

Ethical considerations in sudden unexpected death in epilepsy (SUDEP)

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Abstract: *Epilepsy is one of the world's oldest diseases. Social stigma, misunderstanding and thus, discrimination have surrounded patients and their families from the beginnings until nowadays. Approximately up to 80% of epilepsy cases worldwide are found in developing regions. The risk of premature death is two to three times higher than for the general population. There is contradictory evidences concerning the question of whether to inform patients about the possibility of sudden unexpected death in epilepsy (SUDEP). Actual guidelines states that individuals with epilepsy and their families or careers should be given access to information on SUDEP. We have information about how, when and what to say to the patients and families about SUDEP. But it's a delicate subject, and some patients do not want to know that they are at risk for this.*

Keywords: *epilepsy, SUDEP, ethics*

INTRODUCTION

Despite age, racial, social, geographic or national boundaries, epilepsy remain a prevalent chronic neurological disorder.

The incidence of epilepsy was estimated at 24-53 per 100,000 people.

World Health Organization (WHO) estimates that around 50 million people worldwide have epilepsy, 80% from developing regions. Epilepsy is characterized by recurrent seizures due to excessive electrical discharges in a group of

different parts of the brain cells. It is consider that up to 10% of people worldwide have one seizure during their lifetimes. Epilepsy is defined by two or more unprovoked seizures. Only one fourth of affected people in developing countries get the treatment they need and only 70% of these respond to medication. Mortality is higher in patients with epilepsy than in general population. People with epilepsy and their families can suffer from stigma and discrimination in many parts of the world. For example in China and India, epilepsy is a reason for prohibiting or annulling marriages.

In the United Kingdom, a law forbidding people with epilepsy to marry was repealed only in 1970. In the USA, until the same years, it was illegal that people with seizures have access to restaurants, theatres,

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recreational centers and other public buildings. Even nowadays patients have reduced access to health and life insurance, to obtain a driving license, to get a job or have other limitations.[1-5] Still now a person may be identified as an “epileptic” rather than “a person with epilepsy”. [6] SUDEP is the second death cause in epilepsy after status epilepticus. Unusually, the diagnostic of SUDEP is retrospective. Is defined as sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death in patients with epilepsy, with or without evidence of a seizure and excluding documented status epilepticus, in which postmortem examination does not reveal a toxicological or anatomical cause of death. [7] It is responsible for 7.5–17% of all epilepsy deaths and has an incidence among adults between 1:500 and 1:1000 patients per year. [8] Epileptologists agreed that SUDEP is mainly, but not exclusively, a problem for patients with refractory epilepsy. Epilepsy-related mortality is a significant risk in pregnancy, 1:1000 women died from epilepsy (mostly SUDEP) during or shortly after pregnancy. [9] SUDEP has an estimated annual incidence rate of 0.81 cases per 100000 population, or 1.16 cases per 1000 patients with epilepsy. Comparing years of potential life lost from SUDEP with selected other neurologic diseases, SUDEP ranks second only to stroke. [4] There are some risk factors like: generalized tonic-clonic seizures (GTCS), nocturnal seizures, variability of EEG records, and duration of the disease ranging from 15 to 20 years, early onset of epilepsy, poly-medications, cold temperatures, alcohol abuse, and street drugs. [10-14] It has been suggested that the most common pathogenic mechanism underlying SUDEP is heritable arrhythmogenic syndromes, or cardiac channelopathies, such as familial long QT syndrome (LQTS).[15,16] LQTS associated with syncope, seizures and sudden cardiac death is caused by mutations in more than 10 genes, encoding potassium and sodium ions channels.

Among cardiac arrhythmias, respiratory dysfunction, neurogenic pulmonary edema and dysregulation of systemic and cerebral circulation are other proposed pathophysiological events implicated in SUDEP.[17-19]

ETHICS ON SUDEP

There is a reasonable question about SUDEP: must it be discussed with all patients with epilepsy who are at risk of SUDEP, or not? The Task Force of the American Epilepsy Society and the Epilepsy Foundation have guidelines concerning what, how, when SUDEP should be discussed with patients, their families and caregivers. In Europe, the National Institute of Clinical Excellence (NICE) has the same attitude. [3]

The topic of SUDEP involves many moral dilemmas, most of which do not have absolute solutions. Advocates of universal SUDEP counseling cite the “right to know,” but others point to the “right not to know”. There is neither empirical evidence nor consensus on the question of whether to inform patients and parents about the possibility of SUDEP.[20]

Arguments to inform patients about SUDEP

In recent times there has emerged a debate regarding the obligation to warn even newly diagnosed patients of the risk of SUDEP. If there is a reasonable chance of preventing SUDEP, it must be discussed with all patients with epilepsy who are at highest risk of SUDEP. A few strategies that patients with epilepsy and their careers can take to reduce death risk could then be share by the physician.

