



SOME ASPECTS OF EPILEPSY



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Epilepsy and Psychiatric Disorders

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Introduction

Epilepsy represents a global health problem, because according to reports from the World Health Organization (WHO), an estimated 50 to 69 million people suffer from it [1-3].

It is considered as old as humanity itself and one of the most frequent disorders of the Central Nervous System (CNS) [4].

Of significance should be mentioned the involvement in the psychological and social sphere of patients who suffer from it, because they are among the most vulnerable in any society, related to the particular stigma that this disease carries, which has been transmitted for generations through millennia [5].

People who suffer from epilepsy, experience a discriminatory behavior in many areas of life, with an associated psychiatric comorbidity, all of which implies that it is considered a complex pathology, with social, psychobiological and economic consequences [6,7].

This disease, in turn, can significantly compromise the quality of life of those who suffer from it, since in many cases it affects, albeit in a variable way; emotional state, behavior, social and cognitive functioning [8].

Since ancient times, in the first descriptions of epileptic disease it is related to alterations in behavior, thought and humor [9].

The conceptual definition of epilepsy, according to the report of the working group of the International League Against Epilepsy (ILAE) of 2005, states the following [10].

Brain disorder characterized by a continuous predisposition to the onset of epileptic seizures and the neurobiological, cognitive, psychological and social consequences of this disease. The definition of epilepsy requires the presence of at least one epileptic seizure.

Recently (2014) has been published by a group of experts from the ILAE, the operational (practical) clinical definition of this disease [11] considers that epilepsy presents a patient who has suffered a crisis and whose brain, for whatever reason, shows a pathological and continuous tendency to suffer recurrent crises with biological, cognitive, psychological and social consequences.

In fact, there is a consensus that the incidence of neurobehavioral disorders is higher in patients with epilepsy than in the general population and many authors establish a relationship between these disorders and complex partial epilepsy of the temporal lobe [12].

Taking into account that psychiatric comorbidity in patients suffering from epilepsy is frequent and of multifactorial cause, it becomes of significant interest for the physician to be able to identify early the risk factors that are related to neurobehav-



ioral symptoms, in order to minimize their effects and improve their quality of life.

Related factors between epilepsy and behavior disorders

Multiple biological and psychosocial factors interacting, determine the risk for the development of schizophreniform psychosis, major depression and behavioral disorders in patients with epilepsy [7].

Despite being frequent and important, mental disorders are under diagnosed in patients with this disease, whose causes are usually: tendency to minimize symptoms; difficulty in recognizing unusual, atypical symptoms in the population with epilepsy; tendency on the part of patients to minimize complaints for fear of being discriminated against and fear that psychotropic drugs will lower the seizure threshold [13].

The association between epilepsy and psychiatry has a long history. The traditional approach to the care of epilepsy has been directed to the crisis and its treatment. However, this only occupies a small proportion in the affectation of the patient with epilepsy and their quality of life. Sackellares and Berent considered that an adequate care of the patient with epilepsy requires "attention to the psychological and social consequences as well as to the control of the crisis" [14].

Frequency of psychiatric disorders in patients with epilepsy

The psychiatric symptoms characteristic of the neurobehavioral syndrome in epilepsy tend to be distinguished by being atypical, episodic and pleomorphic.

It is estimated that between 20-30% of patients with epilepsy have psychiatric disorders [9,15].

Of patients with intractable complex partial seizures, 70% may have 1 or more diagnoses, included in the Diagnostic and Statistical Manual of Mental Disorders, fourth revised edition (DSM-IV); 58% of these patients have a history of depressive episodes, 32% have agoraphobia without panic or other anxiety disorders and 13% have psychosis.

The risk of psychosis in patients with epilepsy can be 6-12 times more than the general population, with a prevalence of around 7-8%; In patients with temporal lobe epilepsy refractory to treatment, prevalence has been reported in a range of 0-16%.

The most common psychiatric conditions in epilepsy are depression, anxiety and psychosis.

Psychotic Disorders

Psychotic disorders are severe mental disorders that cause abnormal perception and thinking [16-18].

Vuilleumier and Jallon found that 2-9% of patients with epilepsy have psychotic disorders [19]. These are more common in patients with epilepsy than in the general population.

However, many questions hover around this issue [20].

They can be classified according to their relationship with the occurrence of epileptic seizures in periictal (preictal, ictal or postictal) and interictal [21-24].

The etiology and pathogenesis of psychosis in epilepsy is still poorly understood, however, neuroanatomical changes have

been observed in patients with psychosis [25].

In general, patients have a significantly smaller brain volume than patients with epilepsy alone.

Trimble and Schmitz estimate that the conclusions presented in the literature in relation to risk factors are controversial [26].

In a review of patients with epilepsy who developed psychosis, the researchers found that patients with psychosis were generally a form of schizophrenia, most commonly the paranoid.

