QT interval in Temporal lobe epilepsy versus non temporal lobe epilepsy

Thesis
Submitted for Partial Fulfilment of Master's Degree in
Neurology and Psychiatry

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Cairo-Egypt
2020

Acknowledgment

In the name of **"Allah"** the most Gracious and most Merciful for bestowing his blessings upon me, granting me the power to proceed and for stretching out his hand with knowledge to help me accomplish this work.

I would like to express my gratitude to Prof. ***Dr. Ahmed Abd Elmenom Gaber,*** Professor of Neurology, Faculty of Medicine, Ain Shams University for the benefit of his extensive experience. And for giving me the time and chance for completion of this thesis.

With considerable appreciation I would like to express my indebtedness for ***Prof. Dr. Yousry Aboelnaga Abdelhamid***, Professor of Neurology, Faculty of Medicine Ain Shams University for his great help and kind supervision. Couldn't have completed it with his valuable comments and recommendations.

A special word of appreciation for ***Dr. Mona Mokhtar Wahid El din***, Lecturer of Neurology, Faculty of Medicine, Ain Shams University for her kind support, advice and encouragement in every step of this thesis.

I would like to express my thanks and gratitude to ***Dr. Islam Mahmoud Bastawy,*** Lecturer of cardiology, Faculty of Medicine, Ain Shams University. For his advice in academic writing and for his time in helping me calculate QT values for the thesis.

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List of Abbreviations

Abb.	Meaning
AAN	American Academy of Neurology
AED	Antiepileptic drug
AP	Action potential
CBZ	Carbamazepine
ECG	Electrocardiogram
EEG	Electroencephalogram
GABA	γ-aminobutyric acid
hERG	Potassium repolarization channels
HR	Heart rate
IKr	Rapid delayed rectifier potassium current
Iks	Slow delayed rectifier potassium current
Ina	Cardiac sodium current
INaL	Sustained late component of sodium current
LQT	Long QT
LQTs	Long QT syndrome
LTG	Lamotrogine
LVT	Levetiracetam
Ms	Milliseconds
Navs	High density of fast Na channels
NICE	National institute of health and care excellence
nNavs	Neuronal type of sodium channels
PHT	Phenytoin
PRM	Primidone
QTc	Corrected QT
RUF	Rufinamide
SCA	Sudden cardiac arrest
SUDEP	Sudden unexpected death in epilepsy
TdP	Torsade de pointes
TTX	Tetrodotoxin

INTRODUCTION

Epilepsy is one of the most common disabling chronic condition of the nervous system. The incidence of sudden death is 20 times more common in epilepsy patients than the rest of the population ***(Shankar et al., 2013).*** Sudden unexpected death in epilepsy (SUDEP) is defined as a sudden, non-traumatic, witnessed or unwitnessed unexpected death and without any obvious cause ***(Laurence and Kocheril, 2012).*** SUDEP affects 1 in 1000 cases per year ***(Chyou et al., 2016).***

A recent study found that people with epilepsy had a twofold to threefold increased risk of sudden cardiac arrest (SCA) that's ECG confirmed, irrespective of the traditional cardiac risk factors for SCA. Leading to the idea of using 12 lead ECG as a potential low cost screening test for SCA ***(Wilder-Smith and Lim, 2001; Lamberts et al., 2015).***

ECG indicators for the risk of SCA include pathological cardiac repolarization such as shortening or prolongation of QT interval and increased QT dispersion***(Shmuely et al., 2017).*** The QT interval is the measure of the duration of ventricular depolarization and repolarization. It's calculated over three to five heartbeats preferably in leads II, V5 and V6 with longest value used ***(Surges et al., 2010).***

QT corrected according to heart rate (QTc) prolongation was found in interictal ECGs of people with epilepsy more frequently than in those without epilepsy ***(Shmuely et al., 2017; Lamberts et al., 2015).*** There are also studies that suggest there is a genetic link between long QT (LQT) syndrome pathoetiology and epilepsy and that their co-existence can lead to SUDEP ***(Omichi et al., 2010.; Smith, 2016).***

