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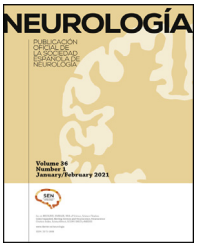

REVIEW ARTICLE

Do patients diagnosed with a neurological disease present increased risk of suicide?

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Abstract
Introduction: Neurological diseases are the leading cause of disability and the second leading cause of death worldwide. Physical and psychological pain, despair, and disconnection with the environment are observed after the diagnosis of numerous neurological processes, particularly neurodegenerative diseases.
Development: A higher risk of suicide is observed in patients with such common neurological diseases as epilepsy, migraine, and multiple sclerosis, as well as in those with such degenerative disorders as Alzheimer disease, Huntington disease, amyotrophic lateral sclerosis, and Parkinson's disease. In most cases, suicidal ideation appears in the early stages after diagnosis, in the presence of disabling symptoms, and/or in patients with psychiatric comorbidities (often associated with these neurological diseases).
Conclusions: Effective suicide prevention in this population group requires assessment of the risk of suicide mainly in newly diagnosed patients, in patients showing unmistakable despair or disabling symptoms, and in patients presenting psychiatric comorbidities (especially depressive symptoms). It is essential to train specialists to detect warning signs in order that they may adopt a suitable approach and determine when psychiatric assessment is required.

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PALABRAS CLAVE
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Factor de riesgo;
Prevención

¿Existe mayor riesgo de suicidio en pacientes diagnosticados de una enfermedad neurológica?

Resumen
Introducción: Las enfermedades neurológicas representan la principal causa de discapacidad y la segunda causa de muerte a nivel mundial. El dolor físico y psicológico, la desesperanza y la desconexión con el medio están presentes tras el diagnóstico de numerosos procesos neurológicos y especialmente de las enfermedades neurodegenerativas.
Desarrollo: Existe un mayor riesgo de suicidio en pacientes con enfermedades neurológicas comunes como la epilepsia, la migraña y la esclerosis múltiple, así como en quienes padecen trastornos degenerativos como la enfermedad de Alzheimer, la enfermedad de Huntington, la esclerosis lateral amiotrófica o la enfermedad de Parkinson. En la mayoría de los casos, la ideación suicida aparece en la etapa próxima al diagnóstico, ante sintomatología invalidante, y/o en pacientes que presentan comorbilidad psiquiátrica (a menudo asociada con dichas dolencias neurológicas).
Conclusiones: Para una prevención efectiva del suicidio en este grupo de la población debe evaluarse el riesgo principalmente en pacientes recién diagnosticados, ante la expresión de marcada desesperanza, ante sintomatología invalidante y en pacientes que presentan comorbilidad psiquiátrica (especialmente síntomas depresivos). La formación de los especialistas para detectar signos de alerta es fundamental tanto para que puedan hacer un correcto abordaje como para que sean capaces de determinar cuándo es necesaria la valoración de un especialista en psiquiatría.

Introduction

Around 804 000 people worldwide are estimated to die by suicide each year; furthermore, for each suicide, there are 20 attempts.[1] In Spain, suicide is the main cause of violent death[2]; since 2008, the number of deaths by suicide has exceeded the number of deaths due to traffic accidents.

People who commit suicide frequently have mental health disorders: history of psychiatric disorders is found in up to 90% of cases.[3,4] Depressive syndrome has been identified as one of the main predictors of suicide.

Physical pain has also been found to be a risk factor for suicidal thoughts, although this factor has been studied less extensively. Furthermore, depression is a frequent comorbidity in numerous diseases, and the risk of suicide increases with the number of comorbid diagnoses.

