



Sudden unexpected death in epilepsy

Principal investigator

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Background

Mortality in children with epilepsy exceeds that in the general population. While many deaths may be explained by the underlying cause of seizures or comorbid conditions, a proportion of deaths in children with epilepsy remain unexplained. Sudden unexpected death in epilepsy (SUDEP) refers to the death of a person with epilepsy that is sudden, unexpected and unexplained.¹

The Canadian Paediatric SUDEP Registry is a multi-centre, population-based registry for SUDEP in children, funded by a peer-reviewed grant from Citizens United for Research in Epilepsy. Paediatric neurologist collaborators representing all academic paediatric health science centres across Canada have committed to identifying cases of SUDEP.

The Canadian health care environment represents a unique opportunity to capture data on SUDEP in children; however, it is well recognized that only a small subset of children with epilepsy receive care from a paediatric neurologist. Dr. Jette, a co-investigator on this project, is currently leading a study examining the health care utilization of 26,000 people with epilepsy in Alberta. Dr. Jette has demonstrated that only 15% of children under 18 years of age were evaluated every two years by a neurologist or neurosurgeon, and 53% of these children had never been evaluated by a subspecialist in neurology care (ongoing study; unpublished data). This data is supported by a recent report for Health Quality Ontario, which determined that only 3.75% of adults and children with drug-resistant epilepsy were assessed by specialized neurology centres.² Given that drug-resistant epilepsy is a risk factor for SUDEP, this data suggests that children at risk of SUDEP are not routinely followed by subspecialist paediatric neurologists.³

Furthermore, poor awareness of SUDEP has been documented in multiple jurisdictions. An audit of epilepsy deaths in the UK found that the term 'epilepsy' was included on only 7% of death certificates.^{4,5} A survey of US coroners demonstrated that SUDEP was used as a final diagnosis infrequently and often mistakenly diagnosed as 'status epilepticus'.⁶

In August 2011, we collaborated on a one-time survey circulated to all CPSP participants to evaluate paediatrician knowledge of SUDEP. The purpose of the survey was to



determine whether a gap in knowledge of SUDEP exists among Canadian paediatricians and inform strategies for a prospective study of SUDEP among Canadian children. Among paediatricians who report that they care for children with epilepsy, only 56% (380) had prior knowledge that children with epilepsy are at an increased risk of sudden unexplained death. Only 33% (225) of these paediatricians were aware of the term SUDEP. Fourteen paediatricians reported knowledge of a case of sudden unexpected death in a child with epilepsy within the previous 24 months. Of the 11 cases for which details of the death investigation process were reported, five children (45%) did not undergo autopsy, suggesting inadequate investigation of deaths in children with epilepsy.

The incidence of SUDEP in adults is estimated to be 1 death per 1,000 people with epilepsy per year, with rates approaching 1 per 100 person-years in drug-resistant epilepsy.⁷ The incidence of SUDEP in children has not been explored adequately; limited literature suggests lower rates than in adults, from 0.2 to 0.4 per 1,000 person-years.^{8,9} These rates were generated from retrospective studies, which are hampered by poor awareness of SUDEP. No surveillance studies of SUDEP in children are available to allow for accurate incidence figures.

SUDEP is a potentially avoidable cause of death in children. A better understanding of which children are at risk of SUDEP will allow for the application of preventative strategies, such as increased nocturnal surveillance and aggressive seizure control methods.

Methods

Using the established methodology of the CPSP, participating paediatricians and paediatric subspecialists will be actively surveyed on a monthly basis for cases of SUDEP in Canadian children. At the launch of the study, participants will receive case definitions. For each reported case, a three-member adjudication panel will determine that the case meets definition for definite or probable SUDEP. Participants will be asked to complete a questionnaire to provide clinical data.