The mechanism of QT interval prolongation in epilepsy remains unknown ***(Biet et al., 2015).*** However, QTc was found significantly longer in partial epilepsy patients when compared to control group ***(Dogan et al., 2010; Lamberts et al. ,2015).*** In another study comparing QT interval between types of epilepsy, its results showed prolonged QT in complex partial seizures more than other epileptic patients ***(Drake et al., 1993).*** Even though the diagnostic yield of routine 12 lead ECG for suspected epilepsy patients isn't well known and neither listed in AEN/AAN guidelines, it's currently recommended by NICE guidelines ***(Lamberts et al., 2015)***.

AIM OF THE WORK

The aim of this study to determine through routine 12 lead ECG in epileptic patients whether:

There is prolonged QT interval in Epileptic patients in comparison with health controls.

There's a difference in QT interval between temporal lobe epilepsy patients and other types of epilepsy.

There is necessity to perform 12 lead ECG for epileptic patients as part of routine investigations.

TEMPORAL LOBE EPILEPSY

Temporal lobe epilepsy is the most common type of focal epilepsy in adults. Many of which its cases have shown pharmaco-resistance and candidates for surgery ***(Muhlhofer et al., 2017).*** Frontal lobe seizures are second most common seizures to temporal lobe and are sometimes hard to differentiate ***(Blair, 2012)***.

Cardinal signs of temporal lobe epilepsy:

Prodrome: Some patients experience preictal events that help predicting a coming seizure. They sometimes last from several minutes to hours, sometimes even days. They may include headaches, anxiety, personality changes, irritability, or nervousness. They are recognized mainly by family and friends but not the patient himself.

Aura: Mostly happen at the onset of complex partial seizures, but some are simple partial seizures that can occur alone. They usually last from 1-2 minutes before losing of conscious state. The auras usually correlate with site of seizure onset. Though some papers have questioned the value of auras in localizing ictal origin in cases of complex partial seizures ***(Blair, 2012)***. Sensory auras have been found in close association with temporal lobe seizures. They include symptoms such as experiential phenomena, rising epigastric sensations, visceral and auditory illusions, and complex

auditory or visual hallucinations ***(Fogarasi et al., 2007).*** Semiological classifications of seizures associate the anatomical focus of seizure origin with the clinical features. The localization may be inaccurate if the seizure begins in an area inaccessible to scalp EEG recording. Seizure semiology may signify seizure propagation rather than seizure origin if it originated in "non-eloquent area" to "eloquent area".

Altered consciousness: Complex partial seizures are commonly associated with altered consciousness and amnesia for the event. Temporary block of verbal output or verbal comprehension or motor output with maintained consciousness should be deffrentiated from impaired awareness.

Amnesia: Patients with complex partial seizures don't recall that they had a seizure minutes earlier. They also may have difficulty recalling the events that happened prior to the seizure onset. There is a variability in the degree of retrograde and anterograde amnesia. Bilateral impairment of hippocampal function causes post ictal amnesia ***(Blair, 2012)***.

Automatism: Automatism represent a coordinated involuntary motor activity always accompanied by altered conscious state and subsequent amnesia. They may be divided into de novo and preservative automatisms. De novo occur at seizure onset. They may be classified into "reactive phenomena" which appear to be reactions to external stimuli and "release phenomena" which include actions that are

normally socially inhibited. Continuation of complex motor acts initiated prior to the seizure may be consedired preservative automatisms ***(Fogarasi et al., 2007).*** Vocalization, ictal speech and affective behaviour are less common automatisms that are associated with temporal lobe seizures. Less common leaving behavior, dycrastic and gelastic have been reported ***(Hartl et al., 2018)***.

