Epilepsy & Behavior xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Review

Incidence rate of sudden death in epilepsy: A systematic review and meta-analysis

Erik Saetre [a,*], Michael Abdelnoor [b,c]

[a] National Centre for Epilepsy, Oslo University Hospital, Oslo, Norway
[b] Centre of Epidemiology and Biostatistics, Oslo University Hospital, Oslo, Norway
[c] Centre of Clinical Heart Research, Oslo University Hospital, Oslo, Norway

ARTICLE INFO

Article history:
Received 24 May 2018
Revised 17 June 2018
Accepted 20 June 2018
Available online xxxx

Keywords:
SUDEP
Mortality
Epilepsy
Meta-analysis

ABSTRACT

Objective: The aim of the study was to summarize the pooled incidence rate of sudden unexpected death in epilepsy (SUDEP) in patients. Meta-regression analysis was applied to identify factors influencing the incidence rate.
Design: The study was a systematic review and critical appraisal with a meta-analysis of cohort studies, both prospective and retrospective.
Material and method: In a literature search, a total of 45 cohort studies were identified. A random effect model was used to synthesize the results. Heterogeneity between studies was examined by subgroup and meta-regression analysis. The small-study effect was evaluated and not corrected for by the "trim and fill" method because of great heterogeneity.
Results: A substantial heterogeneity was present. The pooled estimated incidence rate for SUDEP was 1.4/1000 patient years. A meta-regression pinpointed a negative association between the incidence rate of SUDEP and the mean follow-up time and a positive association with the mean age of the patient. The definition of epilepsy showed statistical significance, with a higher incidence rate of SUDEP in studies where the definition of epilepsy was described and clear ($p = 0.019$) compared with studies having an inadequate or failing epilepsy definition.
Conclusion: Evidence from this study suggests a high incidence rate of sudden death in epilepsy. Its incidence rate was 23 times the incidence rate of sudden death in the total population of the same age. There was heterogeneity and variability of incidence rate depending on the quality of the study and on the definition of epilepsy and the mean age of the patients.

1. Introduction

Sudden unexpected death in epilepsy (SUDEP) is a sudden, unexpected, nontraumatic, nondrowning death in an individual with epilepsy, witnessed or unwitnessed, in which postmortem examination does not reveal an anatomical or toxicological cause of death. In definite SUDEP, an autopsy has confirmed this absence of an anatomical or toxicological cause. Probable SUDEP are cases without autopsy, with the circumstances of death still being strongly indicative. Possible SUDEP implies that a SUDEP situation should be considered among the explanations of the death. Epilepsy has been shown to be associated with a two- or three-fold mortality risk in people who have it compared with the general population. The underlying cause of the epilepsy as well as the comorbidities may partly explain the reduced lifetime expectancy. Seizure-related death can be attributed to status epilepticus, accidents, or SUDEP [1–4].

Sudden unexpected death in epilepsy is a tragic event with broad impacts in families. In the community, it is a worldwide public health problem. The causes of SUDEP are still unknown, and more than one single mechanism may play a role. An important risk factor seems to be the occurrence of generalized tonic–clonic seizures. Previous estimates indicate that the SUDEP risk in young patients with epilepsy is up to 24 times higher than in the general population of a similar age. However, North American studies have demonstrated a variation in incidence at least ranging from 0.35 to 2.7 cases per 1000 patient years [5,6]. According to Tomson et al. [7], the estimates may be dependent on variation in patient selection criteria and the chosen methods of the study and its analysis. The SUDEP risk seems generally lower in children [8,9]. In young and adult people, the SUDEP incidence increases in cohorts with severe and therapy-resistant epilepsy [4,10].

Hence, the aim of our study was (1) to pool the estimates of the incidence of SUDEP in different populations of patients with epilepsy,

* Corresponding author.
E-mail address: erisa@online.no (E. Saetre).

https://doi.org/10.1016/j.yebeh.2018.06.037
1525-5050/

then (2) to explore if patient level (e.g., gender, age) and study level (e.g., study design) variables were associated with this estimated incidence rate, and (3) to compare the pooled incidence rate with the incidence of SUDEP in the total population matched for age.

2. Methods

2.1. Literature search

Assisted by a qualified medical librarian, we searched the Cochrane Central Register of Controlled Trials (1970–2014), Medline/PubMed (1966–2014), and Embase (1980–2014). A combination of keywords and similar strategies was used to identify previously published meta-analyses and reviews. In addition, we manually searched conference proceedings and textbooks; screened the reference lists of all papers; and contacted investigators, experts, and translators. The last update for research was done on January 1st, 2015. No limitation on language was considered (Fig. 1).

