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Epidemiology and Risk Factors for Suicide Among Adult Patients with Epilepsy

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Abstract

Suicides constitute a serious public health issue worldwide. The number of suicide victims has been increasing over the years. Susceptibility to suicidal behaviour depends on the interaction of a number of factors. The reasons for taking a decision on committing suicide may objectively seem prosaic, and yet, according to the victim, cannot be resolved in any other way. Very often, it is the disease which is a risk factor for suicide. Suicidal thoughts, suicidal behaviours and suicide attempts as well as committed suicides occur far more frequently in epileptic patients than in the general population. There are many reasons for suicides committed by patients suffering from epilepsy. This paper presents basic data on epidemiology and risk factors of suicide attempts among patients with epilepsy. Risk factors in this group of patients include, inter alia, prior suicide attempts, co-morbidity of epilepsy with depression and other mental disorders, early onset (before 18 years of age), type and frequency of epileptic seizures and the use of anti-epileptic drugs, particularly in polytherapy.

Keywords: epilepsy, epidemiology, risk factors for suicide, suicide, antiepileptic drugs

1. Introduction

The World Health Organization (WHO) estimates that every 40 seconds one person dies as a result of suicide somewhere in the world [1]. Pursuant to data collected by the National Police

Headquarters 8579 suicide attempts have been reported, 6101 of which ended in death in the year 2013. The three main determined reasons for the suicides were family discord (n=999), mental illness (n=797) and chronic disease (n=570), and in the majority of cases investigators failed to determine the reasons behind the suicide attempt (n=3,663) [2]. Available literature suggests that the occurrence of a chronic disease is associated with increased vulnerability to suicidal behaviour [3]. The chronic nature of epilepsy, numerous limitations resulting from the disease, myths regarding the disease itself and persons affected by it as well as stigmatisation of patients all adversely affect the patients' well-being and quality of life [74]. Decreased self-esteem may in turn result in the occurrence of suicidal thoughts [4]. The aim of this paper is to describe epidemiological data and present risk factors for suicidal behaviour in patients with epilepsy. Taking these aspects into account in the treatment and secondary prevention regarding epileptic patients can help reduce that risk.

2. Prevalence of suicide in patients with epilepsy

Estimates from an 8-year observation period of epileptic patients confirm that 30% of patients die in accidents, 23% die suddenly, 16% die as a result of an epileptic seizure and 14% commit suicide [5].

Publication	Country	Observation period (in years)	Number of deaths	Number of suicides	Percentage of suicides
Cockerell et al. [10]	England	8	792	1	0.13%
Currie et al. [11]	England	7	666	3	0.45%
Elwes et al. [12]	England	11	102	1	0.98%
Hennessy et al. [13]	England	20	299	1	0.33%
Lhatoo et al. [14]	England	11.8	792	1	0.13%
Lindsay et al. [15]	England	13	100	1	1.00%
Lip et al. [16]	England	5	1000	3	0.30%
White et al. [17]	England	26	1980	21	1.06%
Bladin [18]	Australia	4	110	1	0.91%
McIntosh et al. [19]	Australia	10	325	4	1.23%
Ding et al. [20]	China	2.5	2455	4	0.16%
Dalby [21]	Denmark	16	346	2	0.58%
Lühdorf et al. [22]	Denmark	4	249	1	0.40%
Olesen et al. [23]	Denmark	10	6780	422	6.22%
Aikiä et al. [24]	Finland	>1	105	1	0.95%
Iivanainen and Lehtinen [25]	Finland	76	1481	13	0.88%

