

COMMENTARY

Sudden death in epilepsy: a wake-up call for management

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<http://image.thelancet.com/extras/02cmt85web.pdf>

Sudden unexplained death in epilepsy (SUDEP) is the most common cause of seizure-related mortality in people with chronic epilepsy. Depending on the cohort studied, SUDEP is responsible for 2% to 18% of all deaths in patients with epilepsy,^{1,2} and the incidence may be up to 40 times higher in young adults with epilepsy than among persons without seizures.³ Several studies have emphasised early age of onset of epilepsy, frequent generalised tonic-clonic seizures, and intractability as significant risk factors for SUDEP.²⁻⁶ Polytherapy may be an additional independent risk-factor in adults^{2,5} but not in children.⁷ Although most cases of SUDEP are not observed, the few witnessed cases,^{8,9} as well as circumstantial clinical data⁵ and autopsy findings,^{10,11} suggest that SUDEP is a direct consequence of the seizure itself. Although the pathophysiological mechanisms leading to death are not fully understood, experimental¹² and clinical^{13,14} evidence implicate seizure-related pulmonary effects such as central apnoea and oedema¹⁵ as well as secondary cardiac dysfunction from ischaemia or arrhythmias.¹⁶

The clinical audit by the charity Epilepsy Bereaved of epilepsy-related deaths, released in the UK on May 20, is an important addition to this body of information. This well-organised study looked at the medical care and postmortem assessment received by patients who had died and in whom epilepsy was considered to be the primary cause of death. The audit found 2412 deaths reported with epilepsy on the death certificate, between September, 1999, and August, 2000. 1023 cases underwent autopsy, and the audit reviewed two-fifths of these cases and a tenth of the non-autopsied cases (156 of 1389). The main findings are summarised in the panel.

The audit concludes: "there was concern about many aspects of epilepsy management and, frequently, management did not meet published national criteria. There were particular problems in managing epilepsy in people who had associated problems such as learning difficulties . . . In conclusion, poor epilepsy management results in a substantial number of potentially avoidable deaths." These findings are both unsettling and discouraging in light of the current possibilities for treatment of epilepsy. Because primary-care providers manage most patients with epilepsy in the USA and Canada, results of a similar audit in North America would probably differ only in degree. The UK audit should be a wake-up call to the medical profession and result in a targeted campaign to improve care for people with epilepsy. Neurologists who have the most knowledge and experience of the disorder should take the lead here.

Because many cases of SUDEP are probably avoidable (estimated at 39% of deaths in adults and 59% of deaths in children in the audit), a strategy is needed urgently to address the following recommendations.

SUDEP is not rare among patients with uncontrolled epilepsy. Patients at risk should be identified, and they and their families educated about this possibility. Relatives of patients with SUDEP consistently indicate that they wish they had been informed that epilepsy can be fatal.⁹

Because continuing seizures, especially generalised convulsions, are one of the most important associations with SUDEP, early and aggressive treatment is essential. In addition to antiseizure drugs, effective treatment includes strategies to promote compliance and identification of seizure precipitants. Patients whose seizures do not respond promptly to treatment should be referred early to a neurologist for classification of seizure type and epilepsy syndrome, appropriate diagnostic testing, review of treatment options, and development of a patient-specific management plan.

Main findings from: Epilepsy—death in the shadows. Report of the national sentinel clinical audit of epilepsy related death*

- 1 Medical records were generally poor. In primary-care settings, information related to epilepsy was incomplete or absent, and the situation was only slightly better in specialty settings.
- 2 Therapeutic management was deficient in one-fifth of the adults and in almost half the children.
- 3 Referral to a specialist could take longer than 6 months, and in only 48% of patients was the initial referral to a neurologist. For patients with multiple handicaps, referral to other specialists was rare.
- 4 Even though only a few of the patients who died (none of them children) were seizure-free at the time of their last visit to a physician, 7% were not taking antiseizure drugs at the time of death.
- 5 Follow-up was inconsistent: 37% of the adults who continued to have seizures had not seen a physician in the year before they died.
- 6 Information provided to patients and their families was not documented and probably poor.
- 7 Postmortem examination was frequently not performed when the circumstances of death should have mandated one before a certificate was issued.
- 8 Most (87%) of autopsy investigations were inadequate given the suspected diagnosis.
- 9 Only a few families were contacted by a physician after a patient's death.

*<http://dspace.dial.pipex.com/epilepsybereaved/audit/audit.htm> (accessed on May 20, 2002).

Patients whose seizures persist for more than 2 years despite the best treatment should be referred to a comprehensive epilepsy centre for re-evaluation and consideration of surgery, vagus nerve stimulation, or clinical trials of new antiseizure drugs. Surgery is underused, and probably the treatment of choice, in patients with uncontrolled seizures due to medial temporal lobe epilepsy and other lesional epilepsies. Pathologists should be educated about SUDEP and the need to look specifically for findings, conditions, and circumstances that will support or refute this diagnosis.

Finally, there is need for continued study of causes, triggers, and mechanisms of SUDEP. Do some antiseizure drugs increase the risk? Some investigators have reported carbamazepine to be a factor, possibly through its effects on autonomic responses or cardiac conduction, which may promote rhythmic instability.^{5,17} The evidence for this is far from definitive, however, and it is not possible at this time to recommend one antiseizure regimen over another in patients at risk for SUDEP. It is also possible that there are genetic factors, presently unknown, that contribute to individual susceptibility.

While there remains a critical need for more effective treatments, especially ones that affect the actual process of epileptogenesis, the UK audit emphasises that many patients with epilepsy—perhaps most—could benefit substantially if only current knowledge and available therapeutic options were applied effectively.

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