On the other hand, the term “unexpected” is improper used because in some patients with risk factors SUDEP could be expected.[7] Precise definition and classification of SUDEP is necessary to scientific and medical communication, and is also important from a legal point of view. The new classification consists of six classes and definitions:

1. Definite SUDEP

1a. Definite SUDEP Plus (preexisting condition could have contributed to the death),

2. Probable SUDEP, (meets criteria for SUDEP, but no postmortem examination was done to exclude another pathologic process)

3. Possible SUDEP (postmortem examination may have identified drowning)

4. Near SUDEP (cardiorespiratory arrest that is successfully resuscitate),

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5. Not SUDEP when a clear cause of death is known.
 6. Unclassified: incomplete information available; not possible to classify

The patient suffering from epilepsy is, in many respects, no different to any other patient being treated by medical practitioner. [21] The ethical principle of patient autonomy in health care involve the patient's right to know about medical condition and prognosis. Information should be provided promptly to patients, their families and caregivers if they ask about the potential adverse consequences of the seizures or about the mortality risk associated with epilepsy.

In learning about SUDEP, parents expressed a need to be informed of the risk of that. There was a consensus that it should be the parents' decision as to whether or not the child should be present at the meeting or when to inform the child about the risk of SUDEP.[22]

In some cases the risk of SUDEP may need to be emphasized to encourage compliance with medical and surgical therapy for epilepsy. Recent evidence from a meta-analysis of randomized clinical trials of adjunctive AEDs at efficacious doses provides strong support for AED treatment as mono- or polytherapy to increase seizure control and protect against SUDEP in patients with refractory epilepsy.

For patients for whom seizure control is unattainable, supervision or monitoring may prevent SUDEP, though this has never been formally tested. [15] Increasing awareness of SUDEP may facilitate improved seizure control and possibly decreasing SUDEP incidence.[23]

Furthermore, SUDEP discussion can be encouraging to patients with very low SUDEP risk. Patients with absence epilepsy or benign epilepsy syndromes must know that their risk of SUDEP is negligible.

Arguments for not informing patients about SUDEP

By low, failure to discuss SUDEP with a patient suffering from epilepsy cannot constitute negligence because the outcome cannot be as a consequence of the actions of the doctor based upon current knowledge.

Mainly, if the patient has not asked about his distress, there is not the basis for litigation against the doctor who chooses not to discuss this topic.[20]

Until now, no interventional measures are known to stop the outcome, so we get nothing by warning of SUDEP. To admit the SUDEP, it may seriously deteriorate quality of life. In this case the doctor may deliberately omit information to avoid patient fear and anxiety, respecting in this way the right „do no harm“. The negative influence on quality of life may represent a form of negligence.

It may be possible to show causal connection between impaired quality of life and the doctor divulging information that the patient did not explore. Poly medication is an important risk factor for SUDEP, but a necessary intervention for the epilepsy management. So many patients requiring polytherapy have been refused it for fear of SUDEP.[14]

CONCLUSIONS

Duty of care dictates open and frank discussion if the patient wishes information about mortality and epilepsy. The big dilemma concerning ethics considerations in SUDEP is: the “right to know” or the converse which is the “right not to know”?

This conflict, places the clinician in a serious ethical difficulty because it requires the balancing of these diametrically opposed concepts and demands a value judgement on the part of the clinician. SUDEP is essentially unpredictable for any individual patient. It also confirms that “never” and “always” are dangerous terms when used by doctors.

To assure the patient of something which cannot be assured may represent another form of negligence and failure of duty of care. The doctor provide the patient with accurate and informed response to questions raised .Where the detailed information will not alter the outcome for the patient, failure to provide it cannot be deemed to represent negligence.

The ethical consideration is met if the doctor tries to ascertain what the patient wants to know and responds accordingly by providing that information which the patient requests. Thus, each case must be

managed individually and doctors are advised to document the decision-making process. The patient

care is like a balance between what the career offers, and what the patient accepts.

References:

1. Nakano H, Inoue Y. Epidemiology and cause of epilepsy. *Nihon Rinsho*. 2014 May ; 72 (5) : 785-9.: [accessed 2014 Jul 07] <http://www.ncbi.nlm.nih.gov/pubmed/24912276>
2. Atlas Epilepsy Care in the World 2005, World Health Organization, ISBN-13 9789241563031, ISBN-10 9241563036, 2005: 1-91
3. The Epilepsies. The Diagnosis and Management of the Epilepsies in Adults and Children in Primary and Secondary Care. London: NICE; 2012 [accessed 21.06.14] <http://www.nice.org.uk/nicemedia/live/13635/57784/57784.pdf>
4. Thurman DJ, Hesdorffer DC, French JA. Sudden unexpected death in epilepsy: Assessing the public health burden. *Epilepsia*. 2014 Jun 5 [accessed 2014 jul 01]; <http://www.ncbi.nlm.nih.gov/pubmed/24903551>
5. WHO-Epilepsy-Fact sheet N°999 -October 2012
6. Beran RG. Epilepsy and law. *Epilepsy & Behavior* 12 (2008) 644–651
7. Nashef L, So EL, Ryvlin P, Tomson T. Unifying the definitions of sudden unexpected death in epilepsy. *Epilepsia*, 2012, 53: 227–233.
8. Scorza FA1, Cysneiros RM, de Albuquerque M, Scattolini M, Arida RM. Sudden unexpected death in epilepsy: an important concern. *Clinics (Sao Paulo)*. 2011;66 Suppl 1:65-9.
9. Edey S, Moran N, Nashef L. SUDEP and epilepsy-related mortality in pregnancy. *Epilepsia*. 2014 Apr 22. [accessed 2014 Jul 07]: <http://www.ncbi.nlm.nih.gov/pubmed/24754364>
10. Majkowski J, Sudden Unexpected Death In Epilepsy (SUDEP) – an update. *Journal of Epileptology* 2013 (21): 37–54.
11. Surges R, Thijs RD, Tan HL, Sander JW. Sudden unexpected death in epilepsy: risk factors and potential pathomechanisms. *Nat Rev Neurol*. 2009;5:492–504
12. Hirsch LJ, Hauser WA. Can sudden unexplained death in epilepsy be prevented? *Lancet*. 2004; 364:2157–8.
13. Aurlen D., Larsen J.P., Gjerstad L., Taubøll E.: Increased risk of sudden unexpected death in epilepsy in females using lamotrigine: a nested, case-control study. *Epilepsia*, 2012, 53: 258–266.
14. Hesdorffer D.C., Tomson T. Sudden Unexpected Death in Epilepsy: Potential role of antiepileptic drugs. *CNS Drugs*. 2013 Feb;27(2):113-9. [accessed 2014 jul 01]; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23109241>
15. Agostini S.D., Aniles E., Sirven J., Drazkowski J.F.: The importance of cardiac monitoring in the epilepsy monitoring unit: a case presentation of ictal asystole. *Neurodiagn. J.*, 2012, 52: 250–260
16. Tu E, Bagnall RD, Duflou J, Semsarian C. Post-Mortem Review and Genetic Analysis of Sudden Unexpected Death in Epilepsy (SUDEP). *Cases Brain Pathol*. 2011 Mar; 21 (2):201-8
17. Schuele SU, Widdess-Walsh P, Bermeo A, Lu" ders HO. Sudden unexplained death in epilepsy: the role of the heart. *Cleve Clin J Med*. 2007; 74:S121–27.
18. Meyer S., Shamdeen M.G., Gottschling S., Strittmatter M., Gortner L.: Sudden unexpected death in epilepsy in children. *J. Paediatr. Child. Health.*, 2011, 47: 326–331
19. Velagapudi P., Turagam M., Laurence T., Kocheril A. Cardiac arrhythmias and sudden unexpected death in epilepsy (SUDEP). *Pacing Clin. Electrophysiol.*, 2012, 35: 363–370.
20. Beran R G, Weber S, Sungaran R, Venn N. Review of the legal obligations of the doctor to discuss Sudden Unexplained Death in Epilepsy (SUDEP)- a cohort controlled comparative cross-matched study in an outpatient epilepsy clinic *Seizure* 2004, 13, 523–528.
21. Beran RG. Informed consent, a legal requirement in the management of patients with epilepsy. In: Beran RG, editor. *Epilepsy: duty of care*. Tel Aviv: Yozmot; 2000.p.25–50.
22. Rajesh Ramachandran Nair, S. M. Jack, B. F. Meaney, G. M. Ronen. SUDEP: What do parents want to know? *Epilepsy & Behavior* 2013, 29:560-564.
23. Hirsch LJ, Donner EJ, So EL, Jacobs M, Nashef L, Noebels JL, Buchhalter JR. (2011) Abbreviated report of the NIH/NINDS workshop on sudden unexpected death in epilepsy. *Neurology* 2011 May 31; 76(22): 1932-8, http://www.ninds.nih.gov/news_and_events/proceedings/SUDEP_workshop_nov2008.htm