Rhythm and structural disorders of the heart in patients with primary diagnosis of idiopathic epilepsy

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Abstract

Introduction: Cardiac abnormalities relate idiopathic epilepsy in several ways: Cardiac disease is the most common cause of sudden unexplained death in epilepsy. Some of epileptic syndromes have syncope as one of their major presentations. Syncope can lead to epileptic seizure and might be caused by epileptic seizure. Differentiation between syncope and seizure might be very difficult, which leads to diagnostic and therapeutic errors.

Methods: 101 patients, with primary diagnosis of idiopathic epilepsy were evaluated in this descriptive study. Comprehensive evaluations including precise physical examination, electrocardiography, echocardiography and 24-hour holter monitoring were performed for each patient. Our population was subdivided in two categories: patients with cardiac disease and those without cardiac disease based on investigatory findings.

Results: 24 patients (23.8%) had cardiac disease. The mean age was 34.4±19 years in patients with cardiac disease and 24.3±11 years in patients without cardiac disease. The mean age of onset of epilepsy was 24.5±22 years in patients with cardiac disease and 15.9±10 years in patients without cardiac disease. The mean duration of treatment with antiepileptic drugs was 71±22 months in patients with cardiac disease and 64±10 months in patients without cardiac disease. In 56.1% of patients without cardiac disease, seizure had been controlled excellently with antiepileptic drugs. 34.2% had good control, 7.9% had acceptable control, and 1.8% had unacceptable control. In patients with cardiac disease 27.3% had excellent control, 50% had good control, 18.2% had acceptable control and 4.5% had unacceptable control.

Conclusion: These data suggest that in patients with cardiac disease either a significant percent had syncope as the cause of their symptoms or the etiology of their true seizures had been their cardiac disease. Appropriate cardiac interventions eliminated symptoms in five patients.

Keywords: Idiopathic epilepsy, cardiac structural abnormality, cardiac rhythm abnormality

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Introduction

Epilepsy is a relatively common neurological disorder. The prevalence of epilepsy ranges from 4-10/10000 in developed countries to 57/10000 in developing countries. Only approximately one fourth to one third of epilepsies have known etiologies and the others are idiopathic.[1]

Cardiac abnormalities relate idiopathic epilepsy in several ways: 1-Sudden Unexplained Death in Epilepsy is responsible for 1.7% of nonstatus deaths in epileptic patients[1] and its most common causes are ictal or interictal cardiac abnormalities.[2] Interictal cardiac arrhythmia in ECG (electrocardiography) or holter monitoring increases the risk of sudden unexplained death in epilepsy and this risk decreases by appropriate cardiac intervention.[3] 2-Specific epileptic syndromes have prominent cardiac manifestations. For example, Panayiotopoulos syndrome sometimes has prominent ictal autonomic features and lead to cardiac arrhythmia and syncope (ictal syncope).[4] 3- Occasionally, the difference between cardiac syncopal attacks and true seizure attacks is very difficult.[1,5,6] Cardiac syncopes can lead to anoxic-nonepileptic seizures (i.e. syncopes associated with some clonic or myoclonic jerks resembling convulsive seizures) and cause diagnostic errors.[7] 4- Epileptic patients might have ictal or interictal cardiac arrhythmias. The most common ictal cardiac arrhythmia is sinus tachycardia (90% of patients).[8-12] Ictal sinus bradycardia or asystole is rare (0.5% of patients) and usually is seen in focal epilepsies specially that of left frontal or temporal lobes origin.[3,13] Temporal lobe seizures usually cause ictal tachycardia while frontal lobe seizures can lead to ictal bradycardia.[14] Sinus bradycardia in the morning hours at the interictal period may be a risk factor for occurrence of seizure attacks.[15,16] Interictal parasympathetic activity might influence seizure control. In temporal lobe seizures when parasympathetic cardiac activity is minimal, seizures tend to be more resistant to conventional therapeutic strategies.[17] 5- Cardiac syncopes can cause anoxic-epileptic seizure (AES); True epileptic seizures because of cardiac syncopal attacks.[4,6,17-19] In children, 7-8% of cardiac syncopes can lead to anoxic-epileptic seizure. The best treatment for anoxic-epileptic seizure is the treatment of its precipitating syncopal attack.[7] This study was designed for assessment of these cardiac and seizure associations.

Methods

This prospective clinical study was approved by the Review Board/Ethics committee of Mashhad University of Medical Sciences. The study protocol was explained to all patients and informed consent was obtained.