Lateralizing signs in temporal lobe epilepsy

Unilateral upper limb automatisms: They are associated with ipsilateral seizure onset, though it's debatable. Some others have reported that early unilateral motor automatisms without dystonic posturing localizes origin of seizures to the contralateral temporal lobe neocortex. Postictal nose rubbing or wiping is associated with ipsilateral focus. Post ictal head tilt occurring early with preserved consciousness is usually ipsilateral to seizure onset, but when occurs later its contralateral lobe and is more forceful. Eye deviation with forced head turning occur in the same direction. Version occurs in both temporal and extra temporal onset seizures and is followed by tonic posturing occurring just before or with secondary generalization. Unilateral tonic limb posturing is associated with contralateral focus. The dystonic posturing of arm and leg has been attributed to the spread from the amygdale and hippocampus to the ventral striatum ***(So, 2006)***.

Lower facial weakness (mild to severe): Facial weakness has been noted contralateral to a unilateral temporal lobe focus in ¾ in a sample of 50 patients. It has been reported more prominent with mimetic movements. That's why facial asymmetry may be a useful sign in temporal lobe epilepsy on combination with other semiological features ***(Blair, 2012)***.

Language disturbances: They are associated with temporal lobe seizure, hey can include expressive, receptive, global aphasia or dyslexia. The occurrence of speech arrest at the seizure onset or ictal or postictal aphasia reliably implies dominant hemisphere seizure of origin. Speech arrest may occur is the patient was talking during seizure onset or if the patent is unable to speak despite clear attempts to do so and recalls it after the termination of the clinical event. Its mechanism may be due to the involvement of Wernick's area, Broca's area or the dominant basolateral temporal area as these areas produce speech without motor impairment or loss of consciousness. Post ictal aphasia is a reliable lateralizing sign with prevalence (80-90%) ***(Loddenkemper and Kotagal, 2005)***. Seizures of non- dominant hemisphere origin is predicted reliably by speech preservation. However they may interfere with speech function on the basis of postictal confusion ***(Blair, 2012)***.

Localization reliability of semiological features in temporal lobe epilepsy

Semiology of temporal lobe seizures that occur during wake or sleep show the same features of lateralization in patients. Secondary generalization is more common in temporal lobe seizures that occur during sleep ***(Rodriguez et al., 2007)***. Localizing the onset of seizures based on ictal semiology is in the majority of patients with partial epilepsy has shown great accuracy ***(O'Brien et al., 2008)***. In a paper done by Kotagal and associates on 31 patients who had complex partial seizures of temporal lobe onset to detect symptoms and seizure progression ***(Loddenkemper and Kotagal, 2005***). The most common symptoms were shown to form a tight cluster with several sub clusters:

(i) Ictal emesis, epigastric aura, alimentary and hand automatisms

(ii) Behavioral arrest, staring, bilateral facial contractions and complete loss of consciousness

(iii) Unilateral dystonic posturing of an arm, complex gestures, ictal speech and partial loss of consciousness

(iv) Looking around, vocalization and whole body movements.

A strong association between epigastric sensation and ictal vomiting was noticed in patients with right temporal origin of seizures. Oroalimentary aura was found frequent in mesial temporal seizures. Preservative automatisms and emesis are said to occur in temporal lobe seizures. Experiental auras and olfactory auras that are followed by alimentary and distal upper limb automatisms, behavioral arrest, loss of consciousness, and purposeless looking around coupled with whole body movements are typical of mesial temporal lobe seizures ***(Blair, 2012)***.

Temporal lobe epilepsy is associated with alterations of autonomic nervous system activity. There is evidence of ictal and interictal autonomic dysregulation, predominantly with sympathetic overactivity. Seizure related autonomic hypo- and hyper-activity modifies the function of multiple systems such as gastorintetsinal, respiratory , urogenital and most importantly cardiovascular system, Thee frequent increae in heart rate and blood pressure precede or accompany ictal discharges. Intericatl autonomic modulation has been demonastrated as enhanced sympathetic tone. Some studies have also reported changes of parasypathteic HR modulation in TLE patients. This imvbalance of sympathetic and parasympathetic cardiovascular activity is considered a potential cause of sudden unexpected death in epilepsy ***(M. J. Hilz, 2002).***