

SHORT REPORT

## Sudden unexpected death in epilepsy: a series of witnessed deaths

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**Abstract**

**Objectives**—Sudden unexpected death in epilepsy (SUDEP) represents a significant category of mortality in the population with chronic epilepsy. A consistent feature is that most of these deaths are unwitnessed. The aim was to identify witnessed deaths, examine the circumstances, and relate these findings to the proposed mechanisms for SUDEP.

**Methods**—During the course of case ascertainment for a control study on SUDEP, witnessed deaths were identified and the circumstances examined in detail. Cases were notified by coroners, neurologists, and bereaved families. The findings were related to the proposed mechanisms for SUDEP which include central and obstructive apnoea and cardiac arrhythmia.

**Results**—One hundred and thirty five SUDEP cases have been identified to date, of which 15 were witnessed deaths. Twelve deaths were associated with convulsive seizures, one collapse occurred 5 minutes after a generalised seizure, another collapse occurred after an aura and one patient died while in a probable post ictal state. Witnesses reported that 12 of the 15 cases experienced respiratory difficulty.

**Conclusions**—Most sudden epilepsy deaths are unwitnessed. Where witnessed most occur in association with a seizure and respiratory compromise is a prominent feature. Positioning or stimulation of respiration may be important in the prevention of these deaths.

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Keywords: epilepsy; sudden death; witnessed

Sudden unexpected death in epilepsy (SUDEP) represents a significant category of mortality in the population with epilepsy with an estimated minimum of 500 deaths occurring yearly in the United Kingdom.<sup>1</sup> The mechanism of sudden death in epilepsy is unknown but a consistent finding is that most deaths are unwitnessed.<sup>2-6</sup> Information gained from previous studies suggests that most are consequent on a seizure although this view remains controversial.<sup>2</sup>

In one study it was reported that nine of 37 patients “died as a result of a single seizure or a few seizures in the presence of witnesses”.<sup>5</sup> In another report three of the 12 deaths identified were witnessed with only one having a convulsive seizure before death.<sup>4</sup> In a prospective study it was found that in 38% or 23 out of 60 cases death was witnessed and a convulsive seizure was seen in 14 of these cases.<sup>3</sup> In a series of interviews with self referred bereaved relatives it was found that two of 26 deaths were witnessed<sup>2</sup> and in a study of SUDEP in the Republic of Ireland in one of 15 cases death was witnessed having being preceded by a generalised seizure.<sup>7</sup>

**Methods**

We are carrying out a case-control study on SUDEP and to date 135 cases have been referred by coroners, neurologists via the British Neurological Surveillance Unit (BNSU),<sup>8</sup> and the charity “Epilepsy Bereaved?” with whose assistance families were interviewed. Fifteen of these cases were witnessed, the circumstances were examined in detail, and the findings related to the proposed mechanisms for sudden death in epilepsy which include central and obstructive apnoea and cardiac arrhythmia.

Sudden unexpected death in epilepsy was defined as: sudden, unexpected, non-traumatic, and non-drowning death in an individual with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus where postmortem examination does not reveal a cause for death.<sup>9</sup> Background clinical information, postmortem reports, and, where applicable, inquest transcripts were sought for all cases identified. Ethical approval was obtained from the joint medical ethics committee of the National Hospital for Neurology and Neurosurgery and the Institute of Neurology, University College London. Informed consent was obtained from all families before interview.

**Results**

Nineteen cases were initially considered. Four were excluded, three because the diagnosis of epilepsy was in doubt and one because of previous publicity surrounding the case. In one excluded case, although death was certified as being due to epilepsy it has been subsequently

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*Circumstances of death*

Case	Sex	Age	Seizure	Location
1	F	45	GTCS	Bed
2	M	47	GTCS	Bed
3	M	34	Aura	Home
4	M	28	GTCS	Home
5	M	43	GTCS	Home
6	M	22	GTCS	Bed
7	F	41	GTCS	Outdoors
8	F	21	GTCS	Bed
9	M	34	GTCS	Bed
10	F	30	GTCS	Bed
11	F	17	Post ictal	Outdoors
12	M	32	GTCS	Home
13	M	38	GTCS	Bed
14	F	18	GTCS	Home
15	M	35	Post ictal	Home

decided that this is unlikely given that the patient's mother and sister have been diagnosed with long QT syndrome.

There were nine men and six women ranging in age from 17 to 47 years with a mean age of 32 years. This group comprises 11% of all cases of sudden death identified to date as part of the case-control study. Nine patients had localisation related epilepsy, two had idiopathic generalised epilepsy, and four had epilepsy of undetermined type. Circumstances of death are described in the table. Of the unwitnessed cases 80 (67%) were found dead in bed, 35 (29%) were found dead elsewhere in the home, and five (4%) were found dead outside the home.

Death occurred in association with a witnessed generalised tonic-clonic seizure in 12 of the 15 cases. In the other three one person shouted "I'm going to have a seizure" before collapsing without having a convulsive seizure. One patient had recovered consciousness after a seizure 5 minutes previously before he suddenly collapsed. A young girl with active epilepsy was found collapsed and incoherent in the street and no obvious convulsion was witnessed; however, she had been incontinent of urine and her mother told bystanders that she had had a fit. It seems likely that she was in a postictal state. Bystanders commenced artificial respiration having noticed that she was no longer breathing but this was unsuccessful. A pulse was palpable at the start of resuscitation but subsequently faded. Resuscitation was attempted in 13 of the 15 cases, immediately by staff or family on the scene in eight cases and in five after paramedics arrived. Three resuscitated people subsequently died having been maintained on ventilators for periods ranging from 12 to 48 hours.

In 12 cases witnesses commented on the fact that the persons concerned had difficulty breathing, the following cases being illustrative examples. As the cases were identified through various sources and the quality of information received varied it is not possible to describe cases in a uniform manner.

A 47 year old man had a history of secondary generalised tonic-clonic seizures after a head injury and subsequent meningitis in 1969. He had not had a seizure for 8 years and was on no antiepileptic medication. He came home early from work with a headache and went to bed. On going to investigate noises from the

bedroom his wife found him lying on his side, jerking and with obvious bleeding from his tongue. After a minute or so he suddenly flipped on to his back and the seizing stopped. She noticed that he was blue and was not breathing so she commenced mouth to mouth resuscitation. He apparently began to breathe on his own again and she left the room to telephone for assistance. He was not placed in the recovery position. On her return a few minutes later he was no longer breathing and no pulse was palpable so she restarted cardiopulmonary resuscitation which was continued by the paramedics on their arrival, to no avail. This case suggests central apnoea as a mechanism for SUDEP.

In two other cases breathing difficulty was likely to be obstructive. A 34 year old man woke up feeling unwell, came downstairs, and had a generalised tonic-clonic seizure. He then collapsed across his mother's Zimmer frame with his throat resting across the bar.

In another case an 18 year old woman collapsed in a convulsive seizure and landed under the sink. On their arrival the ambulance crew reported that she was cyanosed and asystolic and it was considered that her airway was compromised due to the position in which she lay.

## Discussion

Various mechanisms have been proposed for sudden death in epilepsy. Apnoea was a frequent finding in a study of ictal cardiorespiratory variables at the telemetry unit of the National Hospital for Neurology and Neurosurgery.<sup>10</sup> This hypoventilation, which was primarily central in nature, occurred in the context of both generalised and partial seizures. Obstructive apnoea occurred less commonly in this study but it is likely that in the controlled environment of the telemetry unit, where nursing intervention is likely to minimise airway compromise, the contribution of obstructive apnoea, whether intrinsic or extrinsic, to SUDEP may be underestimated.

An important role for hypoventilation is supported by an animal model in which seizures are chemically induced in sheep, some of whom die. In the animals who die during a seizure a precipitous drop in the partial pressure of oxygen occurs along with a concomitant rise in pulmonary artery and left atrial pressures resulting in pulmonary oedema. In this animal model care was taken to ensure that airway patency was maintained.<sup>11</sup> This model of SUDEP is consistent with the observation that pulmonary oedema, in itself thought insufficient to cause death, is a frequent finding and almost a pathological hallmark for sudden death in epilepsy.<sup>12</sup> Of note in relation to the role of apnoea are the findings of a study of SUDEP in a residential school for children with epilepsy and learning difficulties. The children were closely supervised by experienced staff while at school, including at night. No cases were witnessed during the period of the study, suggesting that attention to the recovery of the person after a seizure and posi-

tioning or stimulating if necessary may have a role in the prevention of SUDEP.<sup>13</sup>

The development of apnoea during a seizure does not exclude a role for cardiac arrhythmia as a mechanism in SUDEP. Clinical observations of seizures associated with severe cardiac arrhythmias have been reported, mainly sinus arrest and bradycardia. In most of these cases the epileptic focus was located in the temporal lobes.<sup>14-17</sup>

Bradycardias, often transient, have also been noted to occur in the presence of apnoea.<sup>10</sup> Proposed mechanisms for this transient bradycardia include a direct effect of the seizure discharge or a response to apnoea mediated by the cardiorespiratory reflex.<sup>18</sup> Sinus tachycardia is a common accompaniment to seizures<sup>19</sup> but evidence of the occurrence of malignant tachyarrhythmias is limited.<sup>20</sup> Prolongation of the QT interval has been postulated to occur in sudden death. Investigators have found some evidence of ictal prolongation of the QT and QTc intervals but not beyond the normal ranges.<sup>21</sup> It has already been noted that cases of prolonged QT syndrome may be misdiagnosed as epilepsy.<sup>22</sup> A recent study which examined cardiac pathology in SUDEP cases found evidence of perivascular and interstitial fibrosis along with reversible myocyte vacuolisation. The control group, in whom such abnormalities were not detected, did not include those with epilepsy dying of other causes and thus the relevance of these findings is unclear.<sup>23</sup>

To conclude, in this series, the largest collection of sudden deaths to date, only 11% of deaths were witnessed and most of these occurred in association with a seizure. The account of these deaths support the view that both central and obstructive apnoea play important parts in the genesis of SUDEP, with most witnesses stating that the victims experienced breathing difficulties. Airway obstruction seemed to be a significant factor in at least two cases and it is therefore possible that deaths presently categorised as SUDEP occur through various mechanisms. Although resuscitation was unsuccessful in the cases described most sudden deaths remain unwitnessed. One possible explanation for this is that where seizures are witnessed and recovery is monitored timely assistance by positioning of the patient or stimulation of respiration may prevent a fatal outcome in some cases. This raises the important issue of supervision, which

will be examined in the case-control study. Given the association of most witnessed deaths with convulsive seizures, and the previous findings of circumstantial and physical evidence suggestive of seizures in unwitnessed cases,<sup>2</sup> it is likely that optimisation of seizure control is also important in the prevention of these deaths.

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