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The Relationship of Interictal Epileptic Discharges with Duration of Illness in Epileptic Patients

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Abstract

Background Epileptic discharges generally initiated at specific locations and spread after time in preferred directions along specific pathways, this spread will simultaneously change the dynamics of system in which it spread and cause epileptic destabilization of neuronal circuits.

Objectives To study the relationship between single focal epileptic discharge or multiple focal epileptic discharges and the duration of their disease.

Methods Ninety six epileptic patients with partial epilepsy and mean age of 12.5±7.5 years were studied, no one of patients receive antiepileptic drugs or were on irregular treatment. They had been divided according to duration of illness into two groups; those with more than one year illness and those with less than one year illness. Electroencephalography recording were obtained via 10-20 system using bipolar and referential montage with a thirty minutes record for each patient, accordingly. Patients were divided into those with single focal epileptic discharge (unifocal) & those with multifocal (multiple focal) epileptic discharge.

Results A significant difference in mean duration of illness between patients with unifocal and multifocal epileptic discharge were found. Those with multifocal epileptic discharge show higher mean duration of illness (17.8±9.05) months as compared to those with unifocal epileptic discharge (9.1±6) months. Significant positive linear correlation was found (P = 0.01), and the duration of illness increased more in patients with multifocal epileptic discharge.

Conclusion We found that longer duration of exposure to epileptic discharge could lead to generation of new foci not exist previously and that may possibly be due to kindling phenomena and triggering more spread of epileptic discharge.

Key words Epileptic discharge, Kindling phenomena, electroencephalography.

List of Abbreviation: AEDs = Antiepileptic drugs, EEG = Electroencephalography, ED = Epileptic discharge, MRI = Magnetic resonance imaging, CNS = central nervous system.

Introduction

Brain regions vary considerably in their capacity to participate in different forms of epileptic activities. Epileptic discharges generally initiated at specific locations and spread after time in preferred directions along specific pathways [(1)]. In human as well as in experimental animals, cortical epilepsy can begin with abnormal activity at seizure focus followed by synchronization and subsequent spread through the cortex [(2)].

The process of spread of epileptic discharges in central nervous system (CNS) can occur as a propagation of signals in neuronal network or as a process of dynamic changes in neuronal circuits and nets [(3)]. As the spatial extent of the neuronal population involved in seizures is

increased so the question raised weather this spread causing generation of new focuses were not exist before seizure onset [1].

Some researchers suggest that the after discharge will spread in base of space and time from one area like hippocampus to adjacent areas like entorhineal cortex. This spread will simultaneously change the dynamics of system in which it spread and causing epileptic destabilization of neuronal circuits [4].

Aside from the triggers that may potentially induce an epileptic seizure, the spread of epileptic discharge in human is still under debate. Since then, much work has been done in utilizing kindling and its proposed effects on neural plasticity, one of the fundamental properties of neurophysiology [5]. Since neural plasticity is a feature considered universal throughout the CNS, this suggests that changes prompted by kindling within one part of the CNS may occur throughout the body as well [6]. With this in mind, many have viewed kindling as most notably affecting the neuronal cells of the hippocampus and via a Hebbian Learning mechanism (synaptic strength is increased the more frequently it is active), these cells become altered permanently [7], this may be the mechanism by which spontaneous seizures are generated. Although kindling-induced alterations are seen most strikingly in the hippocampus and the limbic system, repeated stimulation of the pathways of the limbic, cortical, subcortical and brain stem regions (either chemically or electrically) induces a progressive sequence of long-lasting cellular and molecular alterations at all levels of biological organization in neural circuits, from gene transcription to patterns of neuronal connectivity [8]. Therefore, the objective of this research was to study the effect of kindling mechanisms on spreading of epileptic discharges in human cerebral cortex by one way or another [6,8].