Publication	Country	Observation period (in years)	Number of deaths	Number of suicides	Percentage of suicides
Jutila et al. [26]	Finland	11	140	1	0.71%
Sillanpaa and Shinnar [27]	Finland	20	233	1	0.43%
Loiseau et al. [28]	France	1	804	1	0.12%
Shackleton et al. [29]	Netherlands	28	1355	7	0.52%
Rafnsson et al. [7]	Iceland	5	244	4	1.64%
Fukuchi et al. [5]	Japan	14	1722	6	0.35%
Camfield et al. [30]	Canada	8	692	3	0.43%
Garcia-Flores [31]	Mexico	20	112	5	4.46%
Guldvog et al. [32]	Norway	36	64	2	3.13%
Krohn [33]	Norway	10	107	3	2.80%
Stepien et al. [34]	Poland	9	54	2	3.70%
Zielinski [35]	Poland	2	6710	16	0.24%
Forsgren et al. [36]	Sweden	7	296	1	0.34%
Nilsson et al. [6]	Sweden	9	6880	26	0.38%
Chen et al. [37]	Taiwan	10	263	2	0.76%
Tsai [38]	Taiwan	1	1224	3	0.25%
Blumer et al. [39]	USA	12	10,739	5	0.05%
Day et al. [40]	USA	14	10,030	2	0.02%
Foldvary et al. [41]	USA	22	79	1	1.27%
Freytag and Lindenberg [42]	USA	11	294	9	3.06%
Quigg et al. [43]	USA	7	107	3	2.80%
Hauser et al. [44]	USA	39	618	3	0.49%
Mendez et al. [45]	USA	8	1611	4	0.25%
Salanova et al. [46]	USA	15	215	2	0.93%
Sperling et al. [47]	USA	4.5	583	2	0.34%
Kelemen et al. [48]	Hungary	6	94	1	1.06%
D'Alessandro et al. [49]	Italy	5	161	1	0.62%

Table 1. Frequency of suicides in the deaths of epileptic patients.

The risk of suicide in patients with epilepsy is greater than in the general population. The standardised mortality ratio (SMR) for suicides in patients with epilepsy as compared with the general population ranges from 3.5 to 5.8 [6, 7]. Based on a review of 21 studies, it has been estimated that on average 11.5% (0–67%) deaths of epileptic deaths are due to suicide [8].

Available epidemiological data indicate that the risk of suicides committed among epileptic patients is ca. 3–10 times greater compared to the general population. However, some researchers believe that this risk can be even greater, up to 25 times more in certain types of disease, e.g. in patients diagnosed with temporal lobe epilepsy [9]. **Table 1** summarises the number of deaths resulting from suicide when compared to all deaths among patients diagnosed with epilepsy within studies conducted in different countries.

The epidemiological data presented in **Table 1** differ substantially depending on the country and the area of the world. This results from the observation period and the population of epileptic patients.

3. Risk factors for suicide among epileptic patients

The motives behind suicide attempts in patients with epilepsy include factors characteristic for both the general population and factors typical of this disease.

Risk factors for suicide attempts have been listed by Patterson in the following abbreviation: SAD PERSONS—S, Sex (male); A, Age (elderly or adolescent); D, Depression; P, Previous suicide attempts; E, Ethanol abuse; R, Rational thinking loss, psychosis; S, Social support lacking; O, Organised plan to commit suicide; N, No spouse; S, Somatic sickness [3].

The above-mentioned risk factors for suicide are confirmed by other authors, adding to that list suicide attempts in the family and in the immediate environment, mental disorders, including anxiety apart from depression [8, 50, 51], white race, self-inflicted injury in the interview, and alcohol abuse [52].

Taking into account patients suffering from chronic diseases, the risk factors for suicide attempts include stigmatisation, discrimination, taking medication that possibly induces depression and easy access to toxic drugs [53]. Specific risk factors for suicide in epileptic patients can be grouped into several major categories.

3.1. Type of epileptic seizures

Additional risk factors in epileptic patients are related to the type of epileptic seizures. The risk of suicide attempts increase in the case of simple partial seizures, in primarily and secondarily generalised seizures with regard to partial complex seizures and temporal lobe epileptic seizures in male patients [54]. Furthermore, more frequent seizures, regardless of their type and the age at which the patient was diagnosed with epilepsy, also constitute risk factor for suicide attempts [9]. Additionally, it was found that the risk of suicide is over 5 times higher in patients with a 6-month history of the disease and that this risk decreases with the disease duration [55]. A study conducted in Finland among children below 16 years of age diagnosed with idiopathic or cryptogenic epilepsy reported two cases of suicide (where $n = 122$), however such self-destructive behaviour was not observed in children with symptomatic epilepsy [56].

3.2. Previous suicide attempts

It was also found that previous suicide attempts among epileptic patients increases the risk of another suicide in the future by ca. 38.4% when compared to the general population [57]. Similar results were obtained in a study conducted in Sweden, where that percentage amounted to 46.2%. Interestingly enough, not only epileptic patients are characterised by increased risk of suicide, but there is also a 5-times greater risk of epilepsy in persons who attempted to commit suicide prior to their diagnosis [58]. It is worth noting that this risk was not associated with the incidence of depressive disorders and alcohol abuse. Deterioration of cognitive functions and personality disorders resulting from the frequency of seizures increase the risk of suicide attempts [59].