The study was conducted in neurology and cardiology divisions of Ghaem hospital, Mashhad, during 2004-2006. Patients with primary diagnosis of epilepsy who had been treated with antiepileptic drugs by another

physician were included. Any of the following: abnormal neurological examination; abnormal brain CT-scan or brain MRI; abnormal routine laboratory tests such as CBC, blood sugar, blood biochemistry, sodium, potassium, calcium; and borderline or lower than normal IQ consisted the exclusion criteria. Regarding these criteria, we supposed that these patients had been treated with the diagnosis of idiopathic epilepsy.

Eligible patients referred to cardiology service and detailed cardiac evaluation including physical examination, electrocardiography (ECG), echocardiography and 24-hour ambulatory ECG (AECG) monitoring was performed for each patient by one cardiologist. Our population was subdivided in two categories: with cardiac disease and without cardiac disease. Definition of "cardiac disease" in our study was: Any significant abnormality in 24-hour AECG monitoring, echocardiography and/or ECG (in expect of nonspecific ST-T changes or abnormalities which are suggestive of coronary artery diseases).

The data including age, sex, past medical history, family history, drug history, age of patient at disease onset, frequency of seizure attacks, the state of seizure control, seizure type, epileptic syndrome and electroencephalographic findings on the last electroencephalogram (EEG) and possible cardiac abnormalities were recorded for each patient in specific data collection sheets and analyzed using SPSS 13 software package. The state of seizure control was defined as: *excellent,* if the patient had ≤ 1 attack in year; *good,* if he or she had ≥ 2 attacks in year; *acceptable,* if he had ≤ 1 attack in month and *unacceptable,* if she had > 1 attack in month. Qualitative variables were expressed using percentages and quantitative data demonstrated with mean, standard deviation, and/or confidence interval.

Results

24 patients (23.8%) had cardiac disease. Mean age of population was 26.7±14 years. The mean age was 34.4±19 years in patients with cardiac disease and 24.3±11 years in patients without cardiac disease. The mean duration of treatment with antiepileptic drugs was 71±22 months in patients with cardiac disease and 64±10 months in patients without cardiac disease. 23.4% of patients without cardiac disease and 16% of patients with cardiac disease had positive familial history of epilepsy.

In 56.1% of patients without cardiac disease, seizure had been controlled excellently with antiepileptic drugs. 34.2% had good control, 7.9% had acceptable control, and 1.8% had unacceptable control. In patients with cardiac disease 27.3% had excellent control, 50% had good control, 18.2% had acceptable control and 4.5% had unacceptable control.

73.9% of patients with cardiac disease and 61% of patients without cardiac disease had generalized tonic-clonic seizure (grandmal). A specific epileptic

syndrome was found in 13.1% of patients with cardiac disease and 29.6% of patients without cardiac disease. 78.3% of patients with cardiac disease and 68.4% of patients without cardiac disease had normal EEG (of course, the last EEG of the patient).

In echocardiography 2 patients had MVP, 3 patients had mitral valve prolapse with mitral regurgitation (MVP+MR) and 2 patients had patent foramen oval (PFO). Rheumatic heart disease (RHD), systolic left ventricular failure, right ventricular dysplasia (RVD), atrial septal aneurysm (ASA) and bicuspid aortic valve each one was found in one patient. The frequency of different abnormalities in 24-hour AECG monitoring has been shown in Table 1.

Table 1: The frequency of different abnormalities in 24-hour

AECG abnormality	Frequency
premature ventricular contraction	*5*
premature atrial contraction	*4*
Second degree A-V block	*3*
sinus pause	*2*
sinus bradycardia	*2*
ventricular tachycardia	*2*
sinus tachycardia	*2*
paroxysmal supraventricular tachyarrhythmia	*1*
significant sinus arrhythmia	*1*
sick sinus syndrome	*1*
paroxysmal atrial fibrillation	*1*
long Q-T interval	*1*

AECG* monitoring

Table 2 demonstrates different EEG patterns, seizure types and epileptic syndromes which were found in different abnormalities of 24-hour AECG monitoring. Different EEG patterns, seizure types and epileptic syndromes in various abnormalities of echocardiography have been demonstrated in table 3.

