryptogenic nature (16.66% vs 18.18%).

Highest rate of photosensitivity was observed in idiopathic rolandic epilepsy (33.33%) followed by lennox-gastaut syndrome (25%), complex focal epilepsy (18.18%) and grandmal epilepsy (13.13%). No photosensitivity was seen in west syndrome, childhood absence epilepsy, juvenile myoclonic epilepsy and myoclonic-astatic epilepsy in Table 2.

Grades of PPR

Among 8 photosensitive patients with grandmal epilepsy half were showing grade 4 PPR, 25% were with grade 3 and remaining 25% were showing grade 2 PPR. Generalized grades of PPR (grade 3 and 4) were significantly more prevalent than non-generalized grades (grade 1 and 2) (p value 0.018). Generalized grades of PPR were more prevalent in photosensitive patients of generalized epilepsy (77.77%; $p=0.05$) and non-generalized grades were more prevalent in focal epilepsy (75%; $p=0.05$). Generalized grades of PPR were more prevalent in photosensitive patients of Idiopathic generalized epilepsy (75%) than in focal epilepsy (25%; $p=0.05$).

Sodium Valproate and Photosensitivity

Patients with generalized epileptic syndromes who were already on sodium valproate, none of these were showing photoparoxysmal response. In 60 patients belonging to grandmal epilepsy 15 patients were on sodium valproate and none of these was showing photosensitivity, while 8 (17.77%) of 45 who were either not on any anti-epileptic or were on some other anti-epileptic drug, were showing photosensitivity. Of total 4 patients of Lennox-Gastaut syndrome one was taking sodium valproate and she was not showing photosensitivity and in the remaining three who were not on sodium valproate, one was showing photosensitivity. Patient in other syndromes were not showing photosensitivity irrespective of their medication status. Similar investigation could not be done in patients of focal epilepsy as none was receiving sodium valproate. Our study might have underestimated the prevalence of photosensitivity as patients of generalized epileptic syndromes who were on sodium valproate were not showing PPR as compared to those who were not on sodium valproate.

DISCUSSION

In this cross-sectional study done on 89 epileptic patients 13 (14.6%) patients were showing a photoparoxysmal response to IPS. The mean age of photosensitive patients was 6.65 ± 3.79 yrs with a male preponderance (16.12% vs 11.11%). The prevalence of photosensitivity in generalized and focal epilepsy was 12.5% and 23.52% respectively. The observed prevalence of photosensitivity in various syndromes was 33.33% in idiopathic rolandic epilepsy, 25% in lennox-gastaut syndrome, 18.18% in Complex focal epilepsy and 13.33% in grandmal epilepsy. None of the patient in generalized epileptic syndromes who were on sodium valproate was showing PPR in contrast to 18% in those who were not on sodium valproate.

According to published reports, a photoparoxysmal response can be elicited, in about 1.6% of healthy adults and in neuro-psychiatric disorders in general but 7.4-9.9% of adult patients with epilepsy have a photoparoxysmal response (Wolf, 1986; Buchthal, 1953 and Obeid, 1991). Higher rates of photosensitivity have been reported in children as compared to adults (Lu, 2008).

About 3-5% of 2.7 million Americans with epilepsy (approximately 1, 00,000 individuals) were photosensitive as indicated by an abnormal response to strobe lights during electroencephalography (Erba, 2006). A study done by Saleem *et al.*, (1994) in North India reported a rather lower prevalence of photosensitivity (0.6%) in epilepsy patients. In our study we observed that 13 (14.60%) of total 89 patients were showing a photoparoxysmal response to IPS. We used the current classification of

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photoparoxysmal response which also include nongeneralized grades (grade 1 and 2). Some older studies did not consider nongeneralized grades (grade 1 and 2) of photoparoxysmal response and this may be the reason of higher prevalence (14.6%) seen in our study (Wolf, 1986 and Kesteleijn-Nolst Trenite 1989). Demographic characteristics of the patient group such as age, gender, the epilepsy type and definition of PPR greatly influence the prevalence of photosensitivity. If photic stimulation is performed before age related appearance of the PPR or after remission of the electroencephalographic trait (Harding, 1997) a photoparoxysmal response may be missed in a given individual. A study by Yang Lu *et al.*, (2008) showed prevalence of photosensitivity of 31% in 566 patients of epilepsy. A lower rate in our study as compared to this study can be explained by use of higher frequencies (upto 50 Hz) , longer duration (maximum 30 sec) of intermittent photic stimulation in the study by Yang Lu *et al.*, (2008).

The mean age of patients with photosensitivity in the present study was 6.65 ± 3.79 years suggesting that photosensitivity was more common in younger age group. A study by Quirk *et al.*, (1995) showed that annual incidence of photosensitivity in all new cases of epilepsy was ~2% but rises to 10% in subjects who were 7-19 years old. A study by Hideaki Shiraishi et al (2001) showed that the incidence of PPR increased in patients till 15 years of age and suddenly decreased after 20 years of age. On the contrary, our study show a prevalence of 10.52% in 10-15 years age group but this is less than that observed in those between 1-10 years (15.71%). In our study 78.65 % patients were young (between 1 and 10 years) and this may be responsible for a observed higher prevalence of photosensitivity in younger age.

