Mortality Due to SUDEP and Status Epilepticus

Abstract:

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Abstract
Mortality in patients with epilepsy (PWE) is increased compared to the general population. For this reason the National Programme of Epilepsy Care, which was established under the Health Service Executive's National Director for Clinical Strategy and Programmes, identified a reduction in mortality from epilepsy as a key quality metric to monitor the success of the programme. The increased mortality is greatest in the first years after diagnosis where it is predominantly related to the underlying cause but there remains a persistent elevation in mortality rates especially amongst those with longstanding epilepsy. This group of patients is more likely to die from epilepsy, predominantly sudden unexpected death in epilepsy (SUDEP) or status epilepticus (SE). This paper identifies a number of studies on mortality in epilepsy from SE and SUDEP and uses this data to generate an estimate for annual mortality from SUDEP and SE in Ireland. These estimates indicate that mortality in patients with epilepsy due to SUDEP and SE account for between 48 and 162 deaths per year in Ireland and sources of mortality information currently available possibly underestimate the numbers involved especially if deaths due to non-convulsive status are included.

Introduction
Patients with epilepsy have higher mortality rates than the general population. The greatest excess in mortality is found in cohorts of hospital patients with longstanding severe epilepsy. A large general hospital based population of patients with epilepsy had a Standardized Mortality Ratio (SMR) of 3[1] and a cohort of epilepsy surgery patients was found to have an SMR of 6.3[2]. Population based studies have shown SMRs between 1.6 and 2.5[3]. Deaths in patients with epilepsy may be unrelated to epilepsy, related to the underlying cause or directly related to seizures. Mortality in newly diagnosed patients is higher and more likely to be related to the underlying cause. The longer a patient is diagnosed the greater the risk of mortality from epilepsy. A review of studies on mortality in cohorts with longstanding epilepsy found between 24-67% of deaths were due to sudden unexpected death in epilepsy (SUDEP), with a further 4-14% of deaths due to status epilepticus (SE)[4]. However, a population based study found only one death due to SE and one due to SUDEP in 14 years of follow-up[5]. This paper identifies a number of studies on mortality in epilepsy from SE and SUDEP and uses this data to generate an estimate for annual mortality from SUDEP and SE in Ireland.

Sudden Unexpected Death in Epilepsy (SUDEP)
SUDEP is defined as the sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death of patients with epilepsy with or without evidence of seizure, excluding documented SE, and in whom post-mortem examination does not reveal a structural or toxicological cause for death[6]. While SUDEP may occur infrequently in community based populations (rates between 0.33 and 2.3[7,8]), the incidence is considerably higher in hospital or residential cohorts (rates between 1.1 and 9.37)[7,8]. Case control studies[7] identified risk factors for SUDEP linked to poorly controlled epilepsy including frequent convulsive seizures and polytherapy with anti-epileptic drugs (AEDs).

Status Epilepticus (SE)
SE can be categorised as either convulsive or non-convulsive. Non-convulsive status, where seizure activity primarily manifests as altered behaviour or depressed consciousness, is often under diagnosed especially if EEG facilities are unavailable[9]. A review paper found incidence rates for SE varied in European studies from 9.9/100,000 per year in Switzerland to 17.1/100,000 in Germany with similar figures in white populations in the United States, with incidence rates of 18.1/100,000 in Rochester and 20.0/100,000 in Richmond[10]. This review found lower mortality rates from SE in European studies than North American studies due to the fact that European studies exclude SE due to anoxic encephalopathy which has a high mortality rate[10]. The paper described case fatality rates (CFRs) for SE in Europe varying between 6.6% in Switzerland, to 9.3% in Germany and 33% (39% including cases of anoxic encephalopathy) in Bologna. In the United States CFRs were 21% in Rochester and 22% in Richmond. When SE due to anoxic encephalopathy was excluded from the Rochester data, the CFR was 13.6%[10]. Preliminary Irish data reported for an elderly cohort admitted with confusion, indicated a mortality rate of 50% in those with confirmed non-convulsive status suggesting that non-convulsive SE in this age group, due to its under-recognised presentation, may be associated with a higher mortality than convulsive status[11].

[1]Derived from Linehan et al 2010[13]
[2]Using 2011 census population,[15]

Data from Irish Studies
Work in Ireland between 1992-1995 in South Dublin and Wicklow found an overall rate of SUDEP of 1:680 per year for the three years of the study[12]. Using an estimated epilepsy prevalence of 0.5% and extrapolating this data to the national population provided an estimated number of cases of SUDEP in Ireland of 25 per year[12]. A study using secondary data sources from 2002-2005 provided an epilepsy prevalence figure for Ireland which had not previously been available. This estimated the prevalence of epilepsy at between 8.3 and 9.0 /1000 persons 5 years and older[13].