Case definition

Sudden unexpected death in a child less than 18 years of age:

- with epilepsy (defined as >1 unprovoked seizure)
- with or without evidence of a recent seizure
- without documented status epilepticus
- without trauma

Definite SUDEP is defined as meeting the above criteria, and a postmortem examination does not reveal a cause of death. *Probable SUDEP* is defined as definite SUDEP, but without autopsy.

Objectives

Primary objective:

- Determine an estimated incidence of SUDEP in Canadian children.

Secondary objectives:

- 1) Describe the clinical features associated with SUDEP in children.
- 2) Improve awareness of SUDEP among Canadian paediatricians.
- 3) Determine proportion of postmortem examination in children with an unexpected death in epilepsy.



Sudden unexpected death in epilepsy (continued)

Duration

January 2014 to December 2015

Expected number of cases

A retrospective review of cases of SUDEP in children less than 18 years of age occurring over a 10-year period in Ontario yielded 27 cases, from 138,620 patient-years of epilepsy, an incidence of 0.2 per 1,000 patient-years.⁸ Based on this incidence, the expected number of SUDEP cases in children in Canada is estimated to be 8.7 per year. It should be noted that the Ontario study included only deaths in which autopsy was performed. The literature suggests that only 12.5% of deaths of children with epilepsy undergo autopsy.¹⁰ Therefore, this figure is likely an underestimate due to poor case ascertainment from retrospective studies. Other studies have demonstrated an incidence of 0.4 per 1,000 patient-years. We anticipate a minimum of 10 cases per year.

Ethical approval

The Research Ethics Board, The Hospital for Sick Children

Analysis and publication

Analysis will include case characteristics and description of clinical features associated with SUDEP. When possible, data will be summarized using descriptive statistics. Completed study results will be presented at national and international scientific meetings and submitted for publication in scientific peer-reviewed journals. Knowledge translation to the epilepsy community will be achieved through collaborations with the epilepsy advocacy groups, Canadian Epilepsy Alliance and SUDEP Aware.

References

1. Nashef L, So EL, Ryvlin P, Tomson T. Unifying the definitions of sudden unexpected death in epilepsy. *Epilepsia* 2012;53(2):227-33.
2. Bowen JM, Snead OC, Chandra K, Blackhouse G, Goeree R. Epilepsy care in Ontario: an economic analysis of increasing access to epilepsy surgery. *Ont Health Technol Assess Ser* 2012;12(18):1-41.
3. Hesdorffer DC, Tomson T, Benn E, Sander JW, Nilsson L et al. Do antiepileptic drugs or generalized tonic-clonic seizure frequency increase SUDEP risk? A combined analysis. *Epilepsia* 2012;53(2):249-52.
4. Coyle HP, Baker-Brian N, Brown SW. Coroners' autopsy reporting of sudden unexplained death in epilepsy (SUDEP) in the UK. *Seizure* 1994;3(4):247-54.
5. Hanna NJ, Black M, Sander JW, Smithson WH, Appleton R et al. National Sentinel Clinical Audit of Epilepsy-Related Death, Report 2002, National Institute for Clinical Excellence.
6. Schraeder PL, Delin K, McClelland RL, So EL. Coroner and medical examiner documentation of sudden unexplained deaths in epilepsy. *Epilepsy Res* 2006;68(2):137-43.
7. Devinsky O. Sudden, unexpected death in epilepsy. *N Engl J Med* 2011;365:1801-11.
8. Donner EJ, Smith CR, Snead OC III. Sudden unexplained death in children with epilepsy. *Neurology* 2001;57(3):430-4.
9. Weber P, Bubl R, Blauenstein U, Tillmann BU, Lütischg J. Sudden unexplained death in children with epilepsy: a cohort study with an eighteen-year follow-up. *Acta Paediatr* 2005;94(5):564-7.
10. Nickels KC, Grossardt BR, Wirrell EC. Epilepsy-related mortality is low in children: A 30-year population-based study in Olmsted County, MN. *Epilepsia* 2012;53(12):2164-71.