



Practice Guideline: Sudden Unexpected Death in Epilepsy Incidence Rates and Risk Factors

This is a summary of the American Academy of Neurology (AAN) and American Epilepsy Society (AES) practice guideline, “Sudden unexpected death in epilepsy incidence rates and risk factors,” which was published in *Neurology*[®] online on April 24, 2017, and in the April 25, 2017, print issue.

Please refer to the full guideline at AAN.com/guidelines for more information, including descriptions of the processes for classifying evidence, deriving conclusions, and making recommendations.

What is the incidence rate of SUDEP in different epilepsy populations?

Rationale

Our systematic review found that the [sudden unexpected death in epilepsy] SUDEP risk in children with epilepsy is 0.22/1,000 patient-years (95% CI 0.16–0.31). The SUDEP risk increases in adults to 1.2/1,000 patient-years (95% CI 0.64–2.32). There is considerable uncertainty regarding the estimates of the adult risk.

People with epilepsy and their families prefer to be informed of the individual’s risk for a catastrophic event such as SUDEP, even when the probability of the event is low.^{e39} This preference is subject to cultural influences. After being informed of an adverse event, people commonly overestimate the risk of that adverse event happening to them.^{e40} Such overestimation unduly increases anxiety related to an adverse event. Overestimation can be lessened by presenting the risk as the probability of both having and not having the event,^{e41} and by using numbers in addition to words^{e40} and frequencies rather than percentages to convey the risk.^{e42}

What is the incidence of SUDEP in childhood?

Level B

Clinicians caring for children with epilepsy *should* inform the children’s parents or guardians that:

- There is a rare risk of SUDEP
- In 1 year, SUDEP typically affects 1 in 4,500 children with epilepsy; in other words, annually, 4,499 of 4,500 children will not be affected by SUDEP

What is the incidence of SUDEP in adulthood?

Level B

Clinicians *should* inform their adult persons with epilepsy that

- There is a small risk of SUDEP
- In 1 year, SUDEP typically affects 1 in 1,000 adults with epilepsy; in other words, annually, 999 of 1,000 adults will not be affected by SUDEP

Are there any risk factors for SUDEP?

Generalized tonic-clonic seizures

Rationale

Our systematic review found that a major risk factor for SUDEP is the presence and frequency of [generalized tonic-clonic seizures] GTCS. For example, people with 3 or more GTCS per year have a 15-fold increased risk of SUDEP. This relative risk increase translates to an absolute risk of up to 18 deaths per 1,000 patient-years^{e20} for people with frequent GTCS.

The large SUDEP risk increase from GTCS, coupled with epilepsy monitoring unit evidence^{e43} demonstrating that a GTCS was always the precipitating event of SUDEP, strongly suggests that GTCS are not just associated with SUDEP but, rather, are in the causal path to SUDEP. From this, it seems reasonable to infer that improved control of an individual’s GTCS will result in a reduced risk of SUDEP. Thus, a reduction in SUDEP risk is an additional benefit to the many benefits resulting from improved seizure control.

As with all benefits associated with improved seizure control, the potential benefit of SUDEP risk reduction needs to be balanced with the risks and burdens associated with antiseizure therapies.

Recommendation

Level B

For persons with epilepsy who continue to experience GTCS, clinicians *should* continue to actively manage epilepsy therapies to reduce seizure occurrences and the risk of SUDEP while incorporating patient preferences and weighing the risks and benefits of any new approach.

Lack of nocturnal supervision

Rationale

GTCS are clear risk factors for SUDEP, and nocturnal seizures may also increase risk. These findings, in conjunction with the observation that postictal respiratory depression is a major mechanism in SUDEP,^{e43} suggest that unwitnessed nocturnal seizures and postictal respiratory depression can cause SUDEP.

Moreover, the presence in the bedroom of another individual at least 10 years of age and of normal intelligence is associated with a decreased SUDEP risk. These results imply that a bedroom observer could detect seizures, check on the patient, and provide sufficient stimulation to prevent respiratory arrest. This association does not indicate that these interventions directly mitigate the mechanism that causes SUDEP.

If it were in accordance with patient and family circumstances and values, nocturnal supervision could reduce SUDEP risk; however, providing nighttime observation might be overly burdensome and intrusive.

Recommendation

Level C

For persons with frequent GTCS and nocturnal seizures, clinicians may advise selected patients and families, if permitted by their individualized epilepsy and psychosocial circumstances, to use nocturnal supervision or other nocturnal precautions, such as the use of a remote listening device, to reduce SUDEP risk.

Uncontrolled epilepsy

Rationale

One of the most consistent findings of this review is that many factors that are indicators of uncontrolled epilepsy, including having GTCS, having frequent GTCS, and the absence of seizure freedom, are strongly associated with SUDEP.

