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COMORBID COURSE OF MENTAL DISORDERS IN EPILEPSY

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ABSTRACT

There are currently about 50 million people in the world diagnosed with epilepsy (WHO, 2001). Clinical epilepsy is represented by two symptom complexes: various types of epileptic seizures and mental disorders (psychotic and non-psychotic levels). Despite the frequency of occurrence of mental disorders in epilepsy, their most important role in the formation of the clinical picture, course and prognosis of the disease, they have not been standardized in any modification of epilepsy classifications.

KEYWORDS: Epilepsy, Mental Disorders, Comorbidity.

INTRODUCTION

Epilepsy, defined as a condition with recurrent unprovoked seizures, is one of the most ancient diseases known to mankind (WHO, 2001). Among diseases of the nervous system, epilepsy ranks third (0.5-2% of cases), affecting all age groups of the population. [4, 5, 6]. The burden of epilepsy is unevenly distributed, and according to current data, there are differences in prevalence and incidence rates. Some of these differences may be related to different research methods and population structures [2, 3, 4, 5]. The increase in prevalence and incidence rates may be associated with low socioeconomic status, limited access to health care, and the influence of the external environment. Also, prevalence and incidence may be underestimated in areas where the disease is heavily stigmatized. This complicates comparative statistical studies of epilepsy and also mental disorders in epilepsy. Prevalence studies use the following

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methodology: analysis of medical records, house-to-house visits, and prevalence in age groups in population-based studies, studies without clearly defined diagnostic criteria, race and ethnicity, socioeconomic status [6, 13, 14, 17, 21]. Several large epidemiological studies have shown that comorbidity rates for many psychiatric and somatic diseases are higher among patients with epilepsy. The results of a cross-sectional population study with an analysis of a sample from the database of outpatients in the UK (IS General Practice Research Database) for 1995-1998, published in 2004 (Gaitatzis A. et al., 2004) indicate that diseases that are widespread in the general population were also widespread among patients with epilepsy.

Among patients with epilepsy, mental illness was observed 2 times more often than among the general population. J.F. Tellez-Zenteno et al., (2005) analyzed data from epilepsy patients and the general population from two independent studies (Canadian health surveys, the National Population Health vey (NPHS, 49,000 people surveyed) and the Community Survey (CHS, 130,882 people), which represented 98% of the Canadian population. The prevalence of epilepsy and 19 other chronic diseases was estimated by asking respondents about diseases previously diagnosed by physicians. Prevalence values, their ratio (PR), and confidence intervals were calculated for the entire population. Among patients with epilepsy, significantly higher prevalence values were observed for most chronic diseases compared with the general population. Interpretation of epidemiological data on the comorbidity of epilepsy is limited by differences in the methodology used, the definitions used, and differences in the structure of the studied populations. Case-control studies provide insight into the degree of association of epilepsy with other diseases, but do not provide information on the frequency or distribution of these diseases among patients with epilepsy or in the study population.

The prevalence of mental disorders in patients with epilepsy, according to the results of various researchers, varies within a very wide range: from 3.8 to 60% (Kalinin V.V. 2010; Tellez-Zenteno J.F. et al., 2007; Lin J.J. et al., 2012; Rai D. et al., 2012). Mental, cognitive and social disorders can complicate the course of epilepsy [10, 12, 14, 15, and 21]. Disorders are detected more among patients with persistent seizures (25-50%). According to the data of epidemiological studies by V.A. Houser in patients with epilepsy, the values of the prevalence of affective and anxiety disorders, attention deficit and motor hyperactivity disorder (ADHD) and other mental illnesses are increased. There is evidence of a bidirectional relationship between some mental disorders and epilepsy (Kalinin V.V. 2009; Tellez-Zenteno J.F. et al., 2007; Lin J.J. et al., 2012; Rai D. et al., 2012). Other evidence of a bidirectional relationship comes from a study of patients with temporal lobe epilepsy, in this study the progression of mental comorbidities successfully controlled before the onset of epilepsy was revealed (Jones J.E. et al., 2007). Obviously, the relationship between mental illness and epilepsy is complex and not only a consequence of epilepsy itself (Kanner A.M. et al., 2003; LaFrance W.C. et al., 2008; Lin J.J. et al., 2012). The effectiveness of some AEDs in both the treatment of epilepsy and affective disorders confirms the mechanism of a bidirectional relationship between these diseases. The moment is not taken into account that against the background of AEP and a decrease in seizures, a "forced" normalization of the EEG occurs, a decrease in epileptic form patterns, focality decreases, a decrease in the amplitude of the background rhythm with an increase in the alpha rhythm index is determined, but psychotic disorders appear up to Landolt's syndrome, acute paranoid and acute affective psychosis. Valproate, carbamazepine and lamotrigine are effective in the treatment of bipolar and schizoaffective disorders, and lamotrigine in the treatment of bipolar disorder.

