

# Relation between plasma concentrations of vitamin e in patients with temporal lobe epilepsy and sudden unexpected death in epilepsy: why, when and who?

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## ABSTRACT

The most common epilepsy-related category of death is sudden unexpected death in epilepsy (SUDEP). The exact causes of SUDEP are unknown, but it is very probable that cardiac arrhythmias during and between seizures play a potential role. Moreover, it has been shown that plasma vitamin E deficiency has a profound effect on the cardiovascular system, indicating their role in the pathogenesis of variability and cardiac events. Based on these facts, the aim of the present study was analyze plasma vitamin E levels in patients with refractory temporal lobe epilepsy and correlate it as a possible “marker” against cardiovascular abnormalities and hence SUDEP. The lower plasma levels of vitamin E in one of our patients, which presents several clinical characteristics that make him a potential candidate to SUDEP, stimulated us to investigate the plasma concentration of vitamin E in all patients considered SUDEP risk.

**Key words:** epilepsy, SUDEP, vitamin E, heart

## RESUMO

O evento mais comum de morte relatado nas epilepsias é a morte súbita e inesperada nas epilepsias (SUDEP). A causa exata da SUDEP ainda é desconhecida, mas é muito provável que as arritmias cardíacas durante e entre as crises estejam associadas ao evento da SUDEP. Além disso, tem sido demonstrado que a deficiência plasmática de vitamina E desempenha um profundo efeito sobre o sistema cardiovascular, sugerindo sua participação na patogênese de eventos cardíacos. Baseando-se nesses fatos, o objetivo do presente estudo foi avaliar os níveis plasmáticos de vitamina E em pacientes com epilepsia do lobo temporal refratária e tentar correlacioná-lo como um possível “marcador” contra alterações cardiovasculares e até mesmo SUDEP. Dos 10 pacientes avaliados, apenas um apresentou níveis plasmáticos diminuídos de vitamina E. Além disso, tal indivíduo apresenta características clínicas que o torna um possível candidato a SUDEP, estimulando nosso grupo de pesquisa verificar a concentração plasmática de vitamina E em todos os pacientes considerados de risco para SUDEP.

**Palavras-chave:** epilepsia, SUDEP, vitamina E, coração.

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## 1. INTRODUCTION

The epilepsies are the most common serious neurological condition and the severity and seriousness of epilepsy in developing countries is well documented<sup>1</sup>. Furthermore, people with epilepsy are two to three-fold increases to die prematurely than those without epilepsy and the most common epilepsy-related category of death is sudden unexpected death in epilepsy (SUDEP)<sup>2</sup>. The exact pathophysiological causes of SUDEP are unknown, but it is very probable that cardiac arrhythmias during and between seizures play a potential role<sup>3</sup>. As we know, although the availability of pharmacological treatment of epilepsy has expanded, the antiepileptic drugs (AEDs) are still limited in clinic efficacy. In these lines, several factors such as genetic, environmental and social can contribute to the inefficacy of therapeutic outcome of patients with epilepsy. Among these factors, nutritional aspects, i.e., vitamin E also have an interesting role in this scenario. In this way, several animal and human studies have demonstrated an association between epilepsy and vitamin E, supporting the hypothesis that vitamin E could be effective in controlling certain types of seizures and to prevent some of the harmful effects of antiepileptic drugs (AEDs)<sup>4</sup>. From a cardiovascular point of view, Vitamin E also may limit the progression of atherosclerosis, perhaps by stabilizing plaque and preventing its rupture and subsequent clot formation<sup>5</sup>. Vitamin E supplementation also leads to a decrease in platelet aggregability<sup>6</sup> and also can reduce the expression of adhesion molecules that can cause neutrophils to stick to the endothelial cells lining the artery<sup>7</sup>. The benefits of vitamin E may be particularly pronounced in patients with existing cardiovascular disease and low dietary antioxidant intake<sup>8</sup>. Quite interesting, plasma vitamin E deficiency has a profound effect on the cardiovascular system, indicating their role in the pathogenesis of variability and cardiac events<sup>9</sup>. Based on these facts, as high seizure frequency is

one of the mainly risk factor for SUDEP and that seizure control seems of paramount importance to prevent SUDEP<sup>3, 10</sup>, the aim of the present study was analyze plasma vitamin E levels in patients with refractory temporal lobe epilepsy and correlate it as a "marker" against cardiovascular abnormalities and hence SUDEP.

## 2. METHODS

The present study examined plasma  $\alpha$ -tocopherol E levels and dietary vitamin E in patients with refractory epilepsy. The study was granted approval by the University of Mogi das Cruzes Human Research Ethics Committee, and subjects gave written informed consent. A senior clinical neurologist determined diagnoses. Plasma  $\alpha$ -tocopherol levels were measured in 10 subjects (07 females (F) and 03 male (M)) and dietary data are available for all of them. Plasma  $\alpha$ -tocopherol levels was measured by high performance liquid chromatography with UV detection<sup>11</sup> and the normal range of plasma  $\alpha$ -tocopherol levels considered in this study was 0,5 to 1,8 mg/l. Dietary intake was assessed by a dietitian by narrative diet history<sup>12</sup>.

## 3. RESULTS

All the patients were detected to be suffering from temporal lobe epilepsy (TLE). The clinical characteristics of the study population are presented in **Table 1**. The levels of  $\alpha$ -tocopherol (mg/l) are expressed in **Table 2**. In brief, there was no difference in plasma  $\alpha$ -tocopherol between four patients. On the other hand,  $\alpha$ -tocopherol levels were significantly lower in one patient (F.C.B). Diet analysis indicates that all of subjects met or exceeded the recommended intake for vitamin E, and dietary intake was not related to plasma  $\alpha$ -tocopherol level in this subject.

## 4. DISCUSSION

The findings of the present study demonstrated that  $\alpha$ -tocopherol levels were significantly lower in one patient (F.C.B) with refractory temporal lobe epilepsy. We are sure that further studies with larger sample sizes are required; however, some pertinent considerations should be evaluated at this moment. Several epidemiological studies and intervention trials have been performed with vitamin E, and the majority of them showed that it prevents cardiovascular abnormalities<sup>13</sup>. Furthermore, it has been purposed that plasma vitamin E deficiency has a profound effect on the cardiovascular system, indicating their role in the pathogenesis of variability and cardiac events<sup>9</sup>. The adequacy of dietary intake for vitamin E, coupled with the lack of association between plasma levels and dietary intake of  $\alpha$ -tocopherol, suggests that lower plasma levels of  $\alpha$ -tocopherol in our patient (F.C.B.) are less likely to be due to poor diet and may be due to some other factor associated with temporal lobe epilepsy. In addition, our specific case (F.C.B) presents several clinical characteristics that make him a potential candidate to SUDEP<sup>2,3</sup>, such as age (35 years old); type of seizures (complex partial seizures with secondary generalization); seizure frequency (07 times/week), AEDs number (mainly carbamazepine) and uncontrolled seizures. Taking these data together, our research group decided a few days ago to send this patient to a detailed cardiovascular evaluation, looking for cardiovascular co-morbidity, cardiovascular risk factors and prior cardiac findings (electrocardiogram and echocardiogram).

On the whole, we believe that is important to emphasize to the physicians pay more attention with our present explanation and consider that lower vitamin E plasma concentration could be a "marker" to future cardiovascular abnormalities and hence SUDEP.

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Name	Age/Gender	Frequency of seizures	MRI Lesion	AEDs
ISRM	29/F	Complex Partial Seizures. 02 times//day.	Left mesial temporal sclerosis,	900 mg/day - Oxcarbazepine; 10 mg/night – Clobazan.
FCB	35/F	Complex Partial Seizures with secondary generalization. 07 times/week	Left mesial temporal sclerosis	1800 mg/day - Carbamazepine; 5 mg/day - Clobazan.
LAG	44/F	Complex Partial Seizures. 04 times/week	Left mesial temporal sclerosis	300 mg/day - Fenitoin; 2,5 mg/day - Clobazan.
ACP	55/M	Complex Partial Seizures. 02 times/month	Left mesial temporal sclerosis, with cortical dysplasia	600 mg/day – Carbamazepine.
CHA	24/F	Complex Partial Seizures. 03 times/month	Right mesial temporal sclerosis	1 g/day - Carbamazepine; 5 mg/day – Clobazan.
KCS	36/F	Complex Partial Seizures with secondary generalization. 07 times/month	Left mesial temporal sclerosis	1800 mg/day – Oxcarbazepine; 20 mg/night – Clobazan.
MLS	46/F	Complex Partial Seizures 02 times/week	Left mesial temporal sclerosis	1200 mg/day – Carbamazepine 20 mg/night – Clobazan.
FBS	29/M	Complex Partial Seizures 01 times/week	Right mesial temporal sclerosis	400 mg/day – Topiramate 20 mg/night – Clobazan.
TCV	33/M	Complex Partial Seizures 01 times/month	Left mesial temporal sclerosis	800 mg/day – Carbamazepine
RLH	26/F	Complex Partial Seizures 01 times/week	Right mesial temporal sclerosis, with cortical dysplasia	900 mg/day - Oxcarbazepine; 10 mg/night – Clobazan

**Table 1.** Clinical characteristics of the study population.

Patient	Plasma $\alpha$ -tocopherol concentration (mg/l)
ISRM	1,2
<b>FCB</b>	<b>0,2</b>
LAG	0,7
ACP	1,1
CHA	1,0
KCS	1.3
MLS	1.1
FBS	1.2
TCV	1.0
RLH	0.9

**Table 2.** Plasma  $\alpha$ -tocopherol level (mg/l) of the patients studied.