AUTOANTIBODIES IN PATIENTS WITH EPILEPSY

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ABSTRACT

Background: Autoimmune processes have been hypothesized as a potential cause of undefined etiologically epilepsies ***Objectives:*** our work aimed to study the presence of autoantibodies in well defined groups of patients with epilepsy which may offer novel tools for the diagnosis and treatment. ***Methods:*** The study was carried out on 120 subjects (80 epileptic patients divided to tow groups, 40 patients on antiepileptic medications group A, and 40 patients newly diagnosed without medications group B, and 40 normal controls). They were subjected to: Clinical assessment, inter-ictal EEG, and detection of anticardiolipin and antinuclear antibodies in sera of the subjects. ***Results:*** a statistically significant difference between two patient groups and the control group as regard serum level of +ve aCL IgG 25% in group A, 30% in group B, IgM 35% in group A, 20% in group B and ANA 10% in group A, 15% in group B. We found aCL antibodies more in patients on phenytoin treatment 75% and all positive ANA cases on carbamazepine monothrapy100%. No statistically significant association was found between moderate aCL IgG , low aCL IgM and ANA results and frequency of seizures and between EEG changes and aCL and ANA results. ***Conclusion:*** There may be a relationship between epilepsy and the presence of ANA and/or aCL antibodies and that an immune dysregulation may be present in epileptic patients. These autoantibodies could suggest alternative therapeutic approaches in difficult cases or in patients not responding to currently used conventional AEDs.

Key Words: autoantibodies, epilepsy

INTRODUCTION

Epilepsies are common heterogeneous neurological disorders, which represents a major health problem. Structural, metabolic and genetic causes are regularly being identified, however the majority of epilepsies are classified as having an unknown cause [1,2]

Autoimmune processes have been hypothesized as a potential cause of these etiologically undefined epilepsies [(3)], with an accumulating evidence that specific neuronal autoantibodies with pathogenic potential may be present in a subset of epileptic patients[4,5]

Many previous studies demonstrated that, different autoantibodies among those patients may be directed against certain brain components or interact with ion-gated channels or neurotransmitters and therefore affect the stability of neuronal membranes or lowering seizure threshold[6,7,8]

Recently it has been shown that some patients with these serum autoantibodies are often refractory to standard antiepileptic drugs and in contrast may respond well to immunomodulatory therapies[2]

The possibility that epilepsy per se might be associated with immunologic alterations and the production of auto-antibodies has not been addressed and the origin and effects of the antibodies remain unclear, so our work aimed to study the presence of autoantibodies in well defined groups of patients with epilepsy which may offer novel tools for the diagnosis and treatment.

SUBJECTS AND METHODS

This study was conducted at the Neurology Department Zagazig University Hospitals with the approval of Ethics Committee of our University. Our patients were selected as 40 epileptic patients on antiepileptic medications. Their ages were ranged form 5 to 47 years, they were 24 (60%) males and 16 (40%) females **(Group A)** and 40 patients with new onset

seizure disorders before starting medications. Their ages were ranged form 8 to 3 8 years, they were 16 (40%) males and 24 (60%) females **(Group B)**, they were diagnosed as having epilepsy based upon history taking, from an eyewitness and from the patients and electroencephalogram(EEG)studies and its type was classified according to the recommendation of International League Against Epilepsy(ILAE) [9]

In addition to a control group which including 40 healthy volunteers matching with the patients age and sex. The ages were ranged from 8 to 39 years, they were 26 (65%) males and 14 (35%) females.

We excluded patients with immune system, connective tissue or rheumatic diseases, patients with history of intracranial operation, cerebrovascular disorders , meningoencephalitis and demylinating illness, patients with systemic failure as respiratory, renal, hepatic and cardiac and patients with psychiatric disorders.

After taking written informed consent, all patients and control were subjected to:

(1)Clinical assessment,

(A) Detailed history of epilepsy from the patient, their mothers and their relatives and from an eyewitness to describe the seizure in detail according to the special sheet of epilepsy and this is consistent with current guide lines of the ILAE[(9)],which included the following items :onset of seizures ,its frequency per month which divided into <1 seizure /month,1-3 seizures/month,≥4 seizures/month[10], seizure type, duration, aura, ictus description, post ictus state and history of status epilepticus.

(B) Complete general and neurological examination: to detect any neurological or psychological abnormalities.

(2) Computerized inter-ictal EEG was done for all patients at the Neurology Department, Zagazig University Hospitals, using a REEGA VIII minihuit-TR, eight channels apparatus Produced by ALVAR electronics. Electrodes were arranged according to the international 10-20 system of surface electrode placement using mono and bipolar montages

(3) Radiological assessment: Computed Tomography (CT scan) and MRI brain to exclude any underlying pathology.