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Compared with healthy individuals, patients with epilepsy and concomitant mental illness had a greater number of days of incapacity for work and more often received disability, which may be associated both with epilepsy itself and at the same time with a greater decrease in cognitive functions and greater stigmatization (Kessler R.C., 2012). Comorbid mental illnesses explain the variance in quality of life indicators to a greater extent than both epileptic seizures and demographic characteristics (Jones J.E. et al., 2007; Kessler R.C., 2012).

Depression is the most common psychiatric comorbid disease of epilepsy, with a lifetime prevalence of 30-35% among patients with epilepsy. Depression is the cause of a decrease in the quality of life and a significant predictor of the quality of life in patients with drug-resistant epilepsy (Karlov V.A., Khabibova A.O., 2000; Choi-Kwon S. et al., 2003; Boylan L.S. et al., 2004; Cramer J. A. et al., 2003; Guekht A. B. et al., 2007). Depression is most common in patients with partial epilepsy arising from the frontal or temporal regions and among patients with poor seizure control. In population studies, the prevalence of depression ranged from 21-33% in patients with epilepsy with persistent seizures and 4-6% in patients without seizures (O'Donoghue M.F. et al., 1999; Edeh J., 1989; Jacoby A., 1996).

The observed high comorbidity is influenced by many factors [8, 9, 18, 19]. Along with research data showing the presence of depression in patients with epilepsy, there are studies that have studied depression as a risk factor for the development of epilepsy.

In these studies, it was found that depression increases the risk of epilepsy, which is evidence of the general pathophysiology of these two diseases (Forsgren L., 1990; Jones J.g et al., 2007). For example, the presence of pathology of the hippocampus has been associated with the presence of depression in patients with epilepsy. A. Quiske et al. (2000) found higher BD1 scores in individuals with hippocampal sclerosis than in patients with temporal lobe epilepsy without hippocampal sclerosis (Series W. et. al., 1999; Guye M. et al., 2002). The size of the area with reduced values of N-acetylaspartate was linearly related to the severity of depression (Gilliam F.G. et al., 2007).

Depression is only part of the multi factorial association between epilepsy and suicidal behavior. According to a number of studies, in patients with epilepsy, the risk of suicidal behavior is approximately 3 times higher than in the general population (Bell G.S. et al., 2009). According to a meta-analysis of 12 studies, the standardized mortality rate among patients with epilepsy was 5.1 (95% CI: 3.9-6.6) (Harris E.C. et al., 1997). In a case-control study using sources from Denmark, data were studied on 20,000 people who died as a result of suicide and more than 400,000 survivors after a suicide attempt, comparable to those who died by sex and age (Christensen J. et al., 2007). Among those who committed suicide, 500 people were patients with epilepsy. The study noted that patients with epilepsy are 3 times more likely to commit suicide than those without epilepsy. Among people with epilepsy, more people had mental illness than those without epilepsy (odds ratio 4.3), but the proportion of people who committed suicide among people with epilepsy was 2 times higher than among people without epilepsy, even after excluding people with mental illness and taking into account others. Factors. In 2005, the FDA expressed concern about the possible increased risk of suicidal ideation, suicide attempts, and actual suicide with AEDs. The results of several macroepidemiological studies have been published, the efforts of which have focused on finding an association between AED and suicidal behavior. According to a study based on data from the Danish National Register of Prescriptions,

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AEDs increased the risk of completed suicide (OR 1.85 (CI95%: 1.4-2.5)), while for clonazepam, valproate, phenobarbital and lamotrigine this increase was statistically significant (Olesen J.B. et al., 2010). E.Patorno et al. (2010) noted that compared with topiramate, gabapentin, lamotrigine, oxcarbazepine, tiagabine and valproic acid had a statistically significant increase in the risk of suicide attempts and completed suicide. A.C. VanCott et al. (2010), analyzing data from elderly patients with a psychiatric history, found that the use of valproic acid, lamotrigine or levetiracetam had a statistically significant, independent correlation with suicidal behavior [14, 15, 21].