Table 2: EEG pattern, seizure type and epileptic syndrome in our patients with arrhythmia

Case number	AECG abnormality	EEG pattern	Seizure type	Epileptic syndrome
1	Heart block	*Generalized epileptic discharge*	*Grandmal*	*rolandic*
2	PSVT[1]	*normal*	*Grandmal*	*no classified*
3	VT[2]	*normal*	*Grandmal*	*no classified*
4	Bigeminal PVC[3]	*normal*	*Grandmal*	*no classified*
5	Heart block	*normal*	*grandmal*	*no classified*
6	SSS[4]	*normal*	*grandmal*	*no classified*
7	Sinus pause	*normal*	*grandmal*	*no classified*
8	VT[5]	*normal*	*grandmal*	*no classified*
9	Heart block	*normal*	*grandmal*	*no classified*

Table 3: EEG pattern, seizure type and epileptic syndrome in our patients with different cardiac structural disorders

Case number	Abnormality in echocardiography	EEG pattern	Seizure type	Epileptic syndrome
1	MVP[6]	*Generalized epileptiform discharge*	*myoclonic*	*No classified*
2	MVP	*Generalized epileptiform discharge*	*Myoclonic + absence*	*JAE*[12]
3	MVP+MR	*normal*	*grandmal*	*No classified*
4	RHD[7]	*normal*	*grandmal*	*No classified*
5	RVD[8]	*normal*	*grandmal*	*No classified*
6	MVP+MR	*normal*	*grandmal*	*No classified*
7	TVP[9]	*normal*	*grandmal*	*No classified*
8	PFO[18]	*normal*	*grandmal*	*No classified*
9	Systolic ventricular failure	*normal*	*grandmal*	*No classified*
10	ASA[11]	*normal*	*grandmal*	*No classified*
11	PFO	*normal*	*grandmal*	*No classified*
12	Bicuspid aortic valve	*normal*	*grandmal*	*No classified*
13	Hypertrophic cardiomyopathy	*normal*	*grandmal*	*No classified*
14	MVP+MR	*normal*	*grandmal*	*No classified*

[1] Paroxysmal supraventricular tachyarrhythmia
[2] Ventricular tachycardia
[3] Premature ventricular contraction
[4] Sick sinus syndrome
[5] Ventricular tachycardia
[6] Mitral valve prolapse
[7] Rheumatic heart disease
[8] Right ventricular dysplasia
[9] Tricuspid valve prolapse
[10] Patent foramen oval
[11] Atrial septal aneurysm
[12] Juvenile Absence Epilepsy

After appropriate cardiac managements, five of our patients became symptom free and their antiepileptic drugs were discontinued. A middle age lady with PSVT in AECG monitoring, had been treated with the diagnosis of epilepsy with valporate for more than three years without acceptable control. She became symptom free by the administration of beta blocker (propranolol) and valporate was discontinued. A 18 year-old woman who had SSS in 24 hour AECG monitoring, had been managed with carbamazepine for 10 years without acceptable control, became symptom free after implantation of permanent pacemaker (PPM). Similarly, implantation of PPM eliminated all the symptoms of a teenager who had been treated for more than 1 year with carbamazepine and had vasovagal (neurally mediated) syncope with positive tilt test. Finally, a 61 year-old gentleman with hypertrophic cardiomyopathy (HCM) who had received valporate, phenytoine and carbamazepine for more than 8 years, treated successfully with implantable cardiac defibrillator (ICD).

Discussion

The prevalence of cardiac disease was 23.8% in our population. We assumed that this disproportional high frequency might be due to either misdiagnosis of cardiac syncopes as true epileptic seizures (anoxic-nonepileptic seizure) or occurrence of true seizures because of cardiac disorders (anoxic-epileptic seizure) in significant percent of our patients. Both of these conditions lead to inappropriate use of long-term antiepileptic drugs with their numerous complications without clinical improvement. All of the patients with cardiac disease referred to cardiology service and requested cardiac interventions were performed for them. Interestingly, five of our patients became symptom free by appropriate cardiac managements.

In epilepsy registries, 20-30% of the patients have excellent prognosis, 30-40% have good prognosis, 10-20% have uncertain prognosis and up to 20% have bad prognosis.[1] In this study, 40.6% of patients had excellent prognosis, 36.6% had good prognosis, and 9.9% had bad prognosis. However, the definition of prognosis was somehow different in our study. 56.1% of our patients without cardiac disease had excellent prognosis whereas only 1.8% of them had unacceptable prognosis. Our epileptic patients with cardiac disease had more prolong time of treatment with antiepileptic drugs (71 versus 64 months), while only 27.3% of them had excellent prognosis and as many as 4.5% had unacceptable prognosis. This finding could be explained that in patients with cardiac disease either the diagnosis of epilepsy has been wrong or the cause of epileptic attacks has been cardiac disorder; i.e., they have been anoxic-epileptic seizures.