(4) Laboratory Investigations:

(A) Routine laboratory investigations at time of examination (complete blood count, erythrocytic sedimentation rate, serum electrolytes, fasting and postprandial blood glucose level, liver and kidney functions and thyroid function).

(B) Special laboratory investigations(including anticardiolipin (aCL) and antinuclear antibodies(ANA) tests.

Specimen collection and preparation :

Five ml venous blood were obtained from all participants, the serum separated from the cells by centrifugation after clot formation .

(a) Anticardiolipin antibody test using REAADS anti - cardiolipin IgG/ IgM Semi - Quantitative test kit

The test was performed as an indirect using enzyme linked immurosorbant assay (ELIZA) the expected values:

Normal range: values > 10 but ≤ 20 GPL or MPL were considered low positive results, while values > 20 GPL or MPL were considered moderately positive[11,12]

(b) Antinuclear antibody test (ANA)

Using indirect fluorescent antibody (IFA) procedures which performed by indirect immunofluorescene (IIF) technique.

Any nuclear staining was considered a positive results and the titres and the staining patterns of the positive sera were determined[11,12]

STATISTICAL ANALYSIS

The data were tabulated and statistically analyzed using Epi-INFO (2000) and SPSS Version 15 soft were package[13] The relationship between categorical variables was tested by Chi-square test . The relationship between continuous variables was calculated by "t" test and ANOVA. P

values of 0.05 or less were considered statistically significant.

RESULTS

I. 1-Clinical Results: This study conducted on 120 subjects, they were 80 epileptic patients, their mean age 22 ± 11.8 years and 40 healthy volunteers their mean age 19 ± 8.6 years. In the group A(40 patients) their ages were ranged form 5 to 47 years (M±SD =22±11.8), they were 24 (60%) males and 16 (40%) females and In the group B (40 patients) with new onset seizure disorders before starting medications their ages were ranged form 8 to 3 8 years (M±SD = 19±8.6), they were 16 (40%) males and 24 (60%) females

2-Seizure Description:

In comparison of the two patient groups, we found a statistically significant difference regarding seizure frequency, with more frequent seizures in group B than A, while no statistically significant difference was found between them as regards age of seizure onset, we found that the mean age of seizure onset in group A was 13.6 ± 8.4 years and in group B was 13.3 ± 9.7 years, duration in group A was 8.4±5.1 years and in group B was 5.7±4.6 years and positive family history in group A was 25% and in group B was 40%. As regard types of seizures, prodroma, aura, time of occurrence of seizures, there were no statistically significant difference between them, also EEG finding in the two patient groups showed no statistically significant difference

II. Inter –ictal EEG Results: No statistically significant association was found between EEG changes and aCL and ANA results

III. Laboratory Work:

we found a statistically significant difference between two patient groups and the control group as 24 patients in group A with +ve aCL antibodies [10 patients (25%) with IgG class and 14 patients (35%) with IgM class], while in group B we found 20 patients with +ve aCL antibodies [12 patients (30%) with IgG class and 8 patients (20%) with IgM class]. As regard ANA, it was +ve in 4 cases (10%) of group A and in 6 patients (15%) of group B, while all subjects in the control group had negative aCL and ANA autoantibodies Table (1)

We found 8 females (20%)of group B and 2 females (5%) of group A had positive aCL IgG (female number in group B was more than that of group A) , and this was statistically significant ,while no statistically significant difference was found between the two groups as regard aCL IgM and also ANA test results

As regard low titre IgG, we found 4 patients (10%)in group A were <15 years and 6 patients (15%) were >15-25 years and this was statistically significant ,while regarding the positive ANA , no statistically significant difference was found between ANA results and age of onset of seizures

In patients with low titre a CL IgG ,4 patients (10%) of group B had≥ 4 seizures per month ,4 patients (10%)of group B had 1-3 seizures per month while 6 patients (15%) of group A had 1-3 seizures per month and 2 patients (5%) of group A had <1 seizure per month and this was statistically significant .

- In patients with moderate a CL IgM ,5 patients (12.5%) of group A had <1 seizure per month, 1 patient (5%) of group A had ≥4 seizures per month ,while 2 patients (5%) of group B had 1-3 seizures per month and this was statistically significant .

No statistically significant association was found between moderate aCL IgG , low aCL IgM and ANA results and frequency of seizures (Table2).

