

Autonomic Dysfunction in Epileptic Patients

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ABSTRACT

Objective: To investigate autonomic symptoms in different types of epilepsy in comparison to control subjects. To observe whether autonomic symptoms cause possible morbidity and mortality and to make a preliminary remedy

Patients and Methods: A retrospective chart review was conducted for 28 patients diagnosed with epilepsy including 18 patients with complex partial epilepsy (CPE) and 10 patients with primary generalized epilepsy (PGE). Their autonomic symptoms were assessed using the COMPASS-31 questionnaire in comparison to a control group of 18 subjects.

Results: No statistically significant differences were found in autonomic dysfunction symptoms between patients with CPE and patients with PGE. However, constipation and insomnia which autonomic symptoms were statistically significantly more common in epileptic patients compared to the control group.

Conclusions: It is important to recognize and watch out for symptoms of autonomic dysfunction in patients with epilepsy. We believe that awareness for these symptoms is essential both to reduce associated disability and develop specific treatment strategies and to predict sudden unexpected death in epileptic patients.

Key Words: Epilepsy, autonomic dysfunction

INTRODUCTION

Epilepsy is associated with fatal or near fatal arrhythmias. Sudden unexpected death in epilepsy (SUDEP) is related to cardiac events. Dysfunction of the autonomous nervous system causes arrhythmias because of sympathetic imbalance or vagal nerve dysfunction or both systems.

Autonomic symptoms that occur during epileptic seizures often accompany other seizure symptoms and can also appear as isolated. Perictal autonomic symptoms in adults are often seen in temporal lobe epilepsy (TLE) and may be associated with cardiovascular, respiratory, gastrointestinal, cutaneous, pupillary, genital, and urinary tract symptoms. Although autonomic changes are frequently seen during or after generalized tonic-clonic (GTC) seizures, these

changes can also occur during focal seizures [1,2].

The regulation of sympathetic and parasympathetic nervous systems involves numerous complex and integrated steps. Dysautonomia refers to a multitude of clinical conditions that develop because of faulty regulation of these complex steps. It presents with multiple symptoms including constipation, insomnia, dizziness, blurred vision, cold and clammy palms and soles, abnormal blood pressure, headaches, lightheadedness with orthostatic intolerance and palpitations. Autonomic dysfunction has also been associated with increased pain sensitivity as in reflex sympathetic dystrophy with pain out of proportion to the cause [3-7].

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Along with the amygdala and hypothalamus, the anterior cingulate-, insular-, posterior orbitofrontal-, and prefrontal cortex affect the autonomic nervous system at the cortical level. The emergence of ictal activity in these structures or spread to these structures can lead to sympathetic and parasympathetic changes that affect the heart rate in patients with epilepsy [8].

PATIENTS AND METHODS

Autonomic dysfunction symptoms were reviewed retrospectively for 28 patients diagnosed with epilepsy. The types of seizures were categorized as per the *International League Against Epilepsy (ILAE) Classification of Epileptic Seizures 1981* criteria.

A control group of 18 healthy subjects was also included in the study. The study was conducted in Gaziantep Sanko University Hospital in 2017. Ethical approval was obtained from the ethics committee of the same hospital. The type and frequency of seizures, duration of illness and demographic characteristics such as patient age and gender were reviewed in detail by a neurologist. Antiepileptic medications received by the patients were also recorded.

Autonomic dysfunction was assessed using the COMPASS-31 (Composite Autonomic Symptom Scale) questionnaire. The COMPASS-31 [9] questionnaire, a validated and internally consistent measure of autonomic functioning across several domains, was adapted to create the “autonomic symptom checklist.” The autonomic symptom checklist assessed the following six symptoms of autonomic dysfunction: “constipation,” “insomnia,” “dizziness,” “blurred vision,” “abnormal blood pressure,” and “cold and clammy palms and soles” (Table 1). The presence of these six symptoms was assessed by reviewing the clinical notes of the neurologist from the initial evaluation for participants in either of the seizure groups or for the control group. Approval from

the hospital’s Institutional Review Board was obtained prior to conducting the retrospective chart review.

RESULTS

The study was conducted on a total of 46 patients including 28 patients with epilepsy and 18 control subjects. Sixteen (57.1%) epileptic patients were female, and the mean age of epileptic patients was 20.9 years. Eighteen patients (64.3%) had a diagnosis of complex partial epilepsy and others had primary generalized epilepsy. Patients had a mean seizure frequency of 2.5 seizures per month and mean disease duration of 3.8 years.

Nine (31.1%) patients were on valproic acid (VPA) therapy, 4 (14.3%) were receiving carbamazepine (CBZ), and 15 (53.6%) were receiving levetiracetam (LEV). There were 11 (61.1%) female and 7 (38.9%) male subjects in the control group with a mean age of 29.7 years. No statistically significant difference was found between control group and epilepsy group with respect to age.

No statistically significant difference was found between the epilepsy groups with respect to autonomous nervous system symptoms (constipation(p=0.430), insomnia(p=0.778), dizziness (p=0.430), blurred vision (p=0.305), cold and clammy palms and soles (p=1) and abnormal blood pressure (p=0.610; Table 2). Compared to control subjects, constipation (p=0.002) and insomnia (p=0.012) symptoms were statistically significantly more common among epileptic patients (Table 3).

As a subgroup, patients with primary generalized epilepsy showed a statistically significantly higher frequency of constipation (p=0.024) in comparison to the control group (Table 4). However, both constipation (p=0.001) and insomnia (p=0.015) symptoms were more common in patients with complex partial epilepsy (Table 5).