2.2. Study selection

Prospective and retrospective cohort studies on patients with epilepsy were included. The major outcome chosen was the incidence rate of SUDEP in events per patient year because of the variability of the follow-up time. Cohorts not permitting quantification of incidence rates of SUDEP in patient years were not included. Two reviewers independently evaluated the reports for eligibility. Finally, 45 cohorts were considered eligible for the incidence study of SUDEP [5,9,11–50] (Table 1).

2.3. Quality assessment of the cohort studies: the component approach

Unfortunately, there is no agreed "gold standard" appraisal tool for evaluating quality in observational epidemiologic studies, and there are many tools from which to choose. For the purpose of critically appraising cohort studies, we used a checklist based on recommendations by Elwood [51] including (a) methods for selecting study participant;

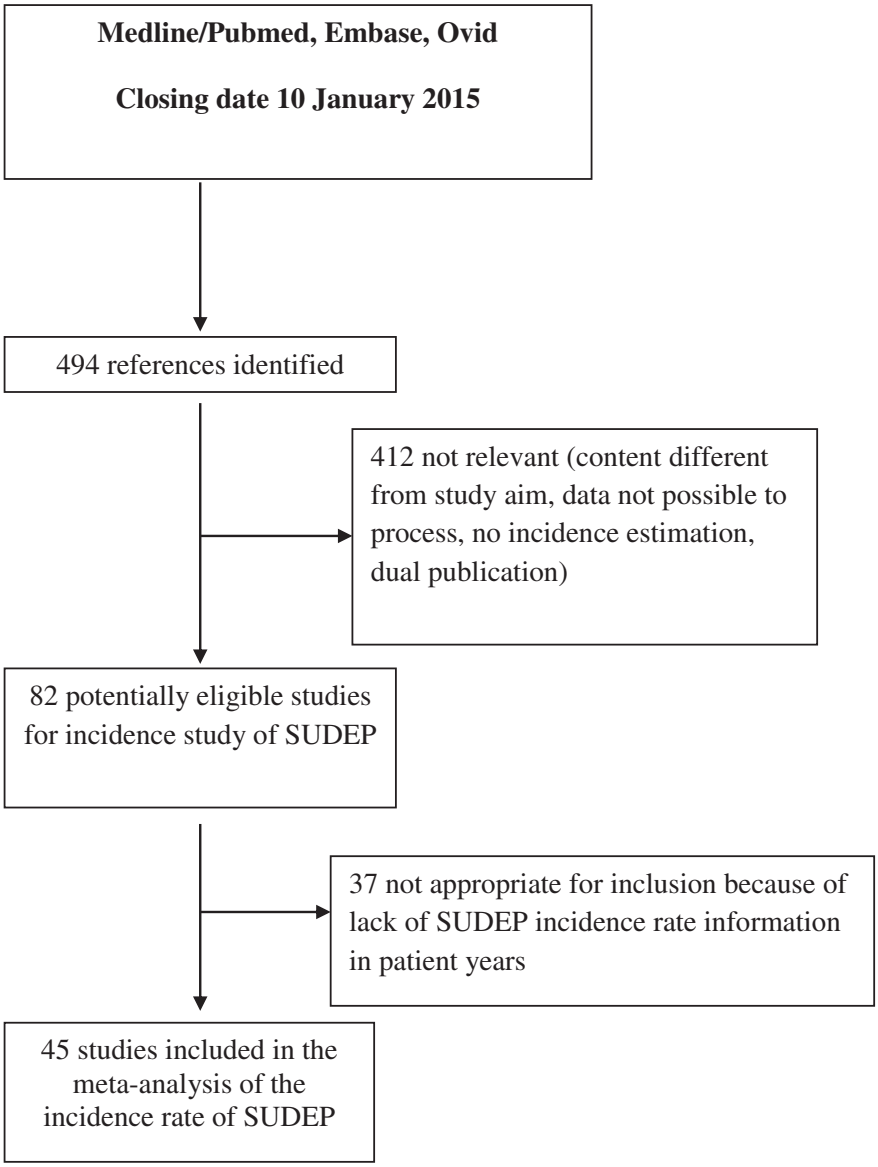

Fig. 1. Flow chart of the literature searches for the systematic review of studies on the incidence of SUDEP.

Please cite this article as: Saetre E, Abdelnoor M, Incidence rate of sudden death in epilepsy: A systematic review and meta-analysis, Epilepsy Behav (2018), https://doi.org/10.1016/j.yebeh.2018.06.037