Stagno reported that the persistent interictal psychosis of epilepsy and the psychosis of epilepsy with schizophrenia like are distinguishable from schizophrenia [27].

Bipolar Affective Disorders

A number of studies have shown that affective disorders in epilepsy represent a common psychiatric comorbidity [28]; however, the neuropsychiatric literature focuses on depression, which is predominant [29]. Our knowledge about the relationship between epilepsy and these disorders is limited, which, in turn, is presented with an episodic course that can be chronic [30].

The incidence of bipolar affective disorders in epilepsy is 1.69 cases per 1000 persons / year, compared with 0.07 in the general population.

Bipolar symptoms were 1.6-2.2 times more common in subjects with epilepsy than with migraine, asthma or diabetes mellitus and they occur 6.6 times more than in healthy subjects.

A total of 49.7% of patients with epilepsy who were selected with positive symptoms of bipolar disorders by a physician, had about twice the rates seen in other disorders.

Other authors, such as Lau, demonstrated in their series that only 12% of epileptic patients had symptoms of bipolar disorder [31].

Depression

Depression is the most frequent psychiatric comorbidity seen in patients with epilepsy, with a prevalence between 10 and 20% in patients with controlled seizures and between 20 and 60% in those with refractory epilepsy [32].

It occurs more frequently in patients with partial frontal and temporal lobe seizures. It is also more frequent in patients with poor control of seizures.

Two etiological possibilities exist: depression as a reaction to epilepsy or depression as part of epilepsy.

Méndez and colleagues found that while 55% of patients with epilepsy reported depression, only 30% of the control group reported it.

Some studies have documented that quality of life improves significantly in patients with epilepsy who are crisis-free. However, Boylan et al have found that quality of life is related to depression, but not to the degree of crisis control [33].

Mania

In a careful and selected series of patients with epilepsy, Williams found that only 165 of 2000 patients had complex ictal experiences, including emotional ones [34].

Mania and hypomania are rare in association with epilepsy.

Manic depressive illness is also rare and was not commonly associated with epilepsy even before the modern use of anti-epileptic drugs.

Suicidal behavior

Suicide is significantly more frequent among patients with epilepsy than in the general population [35].

Depression is one of the psychiatric disorders that increases the risk of suicide. This in depressed patients is considered around 15%.

On average, the risk of suicide in patients with epilepsy is around 13% (prevalence rates of 5-10 times that of the general population).

However, some authors question the methodology and selection techniques of these studies and mention the Barracough meta-analysis, which revealed that the risk of suicide in patients with temporal lobe epilepsy increases as much as 25 times the general population.

Even so, the relationship between epilepsy and suicide is complex and multifactorial.

Adverse psychiatric events, including symptoms of depression and anxiety, have been reported with the use of some Anti-epileptic Drugs (AEDs), particularly barbiturates (Phenobarbiton and Primidone), Topiramate, Tiagabine, Zonisamide, Vigabatrin and Leviteracetam [36].

However, the incidence of suicide phenomena related to AEDs has not been systematically well studied.

Frequent risk factors associated with suicide include:

Current or past anxiety and mood disorders, psychiatric family history or mood disorders, particularly suicidal behaviors and previous suicide attempt.

In the study published by Nillson et al in 2002 [37], conducted in Sweden, it was found that the early onset of epilepsy, the presence of an associated mental illness and the use of antipsychotic drugs were factors associated with suicidal behavior.

In January 2008, the US Food and Drug Administration (FDA) warned about the association between suicide and AED. In the study, suicide occurred in 4.3 of 1,000 patients treated with AED. The result of this study should be considered with great caution and other studies are necessary [36,38].

Anxiety Disorders

Anxiety is common in patients with epilepsy and may also be related to non-epileptic seizures. Anxious symptoms, especially if they are noticeable, can have significant implications for the quality of life of patients with epilepsy [39,40].

The consequences can be disabling, provoking evasive behaviors and isolation [41,42].

GABA is the most important inhibitory transmitter in the central nervous system. Evidence suggests that the abnormal functioning of GABA receptors could be of great importance in the pathophysiology of epilepsy and anxiety disorders.

Anxiety in association with types of epilepsy and frequency of seizures

The highest rates of psychiatric comorbidities, including anx-

ety, are reported in patients with chronic refractory crisis [43].

The risk of anxiety is higher in partial epilepsies (more frequent in the temporal lobe) than generalized epilepsy. In patients with temporal lobe epilepsy, Trimble et al reported that 19% of patients were diagnosed with anxiety and 11% with depression.

Edeh and Toone found that patients with temporal and frontal lobe epilepsy had higher anxiety scores than extratemporal ones [44].

Personality Disorders

Personality disorders in epileptic patients can cause abnormal behaviors, which can have a direct impact on the control of seizures and quality of life [45,46].

