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A POSTICTAL ELECTROCARDIOGRAM (ECG) CHANGES IN CHILDREN (6 MONTHS -12 YEARS) WITH GENERALIZED TONIC-CLONIC SEIZURES (GTCS) TO PREDICT THE RISK OF FURTHER SEIZURES -A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background: The autonomic dysfunction associated with epileptiform activity can lead to cardiac arrhythmia, which may cause Sudden Unexpected Death in Epilepsy (SUDEP), the incidence of which amounts to 0.5% per year. **Aim:** To study the postictal ECG changes in children (6 months to 12 years) with GTCS and to analyse if the postictal ECG changes can predict the risk of further seizures. **Materials and Methods:** A prospective observational study was conducted. 47 children who presented with GTCS to our paediatric casualty were stabilised, and in the postictal state, a 12 lead ECG was taken. Children between 6 months and 12 years of age were included in our study. ECG parameters like Heart Rate (HR), P wave duration, PR interval, QRS duration, QRS type, QTc, ST duration, ST character, T wave character and Rhythm changes were compared between two groups of children - those who developed recurrence and those in whom seizure did not recur within 24 hours of taking ECG. **Result:** The postictal ECG of children with GTCS showed changes in the heart rate, P wave duration, QRS complex, ST segment and T wave. Children below two years of age, those with ECG showing tachycardia, axis deviation, decreased time of P wave, rS type of QRS, ST segment changes and significant T wave inversion were at increased risk of seizure recurrence. **Conclusion:** Postictal ECG can be used as a sensitive bedside tool to prompt the risk of seizure recurrence.

INTRODUCTION

The effects of seizures on the heart have been the subject of many studies in the literature. The lockstep phenomenon is cortical epileptiform activity and postganglionic cardiac sympathetic discharge in a time-locked fashion.[1] This autonomic dysfunction associated with epileptiform activity can lead to cardiac arrhythmia, which may cause Sudden Unexpected Death in Epilepsy (SUDEP), the incidence of which amounts to 0.5% per year.[2,3] The duration of seizure episodes has also been found to impact the prognosis profoundly. International League Against Epilepsy (ILAE) describes two-time points. T1 is the point of time beyond which seizures are less likely to terminate. T2 is the time limit beyond which seizures likely have long-term consequences. These time points (T1) and (T2) for Generalized Tonic-Clonic Seizures (GTCS) are 5 min and 30 mins, respectively.[4] One of the long-term consequences could be the effect on the heart. This demands an easily available, cost-effective and sensitive tool to prompt the risk of further seizures, as Electro Encephalo Gram (EEG) is most often used as a modality to identify epilepsy types and guide treatment.

The heart and brain are highly susceptible to ion channel disturbances. Thus, changes in one organ can be picked up by changes in the other.[5] It has been discussed enough in the literature that the effect of seizures and epilepsy on Electro Cardio Gram (ECG) is far beyond mere heart rate (HR) variations.[6,7] Previous studies have also shown that different brain regions have varied effects on the heart.[2] Thus, a GTCS involving all the brain regions is expected to have a uniform reflection on ECG. Looking for a preictal ECG change becomes meaningless as, practically, most children present with seizures in the ictal, postictal or Non-Convulsive Status Epilepticus (NCSE) phase. The ictal ECG is most commonly subject to artefact due to convulsions, and for a paediatrician, treating the seizure becomes more important than investigating the risk of further seizures.[8]

The primary objective was to study the postictal ECG changes in children with GTCS. The secondary purpose was to analyse if the postictal ECG changes can be used to predict the risk of further seizures.

MATERIALS AND METHODS

This prospective observational study was conducted at a tertiary-care paediatric hospital in Thanjavur medical college hospital, Tamil Nadu, India, after approval from Institutional Ethics Committee between January 2020 and December 2020.

Informed consent was obtained from the guardians of all the enrolled children. The children were not provided with any incentive to participate in the study. Children between 6 months and 12 years of age were included in our study.

Children with focal seizures, children requiring treatment with antiepileptics other than fosphenytoin/levetiracetam and those with known congenital heart disease were excluded from the study.

A Child presenting with GTCS was defined as the one who presented to our PREM (Paediatric Emergency Room) with active convulsions and had established status epilepticus not responding to benzodiazepines, the first line antiepileptics but got controlled with the second line antiepileptics being either fosphenytoin or levetiracetam. The postictal state was taken as 45 minutes within the termination of active convulsions. Recurrence was considered as GTCS occurring within 24 hrs of taking the ECG.

All the 47 Children who presented with GTCS were stabilised. Active convulsion was controlled with two doses of Benzodiazepine and one antiepileptic, either fosphenytoin or levetiracetam. NCSE was clinically ruled out, and the children took a twelve-lead ECG in the postictal state. The child's temperature while taking the ECG was also noted. ECG parameters were read, such as HR, P wave duration, PR interval, QRS duration, QRS type, QTc, ST duration, ST character, T wave character and Rhythm changes. Postictal ECG changes were compared between the two groups of children, i.e., those who developed recurrence and those in whom seizure did not recur within 24 hours of taking ECG.

The data was collected on a structured case record form. Data was represented as percentages and number of cases. The data was entered in MS office excel 2010 and coded. Categorical data between the groups were compared with Pearson's chi-square tests. Significance was defined by P-values less than 0.05 using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Science Inc., Chicago, IL).

RESULTS

The flow of the study is shown in Figure 1. Of the 47 children who presented to our pediatric casualty with GTCS, 34% developed further seizures (Figure 2). Febrile seizure was the most common cause, amounting to 63.8%.

An increased temperature at the time of recording ECG was associated with increased heart rate ($p=0.024$). The duration of the P wave and PR interval was noticed to be decreased by 12.8% and 59.6%, viz., normal in rest, and none showed an increased duration. The QRS showed a predominant RS pattern (47%), with the RS pattern in 8 children and the RS pattern in 17. The QRS duration was normal except for one above five years of age. The corrected QT interval was normal in a maximum number of cases and prolonged in 6.4%. ST segment showed changes of 27.6%. ST duration was normal in all cases. T wave showed abnormalities in 17% of children.

Postictal ECG of those children who developed seizure recurrence showed significant ST segment changes, T wave inversion, decreased duration of P wave, and all those with significant axis deviation had seizure recurrence. Children below two years of age with postictal ECG showing tachycardia and RS type of QRS were at an increased risk of seizure recurrence.

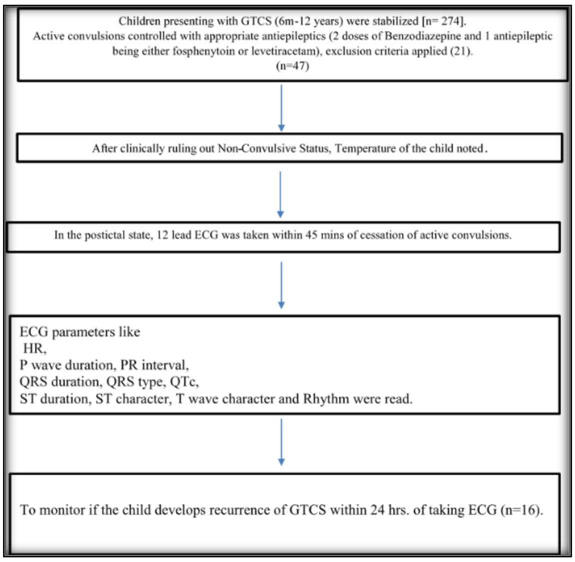

Figure 1: Study flow chart

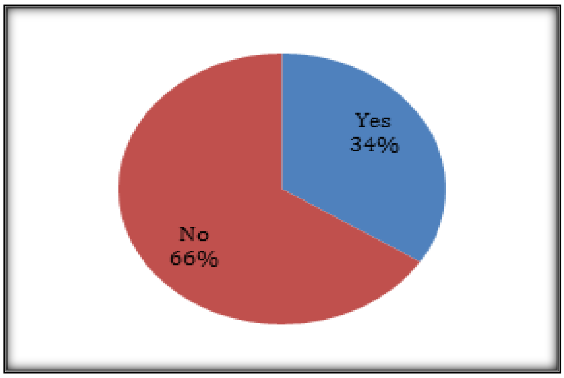

Figure 2: Incidence of seizure recurrence and non-recurrence among the study population (n= 47)

Table 1: Comparison of seizure recurrence with p duration in ECG between the groups (n=47)

Recurrence	P Duration		Total	P-value
	Normal	Decreased		
Yes	11 (68.8%)	5 (31.3%)	16 (100%)	0.006*
No	30 (96.8%)	1 (3.2%)	31 (100%)	
Total	41(87.2%)	6(12.8%)	47 (100%)	

Table 2: Comparison of seizure recurrence with axis changes in ECG between the groups (n= 47)

Recurrence	AXIS			Total	P-value
	Left	Normal	Right		
Yes	1 (6.3%)	13 (81.3%)	2 (12.5%)	16 (100%)	0.045*
No	0	31 (100%)	0	31 (100%)	
Total	1 (2.1%)	44 (93.6%)	2 (4.3%)	47 (100%)	

Table 3: Comparison of ST character in ECG with seizure recurrence between the groups (n= 47)

Recurrence	ST character			Total	P-value
	Normal	Depressed	Elevated		
Yes	6 (37.5%)	7 (43.8%)	3 (18.8%)	16 (100%)	0.001*
No	28 (90.3%)	2 (6.5%)	1 (3.2%)	31 (100%)	
Total	34 (72.3%)	9 (19.1%)	4 (8.5%)	47 (100%)	

Table 4: Comparison of t-wave changes with seizure recurrence between the groups (n= 47)

Recurrence	T wave		Total	P-value
	V1 – V3	> V4		
Yes	10 (62.5%)	6 (37.5%)	16 (100%)	0.007*
No	29 (93.5%)	2 (6.5%)	31 (100%)	
Total	39 (83%)	8 (17%)	47 (100%)	

DISCUSSION

Around 45% of all children and 53.3% of those with febrile seizures had postictal tachycardia. Our results concord with the study by M.Zilmans et al., in which 73% of seizures showed ictal tachycardia.[8] Fritz Leutmezer et al., in their research, also demonstrated ictal tachycardia in 86.9% of seizures.[9] An increased temperature when taking an ECG was associated with an increased heart rate (p=0.024).

Children with increased temperature and tachycardia were at risk of recurrence of seizures. (p=0.01). In febrile seizures, postictal tachycardia (87.5%) increased the risk of further seizures. Children below two years of age had more chance of other seizures (p=0.028). The cause of the seizure showed no relation to recurrence risk. Most children with recurrent seizures were in a state of sleep before seizure onset (39.1% against 29.2% that were awake and developed recurrent seizures).

A decrease in the P wave duration increased the risk of further seizure. This was in contrast to studies by Claire Ufongene et al. and Asadollahi M.et.al., where there was an increase in PR interval noted in cases of epilepsy.[6,10] [Table 1]. In all children with axis deviation, seizures recurred (p=0.045) [Table 2]. The PR interval, QRS duration, and QTc interval had no statistically significant correlation among those with or without recurrent seizures. This was not the result observed in the study by Marian Asadollahi et al., who observed short QRS and long QTc in epileptic children.[10]. RS type of QRS was noted in most cases (50%) of recurrent seizures. Those children with ST-segment changes were at risk of seizure recurrence-43.8% showed ST depression, and 18.8% showed ST elevation (p=0.001) [Table 3]. In febrile seizures, all cases with ST depression had a seizure recurrence (p=0.007). Claire Ufongene et al. also demonstrated preictal and ictal ST changes.[6]. Significant T wave inversion often led to another seizure episode

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(p<0.0001). These changes were also reported in the study by Christian Opherk et al.[11] [Table 4].

The decrease in duration of the P wave has a positive correlation with both lesser age (p=0.004) and an increase in temperature and heart rate, thus the recurrence risk (p=0.003). It can be interpreted that the lesser the age, more the temperature, and the higher the heart rate. Higher the heart rate lesser the PR interval or P wave duration.

The impact of age on ECG changes is that ST segment changes and T wave inversion noted in children below five years of age are likely to have increased recurrence risk. (p=0.001 and <0.0001). The cause of the seizure did not impact the ECG changes. The AED taken did not affect ECG, as was shown in the study by Marian Asadollahi et al.[10]

T wave inversion beyond lead III and state of sleep before seizure onset was associated with increased recurrence risk. These results align with the study by Christian Opherk et al., who also reported that seizures arising during sleep have more chance of ECG changes.[11]

Most literature studies retrospectively integrated ECG changes with EEG-recorded seizure activity. The temperature of the patient was never taken into account. Our study recorded the child's temperature when taking ECG and analyzed the effect of temperature on different ECG parameters. Also, in previous studies, more than one seizure from a patient has been taken into consideration, which is more likely to exaggerate the number of the specific ECG findings and underestimate that of others. Our study considered only the first representative seizure per child. Most were single lead ECGs where assessing T wave inversion and ST changes were impossible. Though around 30 studies discussed ECG in seizures, only seven studies have examined the same in the paediatric age group. Thus, the studies on pediatric age group and the pattern of ECG changes in different age groups is meagre.

The disadvantages of this study are that EEG was not available in hand to correlate the ECG changes and definitively distinguish ECG changes due to the postictal phase and NCSE. The preexisting or underlying cardiac conditions not diagnosed earlier could have accounted for ECG changes. But this is less likely, as ECG is more sensitive to changing the order of ischemia>rhythm disturbances> structural abnormalities. The other causes of seizures, like electrolyte disturbances causing ECG changes, can introduce bias. There was no baseline heart rate or other ECG parameters of the particular child in hand to compare the changes. Incorporation of these into future studies can improve the outcome of this research

CONCLUSION

The study has shown that postictal ECG can be used to predict the risk of further seizures in GTCS. This study can also be extrapolated to seizure detection in newborns, where subtle seizures are challenging to monitor and respond to promptly, and may be incorporated into seizure detection devices in NCSE and paralyzed patients.[12,13] Also, it can be proposed to be a readily available bedside investigation modality for the proposed purpose.

What Is Already Known?
ECG changes occur in a seizure's preictal, ictal and postictal phases, and epileptic patients have specific heart rate abnormalities, T wave, ST segment, PR and QTc interval.

What Does This Study add?
Postictal ECG changes can predict the risk of recurrence of seizures within 24 hrs.

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