According to Klonsky et al.,[5] depression, impulsivity, and hopelessness are the 3 main components of suicide. The authors propose the 3-step theory of suicide, according to which the combination of 3 factors explains the progression from suicidal ideation to behaviour (whether attempt or suicide). The first step involves feelings of pain and hopelessness, which in turn promote suicidal ideation. In the second step, these individuals lose connectedness with their setting as they lack a meaningful life project and lose their personal relationships. The third step is suicide capacity, with impulsivity being the key factor in the progression from ideation to behaviour.

Several neurological diseases cause physical and psychological pain, feelings of hopelessness, and disconnectedness. Recently, several authors have analysed the relationship between these diseases and suicidal behaviour. Our working hypothesis was that the prevalence of suicide is higher among patients with neurological diseases, especially neurodegenerative diseases, than in the general population. We conducted a systematic review of studies into the topic.

Suicide and neurological diseases

Neurological diseases represent the main cause of disability-adjusted life years lost worldwide and the second leading cause of death, after cardiovascular diseases, causing 16.8% of deaths.

In the last 25 years, the number of deaths due to neurological disease has increased by 36.7%, and the number of disability-adjusted life years lost has increased by 7.4%. The 2 most prevalent neurological diseases are tension-type headache and migraine. Alzheimer disease (AD) is the most frequent neurodegenerative disease, as well as the most frequent cause of dementia, affecting over 46 million people worldwide.[6]

Increases in life expectancy due to scientific and technical advances and improvements in healthcare, nutrition, and control of infectious diseases may partially explain the upward trend in the prevalence of neurodegenerative diseases.

Neurological diseases, particularly age-related diseases, have been associated with an increase in suicidal ideation and behaviour. This association is particularly strong in the case of epilepsy, multiple sclerosis, AD and other dementias, Parkinson's disease (PD), Huntington disease (HD), and amyotrophic lateral sclerosis (ALS).[7]

In Denmark, Eliasen et al.[7] compared the prevalence of suicide attempts between patients diagnosed with neurological disease and healthy controls between 2006 and 2013. Interestingly, the researchers observed an increase in suicidal tendencies in patients with neurological disease (11%, vs 3% in controls), finding that the risk of attempting suicide

was highest at 3 months after diagnosis, decreasing thereafter. Other independent risk factors of suicidal behaviour in patients with neurological diseases include early disease onset, cognitive impairment, moderate physical disability, and recent changes in the symptoms associated with the disease.

Epilepsy

There is growing interest in the association between epilepsy and suicide, as these patients have been found to present 5 times higher risk of suicidal behaviour than the general population.

Epilepsy is one of the most frequent neurological diseases, estimated by the World Health Organization to affect 50-69 million people worldwide. Although it is more common among young individuals, its incidence and prevalence have increased in line with the increase in life expectancy, due to the higher incidence of cerebrovascular disease and degenerative dementia, 2 conditions with epileptogenic potential.[8]

Interestingly, epilepsy and suicidal behaviour share several clinical characteristics: both are episodic phenomena presenting similar recurrence rates in the first 5 years (37% for suicide and 32% for epilepsy) and higher recurrence rates in the first 2 years.

The risk of suicide is not homogeneous among patients with epilepsy. Some studies conclude that the risk is greater among patients with temporal lobe epilepsy, women, and patients with early-onset forms. Hesdorffer et al.[9] found a particularly strong association between cryptogenic epilepsy and suicide: in their sample, over 80% of suicide attempts were observed in patients with cryptogenic epilepsy.

The relationship between suicide and epilepsy is bidirectional. On the one hand, the risk of suicidal behaviour is higher in patients with epilepsy; on the other, brain damage secondary to a suicide attempt increases the likelihood of epilepsy.[10] The explanation for this association is not straightforward. Patients with epilepsy have greater predisposition to psychiatric disorders; therefore, the association with suicidal behaviour may be indirect, given the higher risk of suicidal behaviour in patients with psychiatric disorders. Furthermore, from a neurobiological viewpoint, both suicide and epilepsy are associated with neurotransmitter alterations, especially serotonergic alterations. This points to the need to screen for depressive symptoms and suicidal ideation in patients with epilepsy.[10,11]

Epilepsy has been identified as a risk factor for suicide, regardless of the presence of psychiatric comorbidities. According to some researchers, this relationship may be explained by the association between suicide and treatment with certain commonly prescribed antiepileptic drugs; however, recent studies have ruled out this association,[9,10,12] and no alternative explanation is currently available.