In group A, 2 patients (5%) with partial seizures and 8 patients (20%)with generalized seizures had aCL IgG , 1 patient (2.5%) with partial and 13 patients (32.5%)with generalized seizures had a CL IgM and 3 patients (7.5%) with partial and 1 patient (2.5%) with generalized seizures had positive ANA

In group B:12 patients (30%) with generalized seizures had a CL Ig G , 1 patient (2.5%) with partial and 7 patients (17.5%)with generalized seizures had aCL IgM and 4 patients (10%) with partial and 2 patients (5%) with generalized seizures had positive ANA (Table 3).

Anti-epileptic treatment: No statistically significant association was found between drug treatment to aCL IgG & IgM and ANA results regarding monotherapy (14 patients) and polytherapy (14 patients) (Table 5).

We found 16 patients on carbamazepine, 22 patients on valproic and 8 patients on phenytoin , aCL antibodies more in patients on phenytoin treatment (6 pattients) and all positive ANA cases on carbamazepine monothrapy (4 patients) (Table 6).

Table (1): Comparison of the results of aCL (IgG & IgM) and ANA between both patient groups (A, B) and control.

Autoantibodies		Group A N=40		Group B N=40		Control N=40		X^2	P
		No	%	No	%	No	%		
aCL	IgG class	10	25	12	30	0	0.0	13.8	0.001*
	Low titre	8	20	8	20	0	0.0	9.23	0.009*
	Moderate titre	2	5	4	10	0	0.0	4.21	0.12
	IgM class	14	35	8	20	0	0.0	16.47	0.001**
	Low titre	8	20	6	15	0	0.0	8.41	0.014*
	Moderate titre	6	15	2	5	0	0.0	7.5	0.02*
+ve ANA		4	10	6	15	0	0.0	6.11	0.04*

X^2=Chi square P≤0.05(significant) P>0.05(non significant)

a CL Anticardiolipin antibodies ANA antinuclear antibodi

Table (2): Relation of aCL (IgG& IgM) and ANA results with the frequency of seizures among two patient groups.

Frequency of seizures /month	**aCL**																+ve ANA			
	IgG								**IgM**											
	Low titre				**Moderate titre**				**Low titre**				**Moderate titre**							
	Group A No=40		Group B No=40		Group A No=40		Group B No=40		Group A No=40		Group B No=40		Group A No=40		Group B No=40		Group A No=40		Group B No=40	
	No	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
< 1	2	5	-	-	-	-	-	-	6	15	1	2.5	5	12.5	-	-	-	-	1	2.5
1-3	6	15	4	10	1	2.5	3	7.5	1	2.5	4	10	-	-	2	5	2	5	1	2.5
≥ 4	-	-	4	10	1	2.5	1	2.5	1	2.5	1	2.5	1	2.5	-	-	2	5	4	10
X^2	6.4				0.09				5.19				8.0				1.67			
P-value	0.04*				0.75				0.07				0.018*				0.43			

Table (3): The comparison of seizure type in relation to aCL and ANA test results.

Autoantibodies	Group A No=40												Group B No=40											
	Simple partial		Complex partial		C.P with 2ry general.		Generalized						Simple partial		Complex partial		C.P with 2ry general.		Generalized					
							Tonic-clonic		Atonic		Myo-clonic								Tonic-clonic		Atonic		Myo-clonic	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
aCL IgG	1	2.5	1	2.5	-	-	6	15	1	2.5	1	2.5	-	-	-	-	-	-	7	17.5	5	12.5	-	-
aCL IgM	-	-	-	-	1	2.5	8	20	4	10	1	2.5	-	-	-	-	1	2.5	5	12.5	1	2.5	1	2.5
+ve ANA	2	5	1	2.5	-	-	1	2.5	-	-	-	-	2	5	2	5	-	-	2	5	-	-	-	-

Table (4): The comparison of aCL (IgG & IgM) and ANA results in relation to EEG changes.

Autoantibodies	EEG	Group A	Group B	X^2	P
aCL IgG	Normal	-	2	0.51	0.47
	Abnormal				
	- Focal	2	1	0.0	1.0
	- Focal with 2ry generalization	-	2	0.51	0.47
	- Generalized	8	7	0.08	0.77
aC L IgM	Normal	1	2	0.0	1.0
	Abnormal				
	- Focal	-	-	0.0	0.0
	- Focal with 2ry generalization	3	1	0.26	0.6
	- Generalized	10	4	2.05	0.15
+ve ANA	Normal	-	-		
	Abnormal				
	- Focal	2	2	0.0	1.0
	- Focal with 2ry generalization	1	2	0.0	1.0
	- Generalized	1	2	0.0	1.0

Table (5): The comparison of drug treatment in relation to aCL and ANA test results.

autoantibodies	Monotherpay		Polytherapy		X^2	P
	No	%	No	%		
aCL IgG	4	10.0	6	15.0	0.46	0.49
aCL IgM	6	15.0	8	20.0	0.35	0.55
+ve ANA	4	10	-	-	1.4	0.23

Table (6): Number and percentage of patients with positive autoantibodies in relation type of treatment (group A).

Autoantibodies	Carbamazepine No=16		Valproic No=22		Phenytoin No=8	
	No	%	No	%	No	%
aCL	3	18.75	1	4.5	6	75
+ve ANA	4	100	-	-	-	-

DISCUSSION

Epilepsy is a common neurological disorder which associated with significant co-morbidity with other diseases including disorders with proven or suspected autoimmune origin[2,5]

The aetiology of epilepsy in the majority of patients remains undefined but there is evidence for an autoimmune basis in some patients[1,7] Recent studies have suggested that aberrations immune mechanisms may be involved in the pathogenesis of a number of epileptic syndromes either by direct effect of epilepsy on immune system[14,15] or by effect of antiepileptic drugs on the serum immunoglobulin levels[3,16].

The objective of this study was to examine the presence of autoantibodies (aCL and ANA) in patients with epilepsy, which may offer novel tools for the diagnosis and treatment.

In our study aCL IgG was a significantly positive in the epileptic patients especially newly diagnosed(group B) patients(30%) and (25%)group A than the controls with more cases of low titre IgG in both group(8 patients in each group),while moderate titre cases were more in group B{ 4 cases (10%)} than group A { 2 cases (5%)} ,while aCL IgM antibodies as more in group A , 14 (35%) than group B, 8 cases (20%) with low titre more than moderate titre (8 cases to 6 cases)respectively in group A and (6 cases to 2 cases) respectively in group B. Our results were statistically significant when compared with the control ($p<0.05$).

These findings were near to Peltola et al. [11] as they found that aCL IgM class antibodies were +ve in 51 patients, Low titre in 28 patients and moderate titre in 23 patients , while IgG class anticardiolipin antibodies were +ve in 11 patients , Low titre in 8 patients and moderate titre in 3 patients and these results in epileptic patients under treatment in comparison to our first group of our results. While in newly diagnosed epileptic patients without treatment, Peltola et al. [11] found that 11 patients had +ve IgG class a CL with low titre in 9 patients and moderate titre in 2 patients , while IgM a CL were +ve in 17, low titre in 13 patients and moderate titre in 4 patients, also Pardo et al. [17] , Eriksson et al. [18] and Verotti et al. [19] were concluded a significantly higher prevalence of antiphospholipid antibodies which detected in 43% of 36 epileptic patients , most of them with aCL antibodies IgM subtype while in In a study carried out by Cimaz et al. [12], 10.6% were positive for a CL , IgG class were found in 7.7%, IgM class in 1.4% and both isotypes in 1.4% and in

Ranua et al. [10] study, only 4.5% of patients and 5% of the reference subjects were aCL +ve and the surprise was that control subject had more +ve a CL than epileptic patient with no statistically significant difference in the presence of aCL between patients and control while in a most recent study Barrada et al. [20] found that 12% of epileptic patients were +ve for aCL IgG while both the patients and the control were -ve for aCL IgM subtypes

In our study ,all the control subjects were with -ve aCL , like The study of Markic et al. [21] who found only 3 cases 7.5% in 40 epileptic children were +ve aCL and the control group was -ve while Peltola et al. [11] found 7% of control had +ve IgG a CL with low titre in 7% and moderate titre 1%, also 7% of control had +ve IgM aCL with low and moderate titre was 4% for each, Debourdeau et al. [22] as well found that 4% had +ve aCL in epileptic patients and 7% in controls.

In accordance with Verrot et al. [23]Peltola et al. [11], Verotti et al. [19], and Ranua et al. [10], we found 10% of patients in group A and 15% cases in group B had +ve ANA, with a statistically significant difference in comparison to control group ($p<0.05$)while in a more recent study conducted by Barrada et al. [20] ,they found 18 patients (72%) and 5 subjects (50%) of the control had +ve ANA.

As regards the relation between the frequency of seizures to serum level of aCL autoantibodies, in patients with low titre aCL IgG we found 10% of patients in group B had >4 seizures per month and another 10% patients had 1-3 seizures per month ,while 15% of patients in group A had 1-3 seizures per month , this means that prevalence of a CL IgG class increased with increased frequency .

