

Epilepsy Monitor

Lisa Bateman, M.D., FRCPC
Masud Seyal, M.D., Ph.D.

Mortality in patients with epilepsy is increased with a standardized mortality ratio of 1.6 to 9.3 in the general epilepsy population. Causes of increased mortality include accidental death, suicide, status epilepticus and sudden unexpected death in epilepsy (SUDEP). SUDEP is the most common cause of death in patients with epilepsy, with the highest incidence of SUDEP in patients being evaluated in epilepsy referral centers and in patients being assessed for epilepsy surgery. In the latter population the annual incidence is 2.2 – 10 per 1000 population per year.¹

The precise physiological mechanisms of SUDEP are not known. Seizure-associated respiratory dysfunction and cardiac arrhythmias have both been implicated as possible precipitating causes. We have demonstrated that ictal hypoxemia and hypercapnia occur in one-third of patients with intractable localization-related epilepsy undergoing presurgical evaluation with video-EEG telemetry (VET). In some patients, seizures may be accompanied by severe oxygen desaturations (< 60%) and marked rises in end-tidal CO₂ (>70 mm Hg). Seizure-associated apnea, primarily central, is also common.^{2,3} Other respiratory mechanisms have been linked to SUDEP, including neurogenic pulmonary oedema, obstructive apnea and laryngospasm.^{4,5,6}

Cardiac arrhythmia may be primary mechanism of seizure-related death.⁷ There is lengthening of corrected QT interval (QTc), a finding associated with torsade de pointe and sudden cardiac death,⁸ during epileptic seizures, particularly secondarily generalized convulsions.^{9,10} Reduced heart rate variability (HRV), also associated with sudden cardiac death, is seen in chronic epilepsy patients.^{11,12} Mutations in ion channel genes associated with epilepsy and cardiac sudden death may also play a role in SUDEP.^{13,14}

Nocturnal supervision, including regular checks and the use of listening devices, may be protective against SUDEP.¹⁵ There are currently no reliable commercially available devices to detect seizures in the ambulatory setting. Prolonged, multimodality ambulatory monitoring of EKG, respirations and oxygen saturation is technically feasible with existing device technology but has not yet been applied to SUDEP research or prevention.¹⁶ We have been working to develop a prototype system using a PVDF sensor to monitor an epilepsy patient's heart beats and breaths and to wirelessly transmit this information to a base station, where the system detects the cessation of heartbeats and breathing and can sound an alarm. Such a system could provide an alert to a family member that a seizure has occurred, allowing for the potential for interventions which could ultimately reduce the risk of SUDEP.

References

1. Téllez-Zenteno JF, Ronquillo LH, Wiebe S. Sudden unexpected death in epilepsy: evidence-based analysis of incidence and risk factors. *Epilepsy Res* 2005;65:101-15.
2. Bateman LM, Li C-S, Seyal M. (2008). Ictal hypoxemia in localization related epilepsy: analysis of incidence, severity and risk factors. *Brain*, 131:3239-3245. PMID: 18952672
3. Seyal M, Bateman LM, Albertson TE, Lin T-C, Li C-S. (2010). Respiratory changes with seizures in localization-related epilepsy: Analysis of periictal hypercapnia and airflow patterns. *Epilepsia*, 51:1359-1364. PMID: 20163438
4. Swallow RA, Hillier CE, Smith PE. Sudden unexplained death in epilepsy (SUDEP) following previous seizure-related pulmonary oedema: case report and review of possible preventative treatment. *Seizure* 2002;11:446-448.
5. Tavee J and Morris III, H. Severe postictal laryngospasm as a potential mechanism for sudden unexpected death in epilepsy: a near-miss in an EMU. *Epilepsia* 2008;49:2113-2117.
6. Thomas P, Landré E, Suisse G, Breloin J, Dolisi C, Chatel M. Syncope anoxo-ischémique par dyspnée obstructive au cours d'une crise partielle complexe temporale droite. *Epilepsies* 1996;8:339-346.
7. Dasheiff RM, Dickinson LJ. Sudden unexpected death of epileptic patient due to cardiac arrhythmia after seizure. *Arch Neurol* 1986;43:194-196.
8. Elming H, Brendorp B, Kober L, Sahebzadah N, Torp-Petersen C. QTc interval in the assessment of cardiac risk. *Card Electrophysiol Rev* 2002;6:289-294.

9. Brotherstone R, Blackhall B, McLellan A. Lengthening of corrected QT during epileptic seizures. *Epilepsia* 2010;51:221-232.
10. Surges R, Adjei P, Kallis C, Erhuero J, Scott CA, Bell GS, Sander JW, Walker MC. Pathologic cardiac repolarization in pharmaco-resistant epilepsy and its potential role in sudden unexpected death in epilepsy: a case-control study. *Epilepsia* 2010;51:233-242.
11. Stein, P.K., Kleiger, R.E., 1999. Insights from the study of heart rate variability. *Annu. Rev. Med.* 50, 249—261.
12. Ronkainen, E., Ansakorpi, H., Huikuri, H.V., Myllylä, V.V., Isojärvi, J.I., Korpelainen, J.T., 2005. Suppressed circadian heart rate dynamics in temporal lobe epilepsy. *J. Neurol. Neurosurg. Psychiatry* 76, 1382—1386.
13. Goldman AM, Glasscock E, Yoo J, Chen TT, Klassen TL, Noebels JL. Arrhythmia in heart and brain: KCNQ1 mutations link epilepsy and sudden unexplained death. *Sci Transl Med* 2009;1:2-6.
14. Hindocha N, Nashef L, Elmslie F, Birch R, Zuberi S, Al-chalabi A, Crotti L, Schwartz PJ, Makoff A. Two cases of sudden unexpected death in epilepsy in a GEFS+ family with an SCN1A mutation. *Epilepsia* 2008;49:360-365.
15. Langan Y, Nashef L, Sander JW. Case-control study of SUDEP. *Neurology* 2005;64:1131-1133.
16. Hirsch LJ. Is sudden unexpected death in epilepsy due to postictal brain shutdown? *Ann Neurol* 2010;68:773-775.