Migraine

Migraine is one of the most frequent causes of neurological disability, after dementia and cerebrovascular disease. It is characterised by recurrent episodes of moderate-to-severe headache that may be accompanied by visual alterations, phonophobia, or vomiting. Migraine affects 11%-23% of the global population, and frequently starts during puberty. Some patients with migraine present such neurological and psychiatric comorbidities as depression, epilepsy, cerebrovascular disease, and suicidal behaviour.[13]

The association between migraine and suicidal behaviour has been less widely studied. Friedman et al.[13] conducted a meta-analysis of 6 studies including a total of 148 977 patients, finding a positive association between migraine and self-harm, suicide attempts, and suicide mortality. Suicidal ideation in these patients is also associated with higher headache frequency and intensity. In addition to migraine, other less frequent but far more disabling headache disorders, such as cluster headache (also known as Horton disease) and trigeminal neuralgia, have also been associated with increased risk of suicide.

The neurobiological alterations associated with suicidal behaviour are also found in patients with migraine. Polymorphisms in the serotonin transporter gene and hypothalamic-pituitary-adrenal axis dysregulation have been associated with a higher frequency of migraine attacks.

Although the copresence of migraine and depression may explain the association between migraine and suicidal behaviour, a significant association between migraine with aura and suicidal behaviour has also been described, independently of psychiatric comorbidities.[13,14] The underlying mechanisms are poorly understood, and further research into the topic is needed.

Multiple sclerosis

The risk of suicidal ideation, suicide attempt, and suicide in patients with multiple sclerosis (MS) is 1.72 times higher than in the general population. Furthermore, the risk of suicide is higher at the time of diagnosis than at symptom onset (suicide rate ratio of 2.12 vs 1.69).[15] MS is a chronic demyelinating disease of the central nervous system, mainly affecting the periventricular region, optic nerves, and spinal cord. The natural course of the disease is characterised by relapses and periods of remission, with the disease becoming increasingly disabling over time. MS affects 2.5 million people worldwide, with higher prevalence in Europe and North America.

In addition to the typical neurological symptoms (sensory alterations, partial or total vision loss, motor alterations, gait alterations, etc), patients frequently present such psychiatric disorders as depression, anxiety, and psychosis. As is the case with neurodegenerative diseases, suicidal behaviour in patients with MS is most common near the time of diagnosis, particularly in the first year after diagnosis; however, the risk of suicide in patients with MS continues to be higher than in the general population during the first 5 years of disease progression. In a placebo-controlled trial of interferon β-1b, the detection of one completed suicide and several suicide attempts in both treatment arms, with none in the placebo group, led to suggestions of a possible association between the drug and suicidal behaviour; however, this hypothesis was subsequently ruled out.[16,17]

Neurodegenerative diseases

Neurodegenerative diseases are characterised by progressive cerebral dysfunction and have a significant impact on the lives of these patients. Neurodegenerative diseases are frequently associated with depressive symptoms, which may promote suicidal behaviour.[18] Patients with poor quality of life present 4 times higher risk of suicide than those with higher quality of life.[19]

Neurodegenerative processes affect the physical, psychological, and social spheres, and the subjective impact of the disease plays a key role. Impairment of these functions has a negative impact on daily life, potentially affecting self-perception and communication skills and leading to social stigma. Patients diagnosed with a neurodegenerative disease usually present poorer quality of life than the general population; subjective assessment of quality of life is greatly influenced by limitations in professional activity.

