Knowing Is Half the Battle: Underestimating SUDEP

Underestimation of Sudden Deaths Among Patients With Seizures and Epilepsy.

Devinsky O, Friedman S, Cheng JY, Moffatt E, Kim A, Tseng ZH. *Neurology* 2017;89:886–892.

OBJECTIVE: To determine the definite and potential frequency of seizures and epilepsy as a cause of death (COD) and how often this goes unrecognized. METHODS: Prospective determination of seizures or epilepsy and final COD for individuals aged 18–90 years with out-of-hospital sudden cardiac deaths (SCDs) from the population-based San Francisco POST SCD Study. We compared prospective seizure or epilepsy diagnosis and final COD as adjudicated by a multidisciplinary committee (pathologists, electrophysiologists, and a vascular neurologist) vs retrospective adjudication by 2 epileptologists with expertise in seizure-related mortality. RESULTS: Of 541 SCDs identified during the 37-month study period (mean age 62.8 years, 69% men), 525 (97%) were autopsied; 39/525 (7.4%) had seizures or epilepsy (mean age: 58 years, range: 27–92; 67% men), comprising 17% of 231 nonarrhythmic sudden deaths. The multidisciplinary team identified 15 cases of epilepsy, 6 sudden unexpected deaths in epilepsy (SUDEPs), and no deaths related to acute symptomatic seizures. The epileptologists identified 25 cases of epilepsy and 8 definite SUDEPs, 10 possible SUDEPs, and 5 potential cases of acute symptomatic seizures as a COD. CONCLUSIONS: Among the 25 patients identified with epilepsy by the epileptologists, they found definite or possible SUDEP in 72% (18/25) vs 24% (6/25) by the multidisciplinary group (6/15 cases they identified with epilepsy). The epileptologists identified acute symptomatic seizures as a potential COD in 5/14 patients with alcohol-related seizures. Epilepsy is underdiagnosed among decedents. Among patients with seizures and epilepsy who die suddenly, seizures and SUDEP often go unrecognized as a potential or definite COD.

Commentary

For those familiar with the G.I. Joe television cartoon series (you know who you are), you heard the phrase "knowing is half the battle" on a regular basis. This phrase was used by one of the characters at the end of every episode. At face value, it emphasizes the importance of knowledge and understanding in all aspects of life; while this is a valuable lesson for all impressionable minds (young and old alike), it should also resonate with providers regarding sudden unexplained death in epilepsy (SUDEP). Understanding SUDEP is a critical piece of the puzzle, but it is by no means the only piece.

SUDEP is not a newly recognized phenomenon. SUDEP reports date back to the time of the founding of the United States of America. President George Washington's writings detail the treatments for his stepdaughter's seizures that began at about 6 years of age (1). His stepdaughter, Martha Parke (Patsy) Custis, died at 17 years of age. He wrote, "[S]he was seized with one of her usual Fits, and expired in it, in less than 2 minutes without uttering a word, a groan, or scarce a sigh" (1). Despite descriptions of SUDEP dating back hundreds of years, it remained an infrequent topic of discussion among physicians until only recently.

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In fact, it was also not frequently a topic of scholarly inquiry. On November 2, 2017, I performed a Medline search from 1960 to 2017. A total of 189,011 papers were identified with either the keyword or MeSH heading of "epilepsy" or "seizures." If those papers were then limited to those that also include the keyword or MeSH heading of "death, sudden" or "death, sudden, cardiac" or the keyword "sudden unexplained death," one finds 1,133 papers, accounting for just 0.6% of the literature. Encouragingly, a clear rise in interest in the topic can be seen: From 1960 to 1970, only 0.11% of the literature addressed SUDEP, whereas for 2010 to 2017, it is 0.95%. This illustrates another part of the "battle" against SUDEP: recognition. If providers do not recognize SUDEP as an important part of epilepsy care, share information with their patients, actively study the risk factors and ultimately potential interventions, and engage with other providers outside of the neurology and epilepsy community, then knowledge will grow at a slower rate and won't necessarily be disseminated to all who may benefit.

The challenges of patient and provider education have been the subject of other studies, and the snapshot of publication data above demonstrates increasing recognition of the importance of research on SUDEP. The paper by Devinsky and colleagues tackles another aspect of recognition for SUDEP: For us to understand SUDEP, we need to accurately identify patients with definite, probable, or possible SUDEP.

Their study involved a multidisciplinary group composed of cardiologists, cardiac electrophysiologists, forensic patholo-

gists, anatomic pathologists, and a vascular neurologist who evaluated all cases referred to the medical examiner's office in San Francisco from February 2011 to March 2014. To be included, the deceased had to be 18 to 90 years of age and could not have had a severe noncardiac chronic terminal illness such as cancer, not have been a hospice resident, and not have identifiable noncardiac etiologies at the time of presentation (e.g., trauma or signs of overdose). Cases with a history of epilepsy or seizure were independently reviewed by two epileptologists for this study. The cause of death (COD) of SUDEP was established according to the unified criteria proposed by Nashef et al. (2).

Of the 525 consecutive sudden cardiac death cases that underwent autopsy during the study period, 39 (7.4%) had a history of seizures. Among those with seizures, the multidisciplinary team diagnosed epilepsy in 15 (38.5%), whereas the epileptologists diagnosed epilepsy in almost twice as many cases (25; 64%). The multidisciplinary committee identified 6 definite SUDEP cases of the 15 they identified with epilepsy. Of the 25 patients with epilepsy identified by the epileptologists, the COD was definite SUDEP for 6, definite SUDEP Plus for 2, possible SUDEP for 10, and not SUDEP for the remaining 7. Notably, for the 14 cases with a history of seizures that were not identified as epilepsy, acute symptomatic seizures were considered as either a possible COD or a contributing factor. Despite a thorough multidisciplinary process to identify the COD—utilizing record review and autopsy in patients with sudden death—only 33% of patients with definite or probable SUDEP (or SUDEP Plus) were identified; the majority of cases were missed by the multidisciplinary team. It is worth remembering that this represents the review of only the cases for which available records suggested a diagnosis of epilepsy. It is possible that additional cases were not identified due to incomplete information in the available records.

The underreporting of SUDEP on death certificates has been raised as a significant limit to our ability to quantify, study, and ultimately prevent SUDEP by other investigators (3–5). Previous data have demonstrated that a majority of pathologists did not diagnose SUDEP in cases that met the criteria (4). The authors of the current paper explore, in some detail, the challenges surrounding the diagnosis of SUDEP, including nonspecific postmortem and toxicological findings and the probabilistic determinations that may obfuscate the diagnosis of SUDEP or SUDEP Plus. This highlights the need for further study—not just on SUDEP itself but on how we correctly identify SUDEP in the community without the benefit of the rigorous multidisciplinary process employed in this study.

Knowing is indeed half the battle to ultimately eliminate SUDEP, but incomplete recognition limits the scope of our knowledge. Devinsky and colleagues demonstrated the differences in identifying SUDEP between those with expertise in the areas of epilepsy and sudden death versus those with expertise in sudden death and mortality *outside* the epilepsy field. On the path forward, reliable recognition of SUDEP on death certificates is a major hurdle, one that we have yet to clear. In the cartoon world, G.I. Joe faced a clearly defined foe, recognized by everyone without any introduction; SUDEP has proven to be significantly more challenging to recognize, but these continued examinations of discrepancies in diagnoses will help close the gap.

by Chad Carlson, MD

References

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