Usually, people with epilepsy and their families prefer to be informed of factors that are associated with an increased risk of a catastrophic event such as SUDEP. Patients are especially interested in factors that might reduce their risk even when a causal link between the factor and a reduction in risk has not been established. One example of a risk factor that has attracted great interest but remains to be proven is the prone position as a contributor to SUDEP.^{e44} In addition to the need for further supporting evidence to confirm that this is a risk factor, it is unknown whether any contribution of prone position to SUDEP occurrence is due to the initial sleeping position or the final position after a GTCS. Knowledge of these risk factors might suggest behaviors that could modify the risk factors (e.g., improved therapy adherence^{e45}), increase the person's sense of control, and reduce the anxiety that comes from awareness of the risk. Less severe seizure types, such as focal seizures or myoclonic seizures, are not proven to be associated with increased SUDEP risk, but individuals who have them often remain at risk for GTCS in the setting of therapy nonadherence. Therefore, therapy adherence to maintain freedom from GTCS is important even when an individual is not experiencing this severe seizure type.

Recommendation

Level B

Clinicians *should* inform their persons with epilepsy that seizure freedom, particularly freedom from GTCS (which is more likely to occur with medication adherence), is strongly associated with a decreased risk of SUDEP.

Additional conclusions

The evidence is low that the following factors are associated with altering SUDEP risk:

- Nocturnal seizures (associated with increased risk)
- Any specific AED (none associated specifically with increased risk)
- Lamotrigine use in women (associated with increased risk)
- Never having been treated with an AED (associated with increased risk)
- Number of AEDs used overall (associated with increased risk)
- Heart rate variability (not associated with increased risk)
- Extratemporal epilepsy (associated with increased risk)
- Intellectual disability (associated with increased risk)
- Male gender (associated with increased risk)
- Anxiolytic drug use (associated with increased risk)

The evidence is very low or conflicting that the following factors are associated with altering SUDEP risk:

- Overall seizure frequency when evaluated by using all seizure types
- Medically refractory epilepsy vs not having well-controlled seizures defined as no seizures for the past year
- Monotherapy vs polytherapy
- Carbamazepine, phenytoin, or vigabatrin levels that are above, below, or within the reference range
- Psychotropic drug use
- Mental health disorders, lung disorders, or alcohol use
- Lamotrigine use in people with highly refractory epilepsy
- Undergoing a resective epilepsy surgical procedure (although current research does not rule out the possibility of a beneficial effect or, further, the potential effect of epilepsy surgery on reducing GTCS frequency and epilepsy severity on reducing SUDEP risk)
- Frequent changes in AEDs
- Therapeutic drug monitoring
- Engel outcome of epilepsy surgery (although current research does not rule out the possibility of a beneficial effect and, further, the potential effect of epilepsy surgery on reducing GTCS frequency and epilepsy severity on reducing SUDEP risk)
- Vagus nerve stimulator use for more than two years (however, current research does not rule out the possibility of a beneficial effect and, further, the potential effect of epilepsy surgery on reducing GTCS frequency and epilepsy severity on reducing the risk of SUDEP)
- Epilepsy etiology, whether idiopathic or localization related
- Structural lesion on MRI
- Duration of epilepsy
- Age at epilepsy onset
- Postictal EEG suppression

References

- e20. Hesdorffer DC, Tomson T, Benn E, et al.; ILAE Commission on Epidemiology; Subcommission on Mortality. Combined analysis of risk factors for SUDEP. *Epilepsia* 2011;52:1150–1159.
- e39. Xu Z, Ayyappan S, Seneviratne U. Sudden unexpected death in epilepsy (SUDEP). What do patients think? *Epilepsy Behav* 2015;42:29–34.
- e40. Knapp P, Raynor DK, Berry DC. Comparison of two methods of presenting risk information to patients about the side effects of medicine. *Qual Saf Health Care* 2004;13:176–180.
- e41. Kahneman D, Tversky A. Choices, values, and frames. *American Psychologist* 1984;39:341–350.
- e42. Bonner C, Newell BR. How to make a risk seem riskier: The ratio bias versus construal level theory. *Judgment and Decision Making* 2008;3:411–416.
- e43. Ryvlin P, Nashef L, Lhatoo SD, et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. *Lancet Neurol* 2013;12:966–977.
- e44. Liebenthal JA, Wu S, Rose S, Ebersole JS, Tao JX. Association of prone position with sudden unexpected death in epilepsy. *Neurology* 2015;84:703–709.
- e45. Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing compliance with antiepileptic drug regimes. *Seizure* 1997;6:87–93.

This statement is provided as an educational service of the American Academy of Neurology. It is designed to provide AAN members with evidence-based guideline recommendations to assist the decision making in patient care. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, and are based on all of the circumstances involved. Physicians are encouraged to carefully review the full AAN guideline so they understand all recommendations associated with care of these patients.

The AAN develops these summaries as educational tools for neurologists, patients, family members, caregivers, and the public. You may download and retain a single copy for your personal use. Please contact guidelines@aan.com to learn about options for sharing this content beyond your personal use.