3.3. Depression and other mental disorders

Many researchers are convinced that the main risk factor for suicidal thoughts in epileptic patients is co-morbid depression and other mental disorders. A study conducted in Canada demonstrated that during the lifetime of epileptic patients as compared with the general population, the following occur more often: depression (17.4% vs 10.7%), anxiety disorders (22.8% vs 11.2%) and suicidal thoughts (25% vs 13.3%) [60]. This was confirmed by results of a study conducted in Denmark on a group of 492 patients with epilepsy who committed suicide, as compared with the control group. It was proven that the risk of suicide increases over 29 times when an epileptic patient also suffer from a mental illness. In the same study, it was calculated that the risk of suicide in epileptic patients increases almost twofold in the case of a history of a mental illness [55]. It was found that in women suffering from epilepsy and with a history of mental illness, the risk of committing suicide is 23 times greater than in the case of women without these two conditions, and in comparison with men suffering from both epilepsy and a mental disease, that risk is 10 times higher [55].

It was also estimated that the risk of suicide in patients with epilepsy increases almost 14 times in the case of the co-morbidity of mental disorders, including 32 times more in the case of mood disorders and 12 times more in anxiety disorders [55]. Similarly, a study conducted in Sweden showed that co-morbidity of epilepsy with mental disorders is related to 9 times greater increase of suicide risk [6]. The MEPSY study carried out among Korean patients demonstrated that risk factors for suicide among epileptic patients include advanced depression (OR = 6.448; 95% CI = 3.739–11.120; $p < 0.001$), generalised anxiety disorder (OR = 3.561; 95% CI = 1.966–6.452; $p < 0.001$), as well as history of febrile seizures (OR = 2.188; 95% CI = 1.318–3.632; $p = 0.002$) [61]. Kanemoto et al. [62] observed a greater risk of suicide attempts in patients with temporal lobe epilepsy who experienced psychotic episodes (7%) than during acute interictal psychosis (2%) or post-stroke confusion (0%).

3.4. Emotional and social disorders

Risk factors for attempted suicide in adult epileptic patients also include emotional disorders [63]. Buljan et al., a study carried out among hospitalised patients, have shown that next to mental disorders, another statistically significant risk factor for suicide attempts in epileptic

patients is also a difficult family situation. The authors have estimated that 14.6% patients treated in Croatia attempted to commit suicide for that reason [50]. Results of the Hawton et al. [75] paper indicate a much higher percentage of suicide attempts among patients with epilepsy who have trouble finding employment. A multivariate analysis of logistic regression has confirmed that unemployment (Exp (B) 33.9; $p = 0.007$) is associated with suicidal thoughts in epileptic patients treated in Bosnia and Herzegovina, as is the sense of hopelessness (Exp (B) 14.9; $p = 0.001$) [64].

3.5. The use of antiepileptic drugs

Apart from current or past co-morbidity with psychiatric disorders, other risk factors include the use of anti-psychotics and the first instance of a seizure before 18 years of age [65]. In January 2008, the Food and Drug Administration (FDA) alerted that the use of anti-epileptic drugs (AEDs) is associated with an increased risk of suicide in patients who use them. FDA conducted an analysis of 199 placebo-controlled randomised studies on the risk of suicide attempts in connection with the use of 11 anti-epileptic drugs. The study included 27,863 patients treated with AEDs and 16,029 patients administered with placebo. Each group included at least 20 people treated for at least 7 days. The analysis included 25% of patients diagnosed with epilepsy, 27% of patients with mental disorders and 46% suffering from pain associated with the disease. Committed suicide was reported in four patients taking AEDs vs none patients in the placebo group; a suicide attempt was reported in 30 vs 8 persons, respectively, and suicidal thoughts were reported in 67 vs 29 persons, respectively. Relative risk of suicide for patients treated with AEDs vs placebo was 3.5 for people suffering from epilepsy, 1.5 for people with mental disorders and 1.9 for the remainder of the study group. FDA has concluded that patients using anti-epileptic drugs have a higher risk of suicidal thoughts and behaviour than the population taking a placebo [66].

In another study conducted on a population of 269,937 people aged ≥ 15 years of age, treated with anti-epileptic drugs, 26 suicides, 801 suicide attempts and 41 sudden deaths were reported. It was estimated that the risk of suicide behaviour was lower in patients using topiramate than in patients using gabapentin, lamotrigine, oxcarbazepine or tiagabine. However, an elevated risk of a sudden death occurred in a group of younger and older patients using gabapentin, in patients with mood disorders and epilepsy as compared with a group taking carbamazepine [67].