In contrast to our results ,Eriksson et al[18]. and Barrada et al[20] **.** found no statistically significant correlation between seizure frequency and the presence of any antibodies, while Liimatainen et al[5] found high prevalence of IgG class antibodies in patients with recent seizures compared with the patients with controled seizures . Ranua et al[10] **.** as well stated that poor seizure control was associated with increased aCL antibodies among the epileptic patients.

Experimentally provoked seizures in rodents and spontaneous seizures in human induce many proinflammatory mediators such as cytokines that may potentiate B-cell production of autoantibodies[5,24]

We found that positive ANA cases were associated with increased seizures frequency, 2 cases (5%) of group A and 4 cases (10%) had ≥ 4 seizures per month ,2 patients (5%) of group A and 1 patient (2.5%) of group B had 1-3 seizures per month. These results were in accordance with Eriksson et al. [18] and Ranua et al. [10] who stated that suboptimal seizure control tended to increase the presence of ANA (patients with >1 seizure per month tended to have an increased prevalence of ANA (22.3%) compared to patients with <1 seizure per month (19.5%). Also Debourdeau et al[22] stated that ANA tended to be more frequent when patients had more than 10 seizures per year also Luvi[25] , Barrada et al**.** [20] found significant increase in the mean value of the frequency of the attacks among the positive ANA group , stated that ANA were more common with high frequent seizures.

In agreement with Peltola et al.[11] aCL IgM class was found in only 2.5 % of our patients with localized epilepsy and in 32.5% with generalized epilepsy ,while aCL IgG class was found in 5% of localized and 20% of generalized epilepsy . In group B, 2.5% of localized related epilepsy and 17.5% of generalized epilepsy had +ve aCL IgM and +ve aCL IgG was found in 30% of generalized seizures.

Verrot et al.[23] and Verotti et al.[19] found no differences in the prevalence of aCL antibodies among patients with various epileptic syndromes subdivided into focal or generalized. Debourdeau et al. [22] found that 15% of epileptic patients under antiepileptic drugs had +ve aCL ,also they found that 19% of generalized

epilepsy had +ve aCL and 8% of non generalized epilepsy had +ve aCL.

As explained by Chapman et al. [26], Greaves et al. [27], in their experimental studies that aCL can disrupt neuronal function by direct action on nerve terminals and can reduce GABA receptor mediated chloride currents suggesting a direct and reversible mechanism through which aCL might lower seizure threshold. It has also been postulated that antibodies to endothelium frequently coexisting with aCL, may induce apoptosis within the CNS.

As regards ANA in our study 7,5% of patients in group A with partial and 2.5% with generalized seizures had positive ANA and in10% in group B with partial and 5% of patients with generalized seizures had +ve ANA. This means that ANA more in localized than in generalized seizures and this is in agreement with Peltola et al.[11] Eriksson et al. [18] and Ranua et al[10]., as they stated that ANA more frequent in localized than in generalized epilepsies while Verotti et al[19] found that 12 patients (34.2%) with generalized and 10 patients (25.6%) with localized seizures were +ve ANA with no difference between focal and generalized seizures.

We found no statistically significant association between EEG changes and aCL and ANA results and this in accordance with Barrada et al. [20]

The immunological effects of AEDs in epilepsy have not been completely ruled out [5], Several AEDs such as phenytoin and carbamazepine may induce reversible IgA deficiency and activate production of ANA as well as lupus erythematosus like syndrome.[16.28,29]

Pardo et al. [17] studied the prevalence of antiphospholipid antibodies in 36 epileptic patients treated with diverse antiepileptic drugs including phenytoin, antiphospholipid antibodies were detected in 43% of these patients in most of them IgM aCL.

In our results +ve IgG, IgM aCL cases more common in polytherapy epileptic patients (15%,20% respectively) than montherapy (10% ,15%)) without statistically significant difference espicilly in patients receving CBZ and phenytoin .This is in agreement with Peltola et al. [11], who found that the type of AED was not strongly associated with the presence of autoantibodies with possible exceptions of a lower prevalence of IgM class in valproate treated patients ,while in contrast with our results Hagionya et al[30]. found no statistically significant difference between aCL+ve and aCL-ve as regard to polytherapy.

As regards ANA we found all +ve ANA cases were on montherapy,the 4 cases on carbamazepine . More cases with +ve ANA were localized located epilepsy, 3 cases (7.5%) and one case in generalized epilepsy (2.5%)in group A but in group B (10%) with +ve ANA were localized related epilepsy in comparison to(5%)with generalized epilepsy.