Patients with AD and PD, among other conditions, frequently present depressive symptoms of varying intensity at some point over the course of the disease. In some patients, these symptoms may present at early stages or even as the initial manifestation of the disease, although they have also been described at advanced stages. Depression promotes the progression of cognitive impairment.[20]

Numerous neurologists and psychiatrists propose a combination of pharmacological and non-pharmacological treatments for depressive symptoms, as well as promoting the emotional well-being of patients diagnosed with a neurodegenerative disease, as this improves the management of the disease and also helps prevent suicidal behaviour.

Parkinson's disease

The prevalence of major depression in patients with PD is 17%. This condition increases the risk of suicidal ideation, which is observed at some point after diagnosis in over 10% of patients. Death due to suicide is 5 times more frequent in patients with PD than in the general population.[21,22]

PD is a chronic, progressive neurodegenerative disorder characterised by disabling motor (rigidity, bradykinesia, gait alterations, resting tremor) and non-motor symptoms (eg, sleep disorders, neurocognitive alterations, urinary dysfunction).[23,24]

Li et al.[24] found that patients with PD who committed suicide are younger, have fewer comorbidities, and present better cognitive function than patients with other neurological diseases who commit suicide. Motor fluctuations constitute a major predisposing factor for suicidal behaviour, even more so than disease severity. Furthermore, according to Hinkle et al.,[23] patient perception of being untreated for motor fluctuations is in itself a predisposing factor for suicide. Therefore, patient perceptions of treatment effectiveness may be regarded as a crucial factor in preventing suicide among patients with PD.

Huntington disease

Suicide is a major concern in HD.[25] Around 6.5% of patients attempt suicide, and 21% present suicidal ideation.[26] HD is a neurodegenerative disease that follows an autosomal dominant inheritance pattern. It is caused by CAG triplet repeat expansions in the huntingtin gene, located on chromosome 4. The condition manifests between the third and fourth decades of life. Such movement alterations as chorea and dyskinesia are the most common symptoms, and are usually accompanied by psychiatric and neurocognitive alterations.

Over the course of the disease, patients present 2 critical periods for suicidal behaviour: immediately after diagnosis and when they begin to lose their independence. Van Duijn et al.[26] established 5 stages of HD according to functional capacity, with stage V indicating severe dysfunction. Suicidal ideation is more frequent in stage II, regardless of the presence of motor symptoms. However, the number of suicide attempts was higher in patients in stages IV and V, with significant differences between patients in premotor stages (3%) and those in motor stages (7%).

Amyotrophic lateral sclerosis

With an incidence of 1-3 cases per 100 000 person-years, ALS is the most frequent degenerative disease of the motor neuron system.[27] Although its aetiopathogenesis is yet to be fully understood, the condition is characterised by progressive amyotrophy, leading to death usually within several years after diagnosis.[28] As no effective treatment for ALS is currently available, patients gradually lose their independence, the ability to effectively communicate, and bodily functions.[29]

A study conducted in Sweden with data collected between 1965 and 2004 found that the relative risk of suicide is 6 times higher in patients diagnosed with ALS than in the general population.[30]

In a cohort study conducted in France, including 71 patients with ALS, 39% reported suicidal ideation over the 11-month study period. Furthermore, patients with suicidal ideation more frequently presented depressive symptoms and disability than patients who did not present suicidal ideation. Patients not reporting suicidal thoughts also achieved significantly better survival and coping beliefs subscore of the Reasons for Living Inventory.[31]

ALS requires a multidisciplinary approach from the time of diagnosis, including counselling about problems that may arise in the end of life (forgoing artificial nutrition and hydration, mechanical ventilation, sedation, etc), to ensure that patients' wishes and autonomy are respected.[29]

