Acta Neurol Scand 1997: 96: 72–75
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ACTA NEUROLOGICA SCANDINAVICA
ISSN 0001-6314

ECG changes in epilepsy patients

Tigaran S, Rasmussen V, Dam M, Pedersen S, Høgenhaven H, Friberg B. ECG changes in epilepsy patients.
Acta Neurol Scand 1997: 96: 72–75. © Munksgaard 1997.

Objectives – To investigate the frequency of ECG abnormalities suggestive of myocardial ischaemia in patients with severe drug resistant epilepsy and without any indication of previous cardiac disease, assuming that these changes may be of significance for the group of epileptic patients with sudden unexpected death. *Material and methods* – Twelve patients with medically intractable epilepsy were investigated with simultaneous long ECG and EEG recordings while attending either epilepsy surgery investigational procedures or the investigational programme for diagnostic purposes, and one while having an episode of status epilepticus. *Results* – The ECG recording failed in 1 patient. This patient had chest pain and minor yet morphologically conspicuous changes in the ECG, suggestive of myocardial infarction. He died in heart arrest. Eight epilepsy patients had episodes of ST segment depression in the ECG, many of which coincided with video- and EEG documented epileptic seizures. Two patients experiencing simple partial seizures and 1 patient experiencing absence seizures had no ST segment depressions in the ECG. One patient had an episode of status epilepticus secondary to brain damage and no ST segment deviation was seen during the ECG recording which continued until 3 h before the patient died. *Conclusion* – Patients with severe drug resistant epilepsy have episodes of ST segment changes, some of which are closely related to epileptic seizures. Further studies are needed to confirm the present results and to investigate the nature of these changes and document the effect of prophylactic treatment with cardioactive drugs to reduce the risk of sudden death.

S. Tigaran[1], V. Rasmussen[2], M. Dam[1], S. Pedersen[3], H. Høgenhaven[4], B. Friberg[1,*]

[1]University Clinic of Neurology, Hvidovre Hospital, Kettegård Allé 30, 2650 Hvidovre, Denmark, [2]University Clinic of Cardiology, Copenhagen University Hospital, Hvidovre Hospital, [3]Department of Neurology, Frederiksberg Hospital, [4]University Clinic of Neurophysiology, Copenhagen University Hospital, Hvidovre Hospital, Denmark

Key words: epilepsy; myocardial ischaemia; sudden death

S. Tigaran, University Clinic of Neurology, Hvidovre Hospital, Kettegård Allé 30, 2650 Hvidovre, Denmark

Accepted for publication March 5, 1997

Epilepsy is one of the commonest neurological disorders. About 5% of the population will suffer an epileptic episode during their life-time, and 1% have epilepsy (1). In Denmark there are about 45,000 persons who need a continuous treatment of their epileptic seizures (2). It has been estimated that people with epilepsy have an increased mortality risk – approximately 2–3× that of the population at large (3, 4), with the majority of deaths occurring in people aged between 10 and 40 years (5).

A still unexplained phenomenon among epilepsy patients is sudden death (SUDEP), which accounts for up to 15% mortality in this patient group (6).

In some cases instantaneous death has been observed in connection with generalized epileptic seizures, but in most instances the terminal event is unwitnessed and the pathogenesis unknown. Ambulatory long-term ECG registration over 24 h have been made (7) showing cardiac arrhythmias. To our knowledge, no prior reports of long-term EEG monitoring over several days with simultaneous long-term ECG registration in hospitalized patients with refractory epilepsy have been published.

In the present paper the case reports and results of long-term ECG in 13 patients with severe drug resistant epilepsy are presented.

The purpose of this study was to establish the number of epilepsy patients required in a future study aiming at investigating the effect of a combined treatment with a betablocking and a calcium channel blocking agent on the potentially dangerous noxae exerted by the epileptic activity on myocardial tissue as reflected in the ECG.

Material and methods

All patients gave their informed consent before entering the study.