Eriksson et al. [18] found that 16% of their study group on epileptic children had +ve ANA also Ranua et al. [10] found that both epileptic patients and controls had 17% +ve ANA for each and most +ve epileptic cases were unclassified epilepsy and partial epilepsy than primary generalized epilepsy. Also they found that 19% on monotherapy carbamazepine, 9.6% on valproate and 21.3% on phenytoin. But in polytherapy ANA was +ve in 20.6% on carbamazepine,19.6%on valproate and 14.7%on phenytoin In more recent study done by Asadi-Pooya[31] aimed to determine the prevalence of ANA in children with epilepsy who were taking carbamazepine as monotherapy .they found +ve ANA in only one patient and the remaining patients were negative .They concluded that the prevalence of ANA is not among children with epilepsy treated by carbamazepine and this inconsiderable rate of positive ANA seems to have no clinical implications.

Ranua et al. [10] found that AEDs or other medications had no substantial effect on the presence of ANA nor did age at

onset, etiology, type or duration of epilepsy, the presence of aCL was not associated with ANA.

From our study we concluded that there may be a relationship between epilepsy and the presence of ANA and/or aCL antibodies and that an immune dysregulation may be present in epileptic patients. These autoantibodies could suggest alternative therapeutic approaches in difficult cases or in patients not responding to currently used conventional AEDs. So we recommend**:** further studies with large number of patients are needed to define the pathogenesis of aCL and ANA in different types of epilepsy and to evaluate their prevalence in drug- free epileptic patients. Assessment of serum autoantibodies levels could be recommended at starting the administration of AEDs and in serial intervals afterward in epileptic patients and professionals who frequently prescribe these drugs should be alert to this alterations

REFERENCES

1. Berg AT, Berkovics and Brodie MJ: Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE commission on classification and terninology 2005-2009. Epilespsia 2010, 51: 676-685.
2. Irani SR, Bien CG and Lang B: Autoimmune epilepsies. Curr Opin Neurol, 2011, 24: 146-153.
3. Ranua J ,Luoma k. and Auvinen A: Serum IgA ,IgG and IgM concentration in patients with epilepsy and matched controls:a cohort -based cross sectional study .Epilepsy Behav . 2005, 6(2):191-5.
4. McKnight K, Jiang Y, Hart Y, Cavey A, Wroe S, Blank M, Shoenfeld Y, Vincent A, Palace J and Lang B : Serum antibodies in epilepsy and seizures-associated disorders. Neurology 2005, 69: 1730-1736.
5. Liimatainen S,Peltola M,Fallah M, Kharazmi E, Haapala A-M ,Peltola J:The high frequency of antiphospholipid antibodies in refractory focal epilepsy is related to recurrent seizures .European J Neurology, 2009, 16:134-141.
6. Billiau AD, Wouters CH and Lagae LG: Epilepsy and the immune system: is there a link? Eur J Paed Neurol; 2005, 9: 29-48.
7. Majoie HJ, De Bates M, Renier W, Lang B and Vincent A: Antibodies to voltage-gated potassium channels in epilepsy. Epilepsy Res; 2006, 71: 135-141.
8. Rodgers KM, Hutchinson MR. and Northcutt A: The cortical innate immune response increases local neuronal excitability leading to seizures. Brain ; 2009, 132:2478-2486.
9. Commission on Classification and Terminology of International League Against Epilepsy : Proposal for revised clinical and electroencehlaographic classification of epileptic seizures: Epilepsia; 1981, 22: 489-501.
10. Ranua J, Luoma K. and Peltola J.: Anticardiotipin and antinuclear antibodies in epilepsy-a population-based cross-sectional study. Epilepsy Res; 2004, 58: 13-18.
11. Peltola JT, Haapala A. and Isojarvi JI.: Antiphospholipid and antinuclear antibodies in patients with epilepsy or new-onset seizure disorders. Am J Med; 2000, 109: 712-17.
12. Cimaz R, Romeo A.and Scarano A. : Prevalence of anti-cardiolipin, anti-B2 glycoprotein l, and anti-prothrombin antibodies in young patients with epilepsy. Epilepsia; 2002, 43: 52-9.
13. Dean AJ, Dean G and Cloumbier D: Epi-Info, data processing, statistics and epidemiology, software computer package on micro computer CDC, Atlanta, USA. 2000
14. Aarli JA: Epilepsy and the immune system. Arch Neural; 2000, 57: 1689-92.
15. Najjar S,Bernbaum M. and Lai G: Immunology and epilepsy .Rev Neurol Dis ; 2008, 5(3):109-116.
16. Ashrafi MR, Hosseini SA, Biglari M, Abolnaali S,Malamiri RA ,Mombeini H. and Pourpak Z.: Effect of Anti-Epileptic Drugs on Serum Level of IgG Subclasses .Iran J Pediatr; 2010, 20(3):269-276.