Open discussion enables patients to reflect and plan the end of their lives, providing comfort and addressing their fears.[32] Early management is essential, as disease progression may render patients unable to communicate their wishes or affect their decision-making capacities due to cognitive limitations. Furthermore, in countries where physician-assisted suicide is legal, the nature and aggressive course of ALS may result in the patient being unable to self-administer the medication necessary to end their life.[33]

Patients' decisions regarding end-of-life care must be respected by healthcare professionals, always in compliance with the law. Clinical management of patients with advanced ALS should aim to maximise quality of life by minimising physical, psychosocial, and emotional distress. At this stage, the physician's communication skills play a key role.[32]

Alzheimer disease

AD is the leading cause of loss of independence in older adults. From a clinical viewpoint, it is characterised by cognitive dysfunction, which usually affects episodic memory and causes behaviour disorders.[32] AD is associated with moderate risk of suicide.[34]

Several studies have reported a greater risk of suicide among older adults with a diagnosis of AD, especially at disease onset.[35] It has been hypothesised that, during the early stages of the disease, patient awareness of cognitive impairment, feelings of being a burden, and anticipated loss of independence are key factors in suicidal ideation. Furthermore, shortly after diagnosis, cognitive function is sufficiently preserved to plan and commit suicide.[33]

Given the high frequency of psychiatric disorders identified as risk factors for suicide in patients with AD, some researchers have suggested that AD is in itself an independent risk factor for suicide. The risk of suicide increases considerably in patients with AD and comorbid depression. A study including 294 952 patients with dementia concluded that most suicides were committed by patients who were receiving psychiatric treatment.[35] However, we should be aware that such neuropsychiatric symptoms as depression, psychosis, and anxiety are typical of AD and are in fact linked to the pathophysiological basis of the disease.[36,37]

The incidence of neuropsychiatric symptoms is lower at later stages of AD than in age-matched individuals without the disease; it has therefore been hypothesised that severe cognitive impairment and executive dysfunction may protect against suicidal ideation.[38]

Assessment of suicide risk

To evaluate suicide risk, we first need to study risk factors and protective factors. In addition to the physical problems mentioned above, we also describe other risk factors for suicide. Static risk factors include male sex and history of self-harm. Dynamic risk factors include toxic substance use (mainly alcohol or drugs of abuse), acute mental illness, unemployment, living alone, and being single.[39,40]

On the other hand, family support, strong religious faith, having children at home, a sense of responsibility for others, and problem-solving skills are protective factors.[39—41]

Neurologists should be aware of these protective and risk factors, and bear in mind that the risk of suicide increases shortly after diagnosis of neurological disease, when patients begin to develop disabling symptoms, and in patients with psychiatric comorbidities, which are frequently associated with the neurological disease. More specifically, patients with depressive symptoms and other issues should undergo thorough risk assessment and receive both pharmacological treatment and psychological support.[40]

Sinclair and Leach[41] mention several profiles observed during the medical interview that should lead to an assessment of suicide risk, such as severely depressed patients, patients whose behaviour can evoke feelings of boredom in the physician or a sense that they are undeserving, and those with extreme behaviours at consultations (eg, withdrawal, agitation, etc). The authors also provide a list of questions that may be useful during history-taking and indicate the situations requiring referral to the psychiatry department.

Conclusions

The available evidence suggests that the risk of suicide is higher among patients with such neurological diseases as epilepsy, migraine, and MS, or degenerative diseases including AD, HD, and PD. This increased risk is usually observed in patients with a recent diagnosis, disabling symptoms, and/or psychiatric comorbidities, which are frequently associated with the neurological disease.

To ensure effective prevention, healthcare professionals should evaluate the risk of suicide in this population group, especially shortly after diagnosis and in patients with symptoms or psychiatric comorbidities known to be associated with increased risk of suicide. Neurologists and primary care physicians should receive training for suicide risk assessment and management, and follow up these patients. Early identification of warning signs and referral to the appropriate specialist is crucial in suicide prevention.

Conflicts of interest

The authors have no conflicts of interest to declare.

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