Methods

This retrospective study was conducted in Al-Sader Teaching Hospital in Basra in the period from march/2012 up to April/2013 designed to evaluate the epileptic discharge in a group of ninety six patients with partial epilepsy with an age range from 5-20 years and mean age (12.5±7.5years). They were divided according to duration of illness in to two groups:

A: Those with duration of illness twelve months or less.

B: Those with duration of illness more than twelve months.

No one of patients had history of head trauma, meningitis, encephalitis or chronic illness. We included only patients with partial epilepsy; those with Absence, myoclonic or tonic clonic seizure were excluded. All patients show normal neurological exam. Patients were on no treatment or on very irregular treatment. Patients (or the relatives of children patients) were informed about the aim of study and their acceptance obtained. This work is in agreement with the medical ethics provided from the ethical committee in Basra collage of medicine and the Department of Training & Improving Skill - Research & Educational facilities in Al-Sader Teaching Hospital.

A digital electroencephalography (EEG) machine used to examine all patients according to standard 10-20 system, two montages used to read each record, a bipolar and referential montage, and the EEG record obtained after thirty minutes of exam carefully interpreted and patients divided according to EEG results into two groups:

1. Patients with unifocal (single focal epileptic discharge).
2. Patients with multifocal (multiple focal) epileptic discharge.

Data analysis was done by using SPSS version 20 computer software. Descriptive statistics for all data of each set was expressed as mean ± 2SD. The difference in mean duration of illness between groups was assessed by independent sample t-test, $P < 0.05$ considered statistically significant, spearman test used to assess the correlation between duration of illness and interictal epileptic discharge.

Results

Out of the total 96 patients included in the study, 54 (56.3%) were females and 42 (43.8 %) were males, no significant difference found in epileptic discharges (ED) weather unifocal or multifocal between male and female as illustrated in table 1.

Table 1. The sexual distribution of patients with unifocal and multifocal epileptic discharges

Epileptic Discharges	Males		Females		Total
	No.	%	No.	%	
Unifocal	8	19	15	27.8	23
Multifocal	34	81	39	72.2	73
Total	42	100	54	100	96

Twenty three patients (23.95%) were found to have unifocal ED and seventy three (76.05%) have multifocal ED (Table 2).

Table 2. Frequency distribution of the two study groups according to epileptic discharge

Epileptic Discharges	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Unifocal	15	34.9	8	15.1	23	23.95
Multifocal	28	64.9	45	84.9	73	76.05
Total	34	100	53	100	96	100

Patients in group A were further subdivided in to two groups; group A1: Those with duration of illness ≤ 6 months and A2: Those with duration of illness from >6 months up to 12 months. According to these classifications we found that patients with multifocal ED were more in group A2 than in group A1 (Table 3).

Table 3. The number and percentage of unifocal and multifocal epileptic discharge in group A1 and A2 patients

Epileptic Discharges	Group A1		Group A2		Total
	No.	%	No.	%	
Unifocal	10	62.5	5	18.5	15
Multifocal	6	37.5	22	81.5	28
Total	16	100	27	100	43

On taking the patients as a whole or separately into group A and B, the mean duration of illness was significantly longer in those with multifocal as compared to those with unifocal epileptic discharge as illustrated in table 4.

Table 4. The mean duration of illness in patients with unifocal and multifocal epileptic discharges

ED	Group A		Group B		Group A & B	
	N	mean ±SD	N	Mean±SD	N	mean±SD
Unifocal	15	5±2	8	16.6±2.77	22	9.09±6
Multifocal	28	8±2.4	45	23.9±5.5	73	17.8±9.05

ED = epileptic discharges, *P* = 0.01 (for all groups)

For patients in group (A2), the mean duration of illness was significantly longer (*P* = 0.01) in those with multifocal epileptic discharge versus those with unifocal epileptic discharge, whereas there was no difference in the mean duration of illness in those patients belongs to group A1 (Table 5).