Estimates of mortality from SUDEP and SE in Ireland
In estimating a mortality figure for cases of SUDEP and SE in Ireland, a range of incidence rates and CFRs (where relevant) from the studies described above7,8,10 were combined with the 2011 census population for Ireland[14] and the Irish epilepsy prevalence figure[13]. The results are presented in table 1. In estimating mortality due to SUDEP a range of incidence rates [0.33- 2.3]7,8 was combined with the Irish prevalence figure for epilepsy[13] and the 2011 census population[14]. This gave an estimated incidence of SUDEP for the Irish population of 13-95. This range incorporates the figure from the Irish work by Langan et al[12]. To estimate the mortality due to SE, a range of incidence rates for SE [9.9 to 15.8][1] for European studies from the review by Logroscino et al[10] was combined with the 2011 census population from the CSO[14] to provide an estimated annual range of 454 to 724 cases of SE Ireland. Using the CFRs in the review paper for the European studies (Logroscino et al10) but excluding the outlier figure from Bologna, gives an estimated CFR range of 7.6 to 9.3%.[2] This lies in the lower range of CFRs for SE (7.6-22%) given in the review on mortality in epilepsy by Hitiris et al.[3] which included a number of American studies which contained cases due to anoxic encephalopathy. This range of CFRs (7.6-9.3%) provides an estimated range of deaths due to SE of between 35 and 67 deaths per year based on the 2011 Irish population[14] (Table 1). Combining these mortality estimates provides an estimated range of deaths due to SUDEP and SE of between 48 and 162 deaths per year in Ireland (Table 1).

A separate analysis of mortality related to epilepsy was carried out using Health Atlas Ireland[15] to analyse epilepsy-related deaths from the CSO and HIPE datasets. This approach identified 65 deaths (eight occurring in hospital) where epilepsy was the cause of death in 2005, 53 (seven in hospital) in 2006, 64 (14 in hospital) in 2007 and 77 (12 in hospital) in 2008 using the death occurrence data from the CSO. This provides a range of 53 to 77 with a mean value of 65 for deaths where epilepsy was the underlying cause. An examination of the HIPE dataset15 showed that in 2006 there were six deaths where the patient's principal diagnosis was epilepsy and seven where the principal diagnosis was SE. The corresponding figures for 2007 were epilepsy, 11 and SE 11, 2008 epilepsy 11 and SE 4, 2009, epilepsy 21 and SE 11 and in 2010, epilepsy 13 and SE 9. Therefore between 2006 and 2011, the number of deaths recorded in HIPE where the patient's principal diagnosis was either epilepsy or SE ranged from 13 to 32 with a mean of 21.

While it is not possible under data protection rules to link the two datasets, looking at them separately indicates that deaths related to epilepsy occur more commonly outside of the hospital setting which would be consistent with the figures from the review by Tomson et al[4] which showed greater number of deaths from SUDEP than SE. Our figures show a wide range in the estimated numbers of deaths from SUDEP and SE which on an annual basis are low and hence must be interpreted with caution. The CSO figures[15] for epilepsy related deaths fall just within the lower limit of our estimate for SUDEP and SE deaths. The upper estimate provided in this paper is more than 149% greater than the mean number of deaths available from the death occurrence data for the years 2005-2008[15]. Given that the estimates here only involve deaths due to SUDEP and SE, it is likely that, similar to the UK experience[16], there may be some under reporting or under diagnosis of epilepsy related deaths.

The Health Service Executive National Clinical Programme in Epilepsy Care uses international evidence to create a programme of improvement in quality, access and care for PWE and their families. There is evidence that seizure frequency and failure to achieve remission are associated with increased risk for both SE and SUDEP. Evidence and expert opinion would indicate the importance of access to a specialist multidisciplinary service for the assessment and treatment of patients with epilepsy, to improve the management of their epilepsy. It is expected that improved patient care will increase the number of PWE entering remission and decrease their risk of mortality. Central to improved patient care, is the requirement for robust information systems to accurately capture the mortality and morbidity associated with epilepsy. The proposed roll out of an electronic epilepsy patient record as part of the National Programme will allow the prospective collection of accurate data on SE, SUDEP and other epilepsy-associated conditions.

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Comments: