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The incidence of sudden unexpected death in epilepsy (SUDEP) in South Dublin and Wicklow

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Patients with epilepsy have a mortality rate higher than that of the general population. Some of this excess mortality is attributable to sudden unexpected death (SUDEP). We examined the incidence of this phenomenon both retrospectively and prospectively in the population of South Dublin and Wicklow over the period May 1992–1995. Cases were ascertained by examination of post-mortem registers of hospitals serving the area studied. Information on cases was sought from hospital records, general practitioners and families. Fifteen cases (10 male, five female) were identified resulting in an overall incidence rate of SUDEP of 1:680/year for the 3 years of the study. This is the only study of incidence of SUDEP conducted in Ireland and our results are in keeping with incidence rates elsewhere in Europe and the USA.

Key words: epilepsy; sudden unexpected death; mortality; incidence.

INTRODUCTION

Patients with epilepsy have a mortality rate two to three times that of the general population[1]. The cause of death may be related to the underlying cerebral pathological process presenting as epilepsy, particularly in those with recent onset seizures, but excess mortality is also found even in the population with chronic seizure disorder[2]. Accidents, suicide, drowning and, rarely, status epilepticus may account for some of these deaths[3] but it has been recognized that sudden unexpected death in epilepsy (SUDEP) may also occur.

It is possible to define SUDEP as a nontraumatic death in an individual with epilepsy where post-mortem examination does not reveal a cause for death[4]. A proportion of patients are found dead in bed and some have had evidence of a recent seizure[5–7]. There is controversy as to whether those with a witnessed seizure should be included in the definition. As discussed later it seems illogical to exclude these patients as in many cases witnesses are not present at the time of death and a seizure may have occurred without post-mortem evidence.

The aims of our study were to establish the incidence of SUDEP in the population of South Dublin and Wicklow with epilepsy, retrospectively from May 1992 to 1994, and prospectively from May 1994 to 1995, and to identify clinical characteristics which might indicate a predisposition to SUDEP.

MATERIALS AND METHODS

Sudden unexpected death in epilepsy in this study was defined as a nontraumatic death in an individual with epilepsy where post-mortem examination does not reveal a cause for death. The method of case ascertainment was retrospective for the years May 1992–April 1994 and prospective for the year from May 1994 to the end of April 1995. The population under study, 680 000 at the last census, lived in South Dublin, South County Dublin and County Wicklow.

Cases were ascertained by examination of the post-mortem registers of St James's's Hospital, St Vincent's Hospital Dublin and St Colmcille's Hospital, Co. Wicklow. All unexplained deaths reported to the coroner are subject to a post-mortem examination performed by pathologists in these hospitals. Whenever epilepsy was mentioned as a cause or contributory cause of death in the register, including deaths certified as being due

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to status epilepticus, the autopsy report was obtained. Information was collected on the age of sex of the patient, seizure type and frequency, medications, compliance, recent drug levels and alcohol intake from hospital records, general practitioners and families. Postmortem antiepileptic and alcohol levels were obtained where possible. Approval for this study was obtained from St Vincent's Hospital Ethics Committee.

RESULTS

Eighteen patients were identified from the autopsy records and three were excluded because they did not satisfy the criteria for SUDEP. One of these had evidence of aspiration pneumonitis and hypoxic encephalopathy and had survived for some days following a respiratory arrest. Another had evidence of severe coronary artery disease and myocardial infarction was suspected. The third had pneumonia with accompanying hyponatraemia, and had been admitted to hospital in a coma.

Of the remaining 15 cases who satisfied the criteria for SUDEP there were 10 men and five women, with an age range of 14–59 years and a mean age of 37 years. Information on seizure type was available in only nine cases, all of whom had generalized seizures, and one was also known to have had partial seizures. The cause of epilepsy was determined in only one patient who had post-traumatic seizures. One individual was known to have learning difficulties.

Information on location of death was available in 10 cases, the remainder were brought dead into A&E departments. Five patients (33%) were found dead in bed, three (20%) were found dead at home, their exact location being unknown. One was found dead in a public park and one died in a hotel lobby having just had a witnessed seizure.

Information on antiepileptic medication was available in nine cases. Four patients were on phenytoin alone, and two were on a combination of phenytoin and phenobarbitone. One patient was on phenytoin and sodium valproate, and one was on a combination of phenytoin, phenobarbitone and vigabatrin. One patient was known to be on no antiepileptic medication. Postmortem anticonvulsant levels were available on six of the eight patients whose antiepileptic drug regime was known. Two individuals had therapeutic anticonvulsant levels and four subtherapeutic or absent drug levels. Eight patients had alcohol levels measured postmortem, half of these had no evidence of alcohol in the blood while four had levels ranging from 6 mg % to 24 mg %. Thirteen of the 15 cases had pulmonary oedema at post-mortem and all cases had mild cerebral oedema.