The most common type of seizures in patients with anoxic-epileptic seizure (AES) is grandmal. Occasionally,

myoclonic and absence seizure may also be seen.[7,20] In our study most of patients with an abnormality in 24-hour AECG monitoring or echocardiography had grandmal seizure with no classified epileptic syndrome (Table 1 and 2). The only other seizures that were observed in our patients with cardiac disease were myoclonic and absence seizures.

Most of idiopathic epileptic seizures begin in the first decade of life.[1] Mean age of onset of epilepsy in this study was 24.5±22 years in patients with cardiac disease and 15.9±10 years in patients without cardiac disease. Higher age of onset in patients with cardiac disease may suggest that these epilepsies either have not been idiopathic in origin (e.g., they have been a consequence of cardiac disorders) or they have not been true seizures at all.

Most of AES are underdiagnosed. This might be due to either little attention of most neurologists about this disorder or underestimation of its importance by most of them.[7] We believe that AES is a real neurological disorder and its prevalence is high enough to recommend all patients with idiopathic epilepsy be evaluated by an experienced cardiologist. A case-control study with appropriate sample size which can compare differences in prevalence of different cardiac disorders between epileptic and nonepileptic population is suggested.

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اختلالات ریتم و ساختمانی قلب در بیماران با تشخیص اولیه صرع ایدیوپاتیک

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چکیده

زمینه و هدف: اختلالات قلبی و صرع ایدیوپاتیک به چند روش با هم ارتباط دارند: بیماریهای قلبی شایعترین علت مرگ ناگهانی و بدون علت خاص در صرع میباشد. برخی از سندرمهای صرعی به عنوان قسمتی از علایم خود به همراه سنکوپ می باشند. سنکوپ می تواند باعث حمله صرعی شود و یا از حمله صرعی ناشی شود. افتراق بین سنکوپ و صرع ممکن است خیلی مشکل باشد و این مسئله میتواند باعث اشتباهات تشخیصی و درمانی گردد.

روش بررسی: صد و یک بیمار با تشخیص اولیه صرع ایدیوپاتیک در این مطالعه توصیفی مورد بررسی قرارگرفتند. ارزیابی کامل شامل معاینه فیزیکی دقیق، الکتروکاردیوگرافی، اکوکاردیوگرافی و هولترمونیتورینگ ۲۴ ساعته برای تمامی بیماران انجام شد. براساس یافته‌ها جمعیت مورد مطالعه به دو گروه بیماران با بیماری قلبی و بیماران بدون بیماری قلبی تقسیم شدند.

یافته‌ها: ۲۴ نفر از جمعیت مورد مطالعه (۲۳/۸٪) بیماری قلبی داشتند. میانگین سنی ۱۹±۴/ ۳۴سال در بیماران با بیماری قلبی و ۱۱±۲۴/۳ سال در بیماران بدون بیماری قلبی بود. میانگین سن شروع صرع۲۲ ±۲۴/۵ سال در بیماران مبتلا به بیماری قلبی و۱۰ ±۱۵/۹سال در بیماران بدون بیماری قلبی بود. میانگین مدت درمان با داروهای ضد صرع۲۲± ۷۱ ماه در بیماران با بیماری قلبی و۱۰±۶۴ ماه در بیماران بدون بیماری قلبی بود. در بیماران بدون بیماری قلبی در۵۶/۱٪ کنترل صرع عالی ، در ۳۴/۲٪ کنترل خوب ، در ۷/۹٪ کنترل صرع قابل قبول و در ۱/۶٪ کنترل صرع غیر قابل قبول بود. بیماران همراه با بیماری قلبی ۲۷/۳٪ کنترل عالی ،۵۰٪ کنترل خوب ،۱۸/۲٪ کنترل قابل قبول و۴/۵٪ کنترل غیر قابل قبول داشتند.

نتیجه گیری: اطلاعات موجود در این مقاله پیشنهادکننده آنست که یا درصد قابل توجهی از جمعیت مطالعه شده مبتلا به سنکوپ و نه صرع بودند و یا آنکه علت صرع واقعی در آنها بیماری قلبی بود. اقدامات درمانی مناسب قلبی در پنج بیمار منجر به برطرف شدن علائم شد.

واژگان کلیدی: صرع ایدیوپاتیک، اختلال ساختمانی قلب، اختلال ریتم قلب