Table 1. Description of autonomic symptoms assessed

Symptom	Description
Constipation	No bowel movements for greater than 2 days; difficulty, straining or hard bowel movements
Insomnia	Greater than 1 h to fall asleep; frequent waking; unable to maintain sleep
Dizziness	Greater than 15 days of lightheaded/near-syncope; vertigo; unsteadiness
Blurry Vision	Subtle pupillary asymmetry; visual cortex interpretation of sensory imbalance as visual blurriness
Sympathetic Response in Extremities	Cold and clammy palms and soles, palmar and plantar sweating, color changes, and temperature changes associated with sudomotor and vasomotor change
Abnormal Blood Pressure	Blood pressure above or below the normal range for adolescents and children: systolic (110–131 mmHg), diastolic (64–83 mmHg)

The frequency of symptoms was assessed through a review of patient notes utilizing the above criteria

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Table 2. According to the answers given by patients, the number of autonomic findings in epilepsy subgroups

Variables*		Complex Partial Seizure (n=18) n (%)	Primer Generalize Epilepsy (n=10) n (%)	*P
Gender	Female	8 (0.44)	8 (0.8)	0.610
	Male	10 (0.56)	2 (0.2)	
Constipation	Yes	10 (0.56)	4 (0.4)	0.430
	No	8 (0.44)	6 (0.6)	
Insomnia	Yes	10 (0.56)	5 (0.5)	0.778
	No	8 (0.44)	5 (0.5)	
Dizziness	Yes	10 (0.56)	4 (0.4)	0.430
	No	8 (0.44)	6 (0.6)	
Blurring	Yes	7 (0.39)	2 (0.2)	0.305
	No	11 (0.61)	8 (0.8)	
Cold and clammy palms and soles	Yes	9 (0.5)	5 (0.5)	1.000
	No	9 (0.5)	5 (0.5)	
Abnormal blood pressure	Yes	9 (0.5)	4 (0.4)	0.610
	No	9 (0.5)	6 (0.6)	

* Chi-square test

Table 3. Comparison of all epilepsy patients and control group

		Groups				*P
		Patients		Controls		
		n	%	n	%	
Gender	Female	16	57.1	11	61.1	0.790
	Male	12	42.9	7	38.9	
Constipation	Yes	14	50.0	1	5.6	0.002
	No	14	50.0	17	94.4	
Insomnia	Yes	15	53.6	3	16.7	0.012
	No	13	46.4	15	83.3	
Dizziness	Yes	14	50.0	5	27.8	0.135
	No	14	50.0	13	72.2	
Blurring	Yes	9	32.1	7	38.9	0.639
	No	19	67.9	11	61.1	
Cold - Clammy Palms - Soles	Yes	14	50.0	5	27.8	0.135
	No	14	50.0	13	72.2	
Abnormal Blood Pressure	Yes	13	46.4	4	22.2	0.097
	No	15	53.6	14	77.8	

* Chi-square test

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Table 4. Comparison of primary generalized epilepsy patients and control group

		*P
Gender	Female	0.294
	Male	
Constipation	Yes	0.024*
	None	
Insomnia	Yes	0.064
	None	
Dizziness	Yes	0.510
	No	
Blurring	Yes	0.294
	None	
Cold- Clammy Palms-Soles	Yes	0.243
	None	
Abnormal Blood Pressure	Yes	0.324
	None	

*Chi-square test.

Table 5. Comparison of complex partial epilepsy patients and control group

		*P
Gender	Female	0.317
	Male	
Constipation	Yes	0.001
	No	
Insomnia	Yes	0.015
	No	
Dizziness	Yes	0.089
	No	
Blurring	Yes	1.000
	No	
Cold -Clammy Palms -Soles	Yes	0.169
	No	
Abnormal Blood Pressure	Yes	0.080
	None	

* Chi-square test

DISCUSSION

There are several studies which reported heart rate variability and changes in the heart's pumping capacity particularly at diastole in patients with temporal lobe epilepsy during both ictal and interictal periods, resulting in asystole. Specifically, sudden unexpected death in epilepsy has been linked to autonomic dysfunction [10,11]. Increased heart rate at the time of seizure

has been well characterized [12]. Impairment of one or more autonomic function was previously demonstrated in patients with refractory epilepsy [13]. Higher vasomotor tone, higher sympathetic tone, lower parasympathetic tone and reactivity, and severe dysautonomia were demonstrated in some patients with refractory epilepsy [14]. Similarly, in the present study constipation and insomnia, both reflecting reduced parasympathetic activity, were more common in epileptic patients versus control subjects. An interesting finding was the lower frequency of other autonomic symptoms including dizziness, blurred vision, cold and clammy palms and soles and abnormal blood pressure as observed in this study. This may be explained by potential inhibitory effects of antiepileptic medications on the development or manifestation of autonomic symptoms [15].

Our results underline the importance of investigating autonomic function in patients with epilepsy in clinical practice because autonomic symptoms may reflect lower vagal tone and higher sympathetic tone which are predictors of morbidity and sudden death in epilepsy.

On the other hand, investigation of paroxysmal autonomic abnormalities which is frequently observed, would help in the development of algorithms for detection of seizures in advance, and to reduce mortality and morbidity in patients with epilepsy.

Careful analysis and correct evaluation of autonomic symptoms that occur seizures is important in terms of understanding the risk of SUDEP, involvement of neuronal networks, and results and spread pattern of ictal activity. Therefore, we think that, further discussions and long-term studies should question whether the COMPASS-31 tool can be more widely used in chronic neurological conditions.

Conflict of Interests: The author declare that they have no conflict of interest

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