The population of the area under study, South Dublin, South County Dublin and County Wicklow was 681 000 at the last census in 1992, according to information obtained from the Central Statistics Office in Dublin. Taking the prevalence of epilepsy in this population to be 0.5% it can be calculated that, for the 3 years of the study, there are approximately 10 200 person-years of follow-up, giving an incidence of SUDEP of 1:680 over the 3-year period 1992–1995. There were five deaths in the year May 1992–1993 and three deaths in 1993–1994. In the prospectively studied year there were seven deaths giving yearly incidence rates of 1:680(1:290–1:2080), 1:1130(1:390–1:5520) and 1:480(1:220–1:1120), respectively.

DISCUSSION

Other population-based studies have found incidence rates for SUDEP similar to that found in this study; Leestma and colleagues[5] in a prospective study found a yearly incidence of SUDEP of 1:370 to 1:1110, and a community-based study conducted by Tennis and associates[9] in Canada of 0.54 to 1.35 SUDEP per 1000 person years[5–8].

More highly selected populations exhibit a greater risk of SUDEP. A study of patients with epilepsy in long-term care found an incidence of SUDEP of 1:260/year[10]. Nashef in a cohort study in a tertiary referral centre found an incidence of SUDEP of 1:200/year and of 1:295/year in a cohort with epilepsy and learning difficulty[11,12]. Dasheiff reported an incidence rate of 1:50–100/year in a group of patients on an epilepsy surgery programme[13]. A recent study of SUDEP among patients with refractory epilepsy reported an incidence rate of 2.2 per 1000 person-years[14]. One can contrast these findings with that of the National General Practice Study of Epilepsy (NGPSE) in which no SUDEPs occurred in over 3700 person-years of follow-up of patients newly diagnosed with epilepsy[2].

The definition of SUDEP deserves some comment here. There is controversy as to whether those who die having had a witnessed seizure should be included. In the 60 cases collected by Leestma[5], 23 had a witnessed collapse, 14 had a convulsive seizure and seven cases had evidence of recent seizure at post-mortem. If cases such as these are excluded from analysis the incidence rate of SUDEP is reduced[9]. It would seem illogical to exclude such cases, as many patients who are found dead may have had an unwitnessed seizure or one which has left no autopsy evidence.

It is possible that the results of this study represent an underestimation of the risk of SUDEP in the population studied. Our figures are based on the assumption that all those with epilepsy who died suddenly had a post-mortem, and also that epilepsy was mentioned as

a cause of death when an entry was made in the post-mortem registers of the hospitals visited. We estimate that, as in the UK, approximately 90% of SUDEP cases will be referred to the coroner. This possible lack of accuracy on death certificates has been noted by others. Coyle *et al*[15] collected reports of SUDEP from newspapers in the UK and found that in only 42.5% was epilepsy recorded as the primary cause of death. It is not clear from their study the frequency with which it was mentioned as a secondary underlying cause[14]. We also noted that in a number of cases patients were certified as having died from status epilepticus when this could not be substantiated and was unlikely.

It can be seen that given the small number of cases collected, a small change in the numerator could result in an altered incidence rate but it is hoped that our case ascertainment was as accurate as possible, particularly in the prospective year of the study. It is also possible, given the fact that our information on population size is taken from a 1992 census, that our calculation of the denominator may not be wholly accurate. It has been noted in previous studies that similar incidence rates were obtained even where a number of methods were employed to calculate the denominator[8]. Our results are, however, wholly consistent with those found by other investigators.

Studies from the USA have identified the 'at-risk' patient as being a man in his thirties with generalized seizures and noncompliant with medication[5]. In keeping with this, there was a predominance of men in our study, the mean age was 37 years and all had a history of generalized seizures. In the seven cases where post-mortem drug levels were available, four had subtherapeutic or absent anticonvulsant levels. The usefulness of post-mortem drug levels is unclear given that many patients are successfully managed on lower doses of antiepileptic drugs and also the relationship of levels taken after death to ante-mortem blood levels is not established[15]. One of our cases had a high level of phenobarbitone, though this was thought insufficient to cause death.

The fact that approximately one-third of cases of SUDEP occur in bed, as found in this series and supported by others[5,10] is not unexpected as seizures are more frequent in sleep and on purely temporal grounds patients will spend about a third of their life in bed. Many are found face down on the pillow and suffocation has been considered as a possible cause of death but others have found no evidence to support this.

Another interesting feature is the presence of pulmonary congestion which was found in nearly all the cases at autopsy. This is a consistent finding in all studies of SUDEP[17]. The mechanism of death in SUDEP is not understood. Both bradycardia and apnoea have been noted to occur during a seizure[18] and ECG monitoring has also demonstrated ictal cardiac arrhythmias[19], and a case has been reported where a patient with epilepsy died suddenly after a seizure with electrocardiographic evidence of ventricular fibrillation[20].

In our population-based study we have found an incidence of SUDEP of 1:680/year and this is consistent with the findings of other studies. There are approximately 18 000 individuals with epilepsy in the Republic of Ireland, and using the incidence rate which we have calculated, an estimated 25 may die unexpectedly each year. The next step must be to concentrate on the characteristics of these patients with a view to identifying the factors that make them vulnerable.

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