A study conducted on a group of 131,178 patients with epilepsy, pain, bipolar disorder, depressive disorder and schizophrenia demonstrated no difference in the risk of suicide for people using gabapentin [68].

Another study conducted in the United Kingdom compared 453 epileptic patients treated with AEDs with 8962 people in a control group matched in terms of age and gender. The anti-epileptic drugs used were classified into four groups: barbiturates, conventional AEDs, new generation AEDs with a low (lamotrigine, gabapentin, pregabalin, oxcarbazepine) or high (levetiracetam, tiagabine, topiramate, vigabatrin) depression-inducing effect. It was found that new generation AEDs with a high depression-inducing effect increased the risk of self-inflicted injuries/suicidal behaviours, it was however obvious only in patients with co-morbid mental

disorders [69]. Yet another study shows that the use of barbiturates is associated with inducing depressive symptoms, which may lead to abnormal behaviour, depression and suicidal thoughts, particularly in children [70].

Drug	Mechanism of action	Risk of suicide
Phenobarbital	Effect on GABA No effect on glutamate No effect on serotonin	Proven suicidality risk
Phenytoin	Effect of Na ⁺ channels No effect on glutamate No effect on serotonin	Proven suicidality risk
Carbamazepine	Improve cognitive functions and mood	Antisuicidal properties
Oxcarbazepine	in epileptic patients, and effect on serotonin	
Valproate		
Lamotrigine		
Topiramate	Exert negative effects on mood and cognition,	Influence on suicidality has not been proven in
Tiagabine	and no effect on serotonin	evidence-based studies yet
Vigabatrin		
Levetiracetam		
Zonisamide	Exert negative effects on mood and cognition, but effect on serotonin	Influence on suicidality has not been proven in evidence-based studies yet
Gabapentin	Exert positive psychotropic effects on mood and cognition, but no effect on serotonin	Antisuicidal properties

Table 2. Antiepileptic drugs and risk of suicide [71].

A study based on data from the Danish National Prescription Registry concerning 169,725 AEDs (only 2.6% of prescribed for epilepsy treatment) confirmed increased risk of suicide (OR = 1.85; 95% CI = 1.4–2.5), in particular in patients treated with clonazepam, valproic acid, luminal and lamotrigine [23].

Furthermore, it was indicated that the use of anti-epileptic drugs in polytherapy is also a factor in the risk of suicide [65].

On the one hand, some AEDs can cause depression, which itself is the main risk factor for suicidality, but on the other hand, other AEDs have effect similar to antidepressants, and these properties exert antisuicidal effect. The AEDs differ mechanism of action, influence on cognition and mood in epileptic patients and suicidality. Probably, serotonin may play a role in the mechanism of action of some antiepileptic drugs. AEDs with serotonergic properties

should reduce the suicidality risk, because they exert effects similar to antidepressants. Perhaps, psychotropic effects of AEDs may be the result of effects on the receptor functions: γ -gamma-aminobutyric acid (GABA) ergic and antiglutamatergic and neurochemical mechanisms [71]. **Table 2** shows the influence of some AED on suicide risk.

Not much data are available on the risk of suicidal attempts in a group of patients subjected to surgical treatment of epilepsy. A study that involved the observation of 396 patients subjected to surgical treatment of epilepsy indicates that 4 of the 27 reported deaths were caused by suicide, despite good control of epileptic seizures [72]. An analysis of the period which lapsed from the surgery indicates that the risk of a suicide attempt is greatest during the first 6 months after the surgical intervention [73].

During the past few years, a number of studies have been published trying to examine the correlation between AEDs and suicide. However, relationships between suicidal behaviour and AEDs are unclear, show a lack of concordance and are affected by a number of limitations (e.g., observational studies, more than one risk factor in patients with epilepsy).

4. Summary

An essential element of addressing this subject is to know all the possible risk factors for suicide attempts resulting both from the disease itself and additional causes in order to prevent suicide in epileptic patients effectively and in a timely manner. When conducting an interview, neurologists should pay special attention to whether the patient or his/her family has additional mental issues or whether any prior suicide attempts had been reported in the patient or his/her family. Additionally, when monitoring the treatment progress, it is necessary to verify the symptoms of depressed mood, in particular if the patient uses new generation anti-epileptic drugs, which can cause depression. A significant preventive factor also includes assessing the patient's social relationships (family, friends and work), in particular emotional problems, which can significantly impact suicide attempts.

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