Anxiety disorders are the second most common comorbid epilepsy of mental illness, occurring in 15-25% of patients (O'Donoghue M.F., et al., 2010; Edeh J., 2010; Jacoby A., 2011). According to A. Gaitatzis et al. (2004), the proportion of patients with anxiety disorder was 11% of 5834 patients with epilepsy, compared with 5.6% of 831163 people in the population. The relationship between anxiety disorder and epilepsy is complex. That is why it is necessary to distinguish between the various manifestations of anxiety disorder during periods of an attack, after an attack, and in the period between attacks. Existing susceptibility factors, neurobiological factors, iatrogenic consequences [18, 19, 21] (AED, surgery) and psychosocial factors all seem to play a role and have their individual differences. Various forms of anxiety disorders (generalized anxiety, panic, phobic, obsessive-compulsive disorder, PTSD) can be observed in the interictal period with the same clinical manifestations as anxiety disorders in the general population. However, anxiety symptoms in the period often differ from those in the interictal period (Beyenburg S. et al., 2012). Patients with Alzheimer's disease and other types of dementia have a 5-10 times increased risk of developing epilepsy compared with the control group in the population of the same age (Mendez M. et al., 2003). Some clinical and experimental data indicate the existence of a close relationship between the pathophysiological processes underlying epilepsy and cognitive impairment in dementia [3, 12, and 17]. Both diseases are associated with a common risk factor, such as hippocampal atrophy. Seizures in temporal lobe epilepsy rapidly impair cognition and irreversibly damage connections between neurons in the hippocampus, leading to progressive memory loss. In the same way, the accumulation of amyloid proteins that underlies Alzheimer's disease triggers synaptic degeneration, rewiring of neural networks, and abnormal synchronization within them. Because neuronal hyper excitability increases the release of amyloid proteins (ARs) at synapses, seizures create a vicious spiral that accelerates cell death (apoptosis) and the process of cognitive decline (Noebels J., 2011).

In epidemiological studies, it was found that only 4.5% of patients with epilepsy observed by psychiatrists did not reveal mental disorders. Over the past years, there has been a clear increase in the forms of epilepsy with non-psychotic mental disorders, a decrease in the proportion of epileptic psychoses, epileptic dementia, which reflects the obvious pathomorphism of the clinical manifestations of the disease, primarily due to the success of epilepsy pharmacotherapy [1,2,4,15,20]. Dysregulatory processes in epilepsy can be traced from the positions of clinical epileptology, neurophysiology, neurophysiology, neurochemistry, and neuroimmunology. In 1838 E. Esquirol created the first classification of epileptic psychoses. Subsequently, works appeared indicating the influence of AED on the cause of psychopathological disorders in epilepsy. Although there is no single classification of disorders in the higher mental sphere. They can be divided into cognitive impairments; epileptic psychoses; changes in the emotional-

affective sphere, the so-called non-psychotic mental disorders (depression, bipolar disorders) [19, 20].

Epileptic seizures are common in patients who use psychoactive substances [4, 5] and are one of the most severe complications of alcoholism and drug addiction [1]. Long-term substance abuse causes serious complications in many organ systems. Among the numerous complications of chronic alcoholism from the side of the central and peripheral nervous system, epileptic seizures occupy a special position [2]. Drug addiction and substance abuse aggravate the course of epilepsy; contribute to the formation of drug-resistant forms of epilepsy. In the case of psychiatric disorders in patients taking psychoactive substances, higher doses of antiepileptic drugs are required to achieve control over seizures (3).

Epilepsy undoubtedly represents an interdisciplinary pathology of neurology and psychiatry. This is what often unites and at the same time separates neurologists and psychiatrists in the treatment of a disease.

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