Sudden unexpected death in epilepsy: Who are the children at risk?

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CASE 1

A developmentally appropriate 14-year-old girl presented with a history of two generalized tonic-clonic seizures. Further history was positive for myoclonic jerks, most often in the morning. An electroencephalogram demonstrated generalized spike and slow wave discharges, and a diagnosis of juvenile myoclonic epilepsy was established. She was initially treated with valproic acid, which resulted in unwanted side effects and was changed to lamotrigine. During the period of medication changes, she experienced another generalized tonic-clonic seizure. Over the next two years, she had two additional generalized tonic-clonic seizures. With questioning, these seizures could be attributed to forgotten medication doses. She was an excellent student and excelled in athletics.

Three years after her initial diagnosis, at 17 years of age, she was found one morning, dead in her bed in the supine position. There was evidence that a seizure had occurred, including tongue lacerations and disruption of the bed sheets.

Autopsy did not reveal the cause of death. As expected, the family was profoundly distraught, heightened by their anger at never having been told of the risk of death associated with epilepsy. In follow-up discussions with her parents, they expressed concerns about their daughter's compliance with anticonvulsant medications.

CASE 2

A 12-year-old boy was known to have drug-resistant epilepsy, moderately severe cognitive impairment and features of autism. Seizure onset was in the first year of life, characterized by infantile spasms, which resolved with treatment. In the second year of life, seizures recurred and, over time, he developed multiple seizure types including generalized tonic-clonic seizures, atonic seizures and atypical absence seizures. Electroencephalography was consistent with Lennox-Gastaut syndrome. Investigations did not yield an etiology. His seizures did not come under control, despite polytherapy.

Continued medical management reduced the frequency of the generalized tonic-clonic seizures from daily to every three to four weeks, usually occurring in clusters at night. Typically, his mother was awoken when he had seizures at night and would stay with him following a seizure. On the night of his death, she did not hear a seizure. She found him in his bed in the morning, dead in the supine position. It was not clear whether a seizure had occurred before death. An autopsy examination was not performed.

The stories of these two children, based on real cases under study, demonstrate the range of children at risk for sudden unexpected death in epilepsy (SUDEP). SUDEP is the unexpected and unexplained death of a person with epilepsy. Evidence of a preceding seizure is not required. Autopsy does not reveal a cause of death. While SUDEP is more common in people with uncontrolled seizures, all individuals with convulsive seizures are at some risk. Discussing SUDEP with families of individuals with epilepsy and with children and teens, as appropriate, may aid with adherence to treatment and allow people with epilepsy and their families to make informed decisions about their epilepsy care.

LEARNING POINTS

- Children with epilepsy have an increased risk of death compared with the general population. Most deaths in children with epilepsy are not seizure or epilepsy related. Much of the increased risk is attributed to the underlying condition, and children with neurodevelopmental disorders and symptomatic epilepsy are most at risk (1).
- SUDEP occurs in approximately one in 1000 people with epilepsy per year, with rates almost 10 times higher in those with drug-resistant epilepsy (2).
- SUDEP is less frequent during childhood. Reported rates of SUDEP in children range from 0.2 to 0.4 per 1000 person-years (1); however, childhood-onset epilepsy is a risk factor for SUDEP during young adulthood. The risk of SUDEP was 7% in a 40-year follow-up study investigating childhood-onset epilepsy (3).
- The strongest risk factor for SUDEP, established predominantly in the adult population, is frequent generalized tonic-clonic seizures. Other risk factors emerging from the literature include nocturnal seizures and poor adherence to anticonvulsant medications (2).
- Risk factors for SUDEP in children are not well established. Limited literature suggests that children with more severe epilepsy and comorbid conditions are at a higher risk (1). More study is needed to understand whether the risk factors observed in adults also apply in children.
- While not common in children, SUDEP is a potentially preventable cause of death during childhood. A Canadian Pediatric Surveillance Program study is currently underway to investigate the incidence and risk factors for SUDEP in Canadian children. The study protocol can be accessed at: www.cpsp.cps.ca/surveillance/study-etude/sudden-unexpected-death-in-epilepsy.

REFERENCES

1. Berg AT, Nickels K, Wirrell EC, et al. Mortality risks in new-onset childhood epilepsy. Pediatrics 2013;132:124-31.
2. Shorvon S, Tomson T. Sudden unexpected death in epilepsy. Lancet 2011;378:2028-38.
3. Sillanpaa M, Shinnar S. Long-term mortality in childhood-onset epilepsy. N Engl J Med 2010;363:2522-9.

The Canadian Paediatric Surveillance Program (CPSP) is a joint project of the Canadian Paediatric Society and the Public Health Agency of Canada, which undertakes the surveillance of rare diseases and conditions in children and youth. For more information, visit our website at www.cpsp.cps.ca.

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