17. Pardo A, Gonzalez-Porque P, Gobernado JM. Jimenez-Escrig A and Lousa M: Study of antiphospholipid antibodies in patients treated with antiepileptic drugs. Neurologia; 2001, 16 (1): 7-10.

18. Eriksson K, Peltola J, Keranen T, Haapala AM and Koivikko M: High prevalence of antiphosphotipid antibodies in children with epilepsy: a controlled study of 50 cases. Epilepsy Res; 2001, 46: 129-37.

19. Verotti A, Greco R, Latini G, Morgese G, Chiarelli F and Altobelli E: Anticardiolipin, glutamic acid decarboxylase and antinuclear antibodies in epileptic patients. Clin Exp Med; 2003, 3 (1): 32-36.

20. Barrada O,Ismael I,El-Fayoumy N,Abdel-Shafy S,Abdel-Atti A: Immunological aspects in temporal lobe epilepsy .Egypt J Neurol Psychiat Neurosurg; 2010, 47(4):573-578.

21. Markic J, Mestrovic M, Valic I, Sapunar A and Bosnjaki N : Frequency of anticardiolipin, antinuclear and anti-beta-2 glycoprotein in children with epilepsy. Coll Antropol Sep; 2007, 31 (3): 739-42.

22. Debourdeau P,Gerome P,Zammit C, Saillol A,Aletti M, Bargues L. and Cointet F: Frequency of anticardiolipin ,antinuclear and anti β2Gp1 antibodies is not increased in unselected epileptic patients :a case –control study .Seizure; 2004 ,13:205-207.

23. Verrot D, San Marco M. and Dravet C.: Prevalence and signification of antinuclear and anticardiolipin antibodies in patients with epilepsy. Am J Med; 1997, 103: 33-7.

24. Vezzani A and Granata T.: Brain inflammation in epilepsy: experimental and clinical evidence. Epilepsia; 2005, 46 (Suppl 5): 1724-1743.

25. Luvi S.: Refractory focal epilepsy: aetiology and immunological marjers in adult patients. Acta Universitatis Tamperensis; 2009, 1424: 951-78.

26. Chapman J, Cohen-Armon M, Shoefeld Y, and Korczyn AD. : Antiphospholipid antibodies permeabilize and depolarize brain synaptoneurosomes. Lupus; 1999, 8: 127-33.

27. Greaves M.: Antiphospholipid antobodies and thrombosis .Lancet; 1999, 353,1348-1353.

28. Verrotti A, Basciani F, Trotta D, Greco R, Morgese G and Chiarelli F: Effect of anticonvulsant drugs on interleukin-1, -2 and -6 and monocyte chemotactant protein. Clin Exp Med; 2001, 1: 133-136.

29. Moustafa S, Osama A, Saad A, El-Sayed S, and Moustafa N: Immunotoxicity of chronic phenytoin administration in epileptic patients. Egypt J Neurol Psychait Neurosurg; 2006, 43 (2): 435-441.

30. Haginoya K,Yokoyama H,Koda M. Kato R,Limuna K. and Munakata M. :Anticardiolipin antibody and childhood epilepsy .Epilepsia; 2002, ;43(suppl 9):69(abst).

31. Asadia-Pooya AA and Asadia-Pooya K.: Antinuclear antibodies in children with epilepsy treated by carbamazopine. Epilepsy Res.; 2008, 80: 229-230.

الأجسام المضادة الذاتية فى المرضى المصابين بنوبات صرعية

يعتبر مرض الصرع من الأمراض القديمة المزمنة والتى تتميز بالتكرار المفاجئ لهذه النوبات توجد دوث هذه النوبات فى الأمراض المسببة بخلل فى المناعة يثبت أن الصرع له علاقة بهذه الأمراض المناعية وهذا يطرح هل هناك علاقة بين المناعة وأنواع أخرى من نوبات الصرع . أو أن هناك دور للعلاج المناعى لمرض الصرع.

ومفهوم أن الجهاز المناعى يلعب دورا فى تكوين البؤرة الصرعية فى بعض النوبات الصرعية اكتشف منذ أكثر من ثلاثين عاما ومنذ ذلك الحين أجريت دراسات عديدة وحدث أن هناك تغيرات مناعية فى مرضى الصرع بناء على ملاحظة العلاج المناعى فى حالات الصرع المستعصية وأيضا من تزامن أمراض مناعية مع النوبات الصرعية.

ويهدف هذا البحث دراسة عن وجود بعض الأجسام المضادة الذاتية فى المرضى المصابين بنوبات صرعية.