Thirteen patients (6 females, 7 males), mean age: 40 years (range 17–76 years), were investigated. Twelve of the patients were diagnosed as having

* Research nurse

severe, drug resistant epilepsy. Eleven had partial epilepsy with and without secondary generalization and 2 with primary generalized epilepsy. Nine underwent epilepsy surgery investigational procedures, 3 patients were investigated for diagnostic purposes and 1 patient had a long-term ECG recording during a status epilepticus episode.

The epilepsy surgery programme represents a unique test situation as patients are experiencing many seizures within a short time due to withdrawal of standard epilepsy medication according to the special investigational procedure.

One patient (case no. 8) had a history of paroxysmal atrial fibrillation, the other 12 patients had no history of cardiac disease or had ever taken cardioactive drugs.

The patients had never received any kind of cardiac medication. Long-term ECG monitoring (Holter monitor) was performed during 4–5 days in 12 patients. Standard ECG recordings at rest were performed prior to study entry.

All patients had a long-term video electroencephalographic (EEG) registration with special equipment according to standard technique. Holter and long EEG registrations were simultaneous in 12 patients.

Videoregistrations as well as the patients' own observations were recorded. After finishing the monitoring procedures the antiepileptic treatment was re-established.

Results

The long-term ECG recording failed in 1 patient with partial epilepsy (case no. 1). During 4 days with video–EEG monitoring he experienced 8 complex partial seizures and 4 secondarily generalized seizures. At the end of the monitoring the antiepileptic treatment was fully re-established. During the following 6 days the patient experienced 2 more complex partial seizures. Two days after the last seizure the patient complained of chest discomfort. The standard ECG showed reduction of QRS amplitude and small negative T-waves of "coronary" appearance. The patient died in cardiac arrest irresponsive to resuscitation procedures 3 days after the last seizure.

ECG abnormalities suggestive of myocardial ischaemia, such as ST segment depression below 1 mm, each lasting more than 1 min, were found in 8 patients. The majority of ST depressions found in the ECG coincided with video- and EEG-documented epileptic seizures. The most severe ST depression was 4.4 mm.

In 2 patients experiencing simple partial seizures and 1 experiencing absence seizures during the recordings, no ST segment depressions were found.

One patient (case no. 8), operated on for a prostatic cancer in 1992, was admitted to the urologic department for increasing fatigue. Before admission to the hospital the patient fell and possibly injured his head. During hospitalization he developed a severe, drug refractory episode of status epilepticus and he was urgently transferred to the neurological department. The ECG monitoring was started immediately after the transfer and performed over the following 24 h. The ECG monitoring was terminated 3 h before the patient died of respiratory failure. Autopsy revealed a small subdural haemorrhage with a slight impression on the surface of the left frontal lobe of the brain. These findings are detailed in Table 1.

Discussion

Epilepsy, however disabling it may be, is usually not considered to be a fatal condition. It is well known that epilepsy may be secondary to another disease, which implies an increased risk of death, e.g. brain tumour, but both patients and physicians seem to ignore the fact that epilepsy *per se* may constitute a risk factor concerning life expectancy (8).

Even though epilepsy is a chronic condition many deaths which are ascribed to the disorder occur suddenly and unexpectedly. Moreover, clinicians and pathologists are puzzled by the frequency by which deaths of patients with epilepsy remain unexplained despite post-mortem examinations (8).

Several reports have been made reporting cardiac tachycardia as the most common phenomenon related to partial epilepsy, with or without secondary generalization, but bradyarrhythmias also occur (9). Asystolia has been reported as an unusual event (10). ST elevation has only been reported once as a case report (11). It has been published only as a single report regarding autopsy material of myocardium in patients with epilepsy demonstrating interstitial fibrosis connected with atrophy or myofibrillar degeneration (12), which can be caused by heart ischaemia.

The aim of this study was to investigate how many patients with severe drug resistant epilepsy will have ECG changes during a 5 day period of hospital observation, in which the patients undergo either an investigational procedure (10 cases) or a continuous observation due to refractory status epilepticus, in order to establish how many subjects should be enrolled in a future placebo-controlled study aiming at treating these patients with a drug with anti-ischaemic or anti-arrhythmic properties or both and to detect a difference of statistical significance.

