



**Karolinska
Institutet**

Department of Clinical Neuroscience

EPIDEMIOLOGICAL STUDIES OF EPILEPSY: INCIDENCE AND RISK FACTORS

AKADEMISK AVHANDLING

Som för avläggande av medicine doktorsexamen vid Karolinska Institutet
offentligen försvaras i Samuelssonsalen, Tomtebodavägen 6,
Karolinska Institutet

Fredagen den 25 november 2011, kl 09.00

av Cecilia Adelöw, Leg. Läkare

Huvudhandledare:

Professor Torbjörn Tomson
Karolinska Institutet
Institutionen för klinisk neurovetenskap

Bihandledare:

Professor Anders Ahlbom
Karolinska Institutet
Institutionen för miljömedicin

Fakultetsopponent:

Professor Tapani Keränen
University of Eastern Finland, (Kuopio)
Department of Clinical Pharmacology

Betygsnämnd:

Docent Bo Wiksten
Uppsala Universitet
Institutionen för neurovetenskap

Professor Sten Fredriksson
Karolinska Institutet
Institutionen för klinisk neurovetenskap

Docent Karin M Henriksson
Lunds Universitet
Avdelningen för psykiatrisk epidemiologi

Stockholm 2011

ABSTRACT

Epilepsy is one of the most common serious neurological disorders leading to significant consequences for the affected. Despite the wealth of epidemiological data, there are still many unanswered questions. The major challenges in epidemiological research relate to the fact that epilepsy is a heterogeneous condition which hampers the evaluation of subgroups of e.g. different seizure/epilepsy types and age groups.

The overall objective of the present research was to describe the incidence and some selected risk factors for unprovoked seizures/epilepsy in a large representative population based cohort. Four studies were carried out, using the Stockholm Incidence Registry of Epilepsy (SIRE), a large cohort of incident cases with unprovoked seizures and epilepsy. We first analysed the age- and sex-specific incidence of unprovoked seizures/epilepsy in Stockholm, Sweden. The age-adjusted incidence for unprovoked seizures/epilepsy was 40.4 for males, and 30.7 for females, and in the lower range of the incidence rates reported from Europe and the US. Although our incidence rates suggest a possible under-ascertainment in particular among the elderly, the distribution of cases by gender, seizure type and aetiology indicate that there is no major selection bias.

We then performed three separate case-control studies with cases from SIRE, the controls taken from the Population and Housing Census, and exposure defined as a hospital discharge diagnosis using ICD codes from the Swedish Hospital Discharge Registry. Case-control data were linked to the hospital discharge registry to identify a history of in-hospital care for the diagnoses chosen, from 1980 up to the year of the index seizure and also after the index seizure. When analysing the risk of developing unprovoked seizures/epilepsy after hospitalization for stroke, diabetes and myocardial infarction, we could confirm, previously known increased risks of developing unprovoked seizures after intracerebral haemorrhage, odds ratio (OR) 7.2 (95% confidence interval (CI) 3.9-13.6) and cerebral infarction, OR 9.4 (95% CI 6.7-13.1), and a less pronounced risk increase after hospitalization for acute myocardial infarction, OR 1.7 (95% CI 1.4-2.8). The risk of developing unprovoked seizures/epilepsy was substantial even more than 7 years after the stroke.

Socioeconomic belonging was also studied as a potential risk factor for development of unprovoked seizures/epilepsy, and we did not find an association between socioeconomic class and risk of unprovoked seizures. Psychiatric disorders as risk factors for seizures/epilepsy was analysed, and increased rates were observed both predating, (OR 2.5 (95% CI 1.7-3.7) for depression, OR 2.7 (95% CI 1.4-5.3) for bipolar disorder, OR 2.3 (95% CI 1.5-3.5) for psychosis, and OR 2.6 (95% CI 1.7-4.1) for suicide attempt), as well as succeeding seizure onset.

We further analysed the risk, (OR, 95%CI), of developing unprovoked seizures/epilepsy after hospitalization for multiple sclerosis (MS), systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). The risk of unprovoked seizures was increased in patients with a hospital discharge diagnosis of MS, OR 3.5 (95% CI 1.5-8.1) and even more so for patients with SLE, OR 8.0 (95% CI 2.2-30.0), whereas RA was not associated with an increased risk, OR 1.2 (95% CI 0.5-2.9). We also found a comparatively high age and advanced disability at seizure onset as well as a long lag time from diagnosis of MS and SLE until seizure onset.

Keywords: seizure, epilepsy, incidence, risk factor, case-control, stroke, psychiatric disorder, multiple sclerosis