Table 5. Comparison of epileptic discharges in between group A patients

Epileptic Discharges	Group A		Group B	
	No.	mean±SD	No.	mean±SD
Unifocal	10	4±1.6	5	7.4±5.5*
Multifocal	6	4±1.3	22	8.95±1.12

* *P* = 0.01

A significant positive linear relation (*P* = 0.01) was found between mean duration of illness and number of ED (Fig. 1).

Discussion

The results of this study showed that patients with multifocal epileptic discharges have longer duration of illness as compared to those with unifocal epileptic discharge. Which suppose that the development of new epileptic foci is time related and as the brain exposed to epileptic activity for long time their development will be more possible [19].

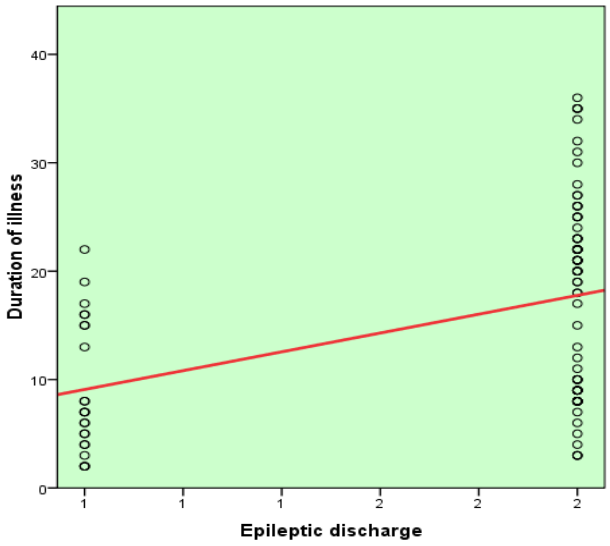

Fig. 1. Correlation between epileptic discharges and duration of illness in epileptic patients

The data of this study also showed a positive relation between mean duration of illness and the development of multifocal ED.

The outcomes obtained in this study agree with findings of other researchers who examined the development of mirror foci in patients who had medically refractory partial seizures secondary to brain tumors that were presumed to represent a single primary epileptogenic lesion[6].

A longer duration of epilepsy and more number of epileptic seizures prior to surgery correlated with failure of these secondary epileptogenic regions to resolve postoperatively.

The mechanisms beyond this spread still under dispute but the most prevalent is the kindling phenomena which assumes that repeated subconvulsive stimulation of a site in one hemisphere leads to increased excitability and abnormal electrical activity at that site and at the homologous site in the opposite hemisphere which will progress through a complex neuronal connectivity [3,11].

These secondary epileptic foci can be developed in patients with partial epilepsy due to kindling like mechanisms and the duration of exposure to such kindling influences can determine whether secondary epileptogenesis become irreversible [9,10].

Also many studied series clearly demonstrated a positive relation between longer duration of an epileptogenic condition prior to medical control and a poorer prognosis [9].

In the study that held by Blume (2007)[10], about secondary bilateral synchrony and its EEG correlate, he found that 91% of patients with duration of illness more than two years have the phenomena of secondary bilateral synchrony which was explained in view of complex interaction of multiple potentially epileptogenic regions and since some forms of epilepsy are progressive [12]; so this progression can be halt by AEDs and prevent continuous sub-threshold activation of adjacent neuronal network.

Furthermore, other readings assume that kindling mechanisms cause progression of epileptic symptoms with time and might interfere with normal cerebral activity.

Since seizure may predispose to further seizures so effective treatment maybe important to prevent evolution into chronic and more intractable multifocal epilepsy [5,7,6].

In conclusion, the duration of epilepsy is very important to determine the spread of epileptic discharge from one focus to other foci in the brain, and since multiple focal epilepsy associated with more adverse effects on brain functions (and development in children), so early treatment of epilepsy is essential to prevent the change of unifocal to multifocal epilepsy.

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Conflict of interest

There is no conflict of interest that could influence the objectivity of the research reported.

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