وقد أجرى هذا البحث على ٨٠ مريضا (٤٠ ذكرا و ٤٠ أنثى) يعانون من مرض الصرع تراوحت أعمارهم من ٥ - ٤٧ سنة بمتوسط (٢٢ + ٨ تم اختيارهم من مرضى عيادة أمراض المخ والأعصاب بمستشفيات جامعة الزقازيق، وكان اختيار المرضى مجموعتين الأولى بالعلاج (مجموعة أ) ومجموعة قبل العلاج (مجموعة ب) وقد تمت مقارنتهم بأربعين شخص من الأشخاص الأصحاء كمجموعة ضابطة مع مراعاة تكافؤ السن والجنس بين المجموعتين.

وفقا للتصنيف الدولى للتشنجات (١٩٨١) عدد المرضى الذين يعانون من تشنجات صرعية عامة ٦٨ بنسبة ٨٥% بينما كان ١٢ مريضا بنسبة ٧٥% يعانون من تشنجات جزئية.

وقد تم إجراء الفحوص الآتية لهؤلاء المرضى :

أخذ التاريخ المرضى تفصيليا حسب نموذج فحص خاص بالصرع.

فحص عام وفحص عصبى شامل.

رسام المخ الكهربى (بين النوبات الصرعية).

عمل أشعة مقطعية أو رنين مغناطيسى على المخ.

أبحاث معملية وتشمل على تحليل الأجسام المضادة لنواة الخلية والأجسام المضادة للكارديوليبين.

وقد تلخصت النتائج فيما يلى :

أظهر رسام المخ الكهربائى وجود بؤرة صرعية فى ٨٨,٧٥% من مرضى كل المجموعتين بنسبة ٩٥% المجموعة (أ) وكذلك ٨٢,٥% من مرضى المجموعة (ب).

كانت نتيجة تحليل الأجسام المضادة للكارديوليبين (IgG) موجبة فى ١٠ من مرضى المجموعة (أ) بنسبة ٢٥% وقد كانوا (٨ ذكور و ٢ إناث). وكذلك الأجسام المضادة للكارديوليبين (IgM) كانت موجبة فى ٤ امريض بنسبة ٣٥% (٦ ذكور و ٨ إناث).

أما بالنسبة للمجموعة (ب) كانت الأجسام المضادة للكارديوليبين IgG موجبة فى ٢ امريض بنسبة ٣٠% (٤ ذكور و ٨ إناث) والأجسام المضادة للكارديوليبين IgM موجبة فى ٨ مرضى بنسبة ٢٠% (٣ ذكور و ٥ إناث).

بالنسبة للأجسام المضادة لنواة الخلية فكانت موجبة فى ٤ حالات (١ ذكر و ٣ إناث) بنسبة ١٠% من مرضى المجموعة (أ) و ست حالات (٢ ذكور و ٤ إناث) بنسبة ١٥% من مرضى المجموعة (ب).

كل المجموعة الضابطة كانت سالبة لهذه الأجسام المضادة.

لم توجد علاقة بين الأجسام المضادة للكارديوليبين والعلاج الدوائى إلا فى حالة العلاج بكاربامازيبين وحمض الفينيتين.

وقد وجد علاقة بين استخدام الكاربامازيبين وزيادة حدوث الأجسام المضادة لنواة الخلية.

لم توجد علاقة بين نتائج رسام المخ الكهربائي و نتائج الاجسام المضادة للكارديوليبين و كذلك الأجسام المضادة لنواة الخلية.

وقد خلصت هذه الدراسة إلى أنه فى مرضى الصرع قد توجد علاقة بين حدوث النوبات الصرعية ووجود بعض الأجسام المضادة لنواة الخلية والكارديوليبين وهذا بدوره قد يكون نتيجة لاضطراب مناعى فى هؤلاء المرضى، كما أن وجود هذه الأجسام المضادة قد يساعد فى تصميم طرق علاجية مختلفة فى الحالات الغير مستجيبة للعلاج الدوائى التقليدى المستخدم حاليا لعلاج الصرع.

ولهذا ننصح بإجراء دراسات أخرى على عدد أكبر من المرضى لتحديد دور الأجسام المضادة لنواة الخلية والكارديوليبين فى الأنواع المختلفة من الصرع ولتحديد مدى انتشارهم فى المرضى الذين لا يستخدمون عقارات مضادة للصرع.

كما نوصى بإجراء روتينى للبحث عن الأجسام المضادة فى المرضى المصابين بالصرع قبل وبعد استخدام العقارات المضادة للصرع وعلى فترات منتظمة .

ونوجه عناية السادة المتخصصون للتغيرات التى قد تحدث فى هؤلاء المرضى.