Table 1. ECG changes in 13 patients with drug resistant epilepsy

Patient number and age	Type of seizures and duration years	ST changes			Number of registered epileptic seizures	Relation between seizures and ECG changes	Other ECG changes	Comcomitant disease	MR brain scan findings
		Number of episodes	Total duration min	Max depression mm					
1, 68 years	CPG, 66		No Holter		8 CP 4 CPG		Coronary T-waves	Pneumonia	Left hippocampus atrophy
2, 50 years	M, 40 PG	38	133	−2.1	21 M 1 PG	Yes	Bradycardia	No	Not performed
3, 45 years	CPG, 38	23	107	−2.0	1 CPG 4 CP	Yes	None	No	Ischaemic lesion on the left side of the temporal lobe
4, 33 years	CP, 4	3	6	−2.1	0	No	None	No	Right hippocampus atrophy and agenesis of the anterior part of the temporal lobe
5, 44 years	CPG, 18	13	58	−4.4	16 CP 1 CPG	Yes	None	No	Right hippocampus atrophy
6, 42 years	CPG, 39	9	43	−2.5	1 CPG	Yes	None	No	Normal
7, 31 years	SP, 28	70	112	−2.1	0	No	None	No	Sequelae after amygdalo hippocampectomy
8, 78 years	SE few days	0	0		SE	No	None	Prostatic cancer	Subdural hematoma on the left side of the frontal lobe
9, 39 years	SPG, 37	38	205	−2.3	5 SP 2 CPG 10 CP	Yes	None	No	Left hippocampus atrophy
10, 26 years	CP, 19 CPG	1	20	−2.1	2 CP 1 CPG	Yes	None	No	Right hippocampus hypoplasia
11, 17 years	A, 5 PG	0	0	0	21 A 1 PG	No	None	No	Hypoplasia of the left temporal pol and right hippocampus hypotrophy
12, 25 years	SP, 16 SCP	0	0	0	0	No	None	No	Left hippocampus gliosis
13, 32 years	SP, 9	0	0	0	11 SP	No	None	No	Left temporal lobe cortex heterotopia and right hippocampus hypotrophy

PG: primary generalized; SP: simple partial; CP: complex partial; SPG: simple partial seizures with secondary generalization; M: myoclon jerks; A: absence; SE: status epilepticus; CPG: complex partial seizures with secondary generalization.

The results of the present pilot study showed that episodes of ST depression appeared in 8 patients with severe partial epilepsy disease, whereas no changes were detected in 1 patient with drug refractory status epilepticus evolved secondary to brain damage. Neither the 2 patients who experienced only simple partial seizures during the recordings, nor the patient experiencing absence seizures and one primary generalized seizure during long EEG registration had ECG changes. In several cases there was registered a temporal relationship between secondarily generalized seizures and ST segment depression. Regular extracardiac activity signals, undoubtedly produced by rapid muscle contraction during the tonic-clonic convulsions, were recorded in the ECG in all the cases having secondarily generalized seizures. The convulsions were preceded by ST depression probably due to generalized tonic phase, and continued for several min after seizures' cessation.

It has to be stressed, that extracardiac activity signal indicating convulsions was seen in ECG of 4 patients with convulsive seizures at a time when no epileptic activity was discovered by EEG or video tape recordings.

The pathophysiologic processes involved in the lethal events are incompletely known. It is known that in seizures cardiac arrhythmia developed probably as a result of sympathetic hyperactivity (13). As death is usually sudden, malignant cardiac arrhythmias are suspected to be the most frequent cause. However, as death often occurs unexpectedly and without close temporal relation to known epileptic seizures, the fatal arrhythmia is thought

to be the result of structural damage to myocardial tissue produced by excessive catecholamine stimulation, ischaemia or both.

The findings of this study showed that almost all patients experiencing frequent secondarily generalized seizures and without indications of previous ischaemic heart disease have episodes of ST depression in the ECG in periods with epileptic activity.

In conclusion this study showed that patients with severe drug resistant partial epilepsy have episodes of ST segment changes, some of which are closely related to the epileptic seizure. Further studies are needed to confirm the present results and to document the effect of prophylactic medical treatment.

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