Most of the studies were showing higher prevalence of photosensitivity in females as compared to males (Wolf 1986 and Erba 2006). A retrospective study performed by Yang Lu *et al.*, (2008) revealed that PPR rate was significantly higher in females (37%) than in males (27%). In the present study no significant difference was observed between the two sexes which may be attributed to small female population in the study group and small sample size.

In our study out of 72 patients with generalized epileptic syndromes 12.5% patients were showing a photoparoxysmal response which was much less than that observed in study by Yang Lu *et al.*, (2008) (46%). Our patients underwent electroencephalography with IPS only once while in the study by Yang Lu *et al.*, (2008) patients had at least two EEG studies yielding more cases or this difference may be because of small sample size of present study.

In our study 16.66% patients with symptomatic/cryptogenic generalized epilepsy were showing photoparoxysmal response, similar to the observation made by Yang Lu *et al.*, (2008) (16%).

The higher PPR rates in our study compared to that by Wolf and Goosses, 1986 could be explained by use of current classification for grading the photoparoxysmal response which also consider nongeneralized grades (grade 1 and 2), in the present study(Wolf, (1986); Waltz, (1992) and Kesteleijn-Nolst Trenite, 2001). Many previous studies considered only generalized spikes and waves or polyspikes as PPR as the classification of photoparoxysmal response in various grades had been proposed in 1992(Wolf, 1986). Out of 66 patients of idiopathic generalized epilepsy group 12.12% patients were found photosensitive and this was much higher as compared to a survey on photosensitivity in relation to epileptic syndromes from an epilepsy center in Japan (5.6%) (Shiraishi, 2001). The higher prevalence in our study may be because of inclusion of nongeneralized grades of PPR which are also considered as a marker of photosensitivity. A higher association of photosensitivity was observed in the study by Yang Lu *et al.*, (2008) (49%) as compared to our study. This may be due to reasons already explained.

Published reports revealed a significant association of photosensitivity to Juvenile myoclonic epilepsy (30.5% in the study by Wolf and Goosses(1986); 17.4% in study by Hideaki Shiraishi *et al.*, (2001); 50% in study by Yang Lu *et al.*, (2008).The present study could not observe such association because of small number of patients with this syndrome. Similarly photosensitivity could not be assessed properly in relation to childhood absence epilepsy, myoclonic astatic epilepsy and juvenile absence epilepsy because of paucity of cases. Apart from grandmal epilepsy no other group of idiopathic generalized epilepsy was found photosensitive.

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Photosensitivity was observed in 23.52% of total 17 patients with focal epileptic syndromes (18.18% in complex focal epilepsies and 33.33% in rolandic epilepsy).

In contrast to study by Yang Lu *et al.*, (2008), present study was showing higher prevalence of photosensitivity in focal epilepsy than in generalized epilepsy (23.52% vs 12.5%). In the study by Yang Lu *et al.*, (2008) photosensitivity was more commonly associated with generalized epilepsy (46%) than focal epilepsy (20%). Further studies on a larger sample are needed to see the strength of association.

The prevalence of photosensitivity in focal epilepsy group was comparable to that observed by Yang Lu *et al.*, 2008 but much higher than the study by Wolf *et al.*, (1986) (2.7%) and by Obeid *et al.*, (1991) (0.6%). The lower value in these studies may be because of inclusion of adult patients in their studies who are known to be less photosensitive than children and adolescents. Also the observation by Wolf and Goosses (1986) and Obeid *et al.*, (1991) did not include patients with Rolandic epilepsy who in our study showed highest rate of photosensitivity (33.33%) similar to that observed in the study by Yang Lu *et al.*, (2008).

Similar to study by Yang Lu *et al.*, (2008) generalized grades of PPR were more prevalent than non-generalized grades (61.53% vs 38.46%) and also, in both the studies all photosensitive patients of symptomatic/cryptogenic generalized epilepsy were showing generalized PPR. Both the studies were showing higher rates of non-generalized PPR in idiopathic focal epilepsy than idiopathic generalized epilepsy.

In our study non-generalized grades were commoner (75%) in focal epilepsy as compared to previous studies which did not consider non-generalized grades as PPR but, study by Yang Lu showed similar results and this was explained as a contribution to multifactorial pathogenesis of focal epilepsy and that higher rates of photosensitivity is restricted to photosensitivity as an EEG trait.

None of the 22 patients with generalized epileptic syndromes who were on sodium valproate at the time of investigation for photosensitivity was found photosensitive while 18% of patients who were showing photosensitivity were either taking no anti-epileptic medication or were on some other anti-epileptic medication ($p=0.03$). This observation supports the fact that sodium valproate is effective in suppressing photosensitivity in generalized epilepsy. Yang Lu *et al.*, (2008) also observed a lower PPR rates in patients taking sodium valproate.

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