This relationship has a long history and remains controversial. In 1975, Woxman and Geschwind described the term they coined as a syndrome of interictal behavior consisting of circumstantiality (excessive verbal expression, hyperviscosity, and hypergraphia), altered sexuality, and animosity in a patient with Temporal Lobe Epilepsy (TLE). This was called Geschwind syndrome [47].

Benson and Herman reported that the data are insufficient to establish a pattern of behavioral changes in patients with TLE. Complex partial epilepsy should not be diagnosed on the basis of the presence of Geschwind syndrome without any paroxysmal episode that may induce epilepsy [48].

The relationship of personality disorders with epilepsy was not only seen in ELT. Trinkka et al found that personality disorders were present in 23% of patients with juvenile myoclonic epilepsy.

Trimble has summarized that the personality profile of a patient with epilepsy can be explained by a complex combination of effects of the relationship with chronic diseases, the effects of AED and the pathology of the temporal lobe.

He asserted that certain personality alterations in epilepsy should be seen as associated with brain abnormalities that are also crisis-inducing [36].

Hyperactivity disorders and attention deficit

Hyperactivity disorder and attention deficit disorder is another psychiatric comorbidity in patients with epilepsy and more common in children. The occurrence may result from the inclusion of altered neurobiological mechanisms in the early development of the brain.

The incidence is around 7.76 cases per 1000 persons / year in patients with epilepsy and 3.22 in patients without epilepsy. In turn, the incidence of epilepsy is 3.24 cases per 1000 person-years in patients with the disorder studied and 0.78 in those without it [38].

Many AEDs can cause symptoms that mimic these disorders and the most common are GABAergic drugs such as barbiturates, benzodiazepines and vigabatrin.

Methylphenidate can cause an increase in epileptic seizures in patients with hyperactivity disorder and attentional deficit, however, it is considered safe in those who are crisis-free [49].

Psychotropic effects of antiepileptic drugs

Knowledge about the psychotropic effects of AEDs is crucial and still very limited in the epileptic population. Evidence suggests that Lamotrigine and the vagal stimulator may have antidepressant properties that could be used in common comorbid depression [50].

Carbamazepine, Valproate, Lamotrigine, and possibly Oxcarbazepine may have mood stabilizing properties. Gabapentin, Pregabalin, and Tiagabine may have anxiolytic benefits.

There is a risk of depression related to barbiturates and topiramate and possibly phenytoin.

The underlying symptoms of depression and anxiety may be exacerbated by Leviteracetam, while psychotic symptoms, although rare, have been reported with Topiramate, Levitracetam, and Zonisamide [51].

Psychiatric disorders in surgery in epilepsy

Generally, psychiatric symptoms improve with surgery in epilepsy. A history of psychiatric disorders before surgery is associated with poor postsurgical remission of epileptic seizures. After resective surgery, only patients with good or excellent seizure control had a substantial improvement over long periods of time in mood [52].

Post-surgical patients had high mortality rates by suicide compared to the general population and people who continued with seizures after surgery had a high mortality rate by suicide, in contrast to those who were crisis-free after surgery (4-5 times) [53].

In a series of 26 patients, with gamma knife radio surgery in patients with mesial Temporal Lobe Epilepsy (LTM), they did not show significant psychiatric changes between the preoperative period and the following 24 months [54].

Risk factors for depression after surgery in epilepsy include preoperative history of mood disorders and LTM surgery [55,56].

Behavioral disorders can interfere with the preoperative evaluation and the patient may not be willing to provide informed consent in the research and surgery.

Stimulation of the vagus nerve showed better responses in patients with major chronic depressive disorders in the 12 months of the study [57,58].

Elger and colleagues in small studies showed that treatment with vagal stimulation improves depression in patients with epilepsy, independent of the effects of the frequency of seizures. Vagal stimulation is a useful therapy in the treatment of resistant depression.

The postoperative decline in memory depends on the volume of tissue that is removed during surgery, the functional reserve of the remaining structures, the age at the time of surgery, the gender and the previous intellectual quotient. Patients who can reduce or stop AED after surgery may experience significant improvement in memory, processing speed, and language, particularly if they were taking multiple AEDs at high doses, as is typical of refractory epilepsy [54].

In analyzing all of the above, it can be understood that we must take measures to arrive at a better understanding of the effects of epilepsy and its treatment, of the results of seizures and the side effects of medications. In turn, areas that may af-

fect the life of a person who has epilepsy must be defined. But also, we must seek the attention and support for the specialties of Psychiatry and Psychology in the management of these patients [59].

Conclusion

Psychiatric comorbidity in patients suffering from epilepsy is frequent and of multifactorial cause, being of significant interest to the physician, to be able to recognize the risk factors that are related to the neurobehavioral symptoms in said patients, in order to minimize their effects and improve the quality of life of them.

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