



CLINICAL PHARMACOLOGICAL APPROACH TO THE USE OF PSYCHOTROPIC DRUGS IN EPILEPSY

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ABSTRACT

The aim of the work is to present clinical characteristics of depressive and anxiety disorders in epilepsy and to substantiate modern psychopharmacotherapy of these disorders. Based on literature data and our own research, the features of affective symptoms characteristic of epilepsy are shown, the significance of cognitive impairment with impaired executive functions is emphasized. A comparison of clinical manifestations of depressive and anxiety disorders with localization and lateralization of the epileptic focus, the factor of the leading hand and the presence of alexithymia is carried out.

INTRODUCTION

Formally being a neurological disease, epilepsy is nevertheless associated with the development of a wide range of mental disorders that require the direct participation of a psychiatrist in their recognition, diagnosis and therapy. The range of psychopathological disorders includes affective disorders [1], personality changes, associated mnestic-intellectual decline [2] and epileptic psychoses [3]. Epilepsy is one of the most common neurological diseases and occurs in at least 0.5–1% of the population [1, 2]. The primary incidence of epilepsy is about 70 cases per 100,000 population per year [2]. Such a high prevalence of epilepsy throughout the world, and currently, according to preliminary estimates, at least 50 million people suffer from it, forces us to look for new methods of its treatment, as well as new antiepileptic drugs (AEDs) [3].

MATERIALS AND METHODS

Affective symptoms in the form of depression are most common [4], although in clinical settings these conditions are not recognized in a timely manner, which is explained by the vagueness of the clinical and psychopathological manifestations of these disorders in patients with epilepsy [5]. At the same time, most epileptologists agree that interictal (interictal) depression in epilepsy most often manifests itself with a variety of symptoms in the form of depression itself, anxiety, irritability, suicidal ideas, somatovegetative manifestations in the form of decreased appetite and libido, and memory impairment. Memory impairment distinguishes depressive disorders in epilepsy from affective pathology of a different genesis [1]. Depression is characterized by a chronic course, which is periodically interrupted by clear intervals, lasting from several hours to several days [2]. Classic symptoms of endogenous depression in the form of guilt, ideas of self-blame, experiences of loss of feelings and



manifestations of daily mood swings in epilepsy are usually rare [3]. In this regard, most authors emphasize that the clinical manifestations of depression in epilepsy are atypical (at least, atypical features are found in at least 50% of patients) [4].

RESULTS AND DISCUSSION

As indicated in the works of Blumer et al. [5], affective disorders in epilepsy are characterized by a multiplicity of manifestations, among which eight key symptoms are distinguished. They include labile depressive symptoms (depressive mood, anergy, pain symptoms, insomnia); labile affective symptoms (fear, anxiety) and supposedly "specific" symptoms in the form of paroxysmal irritability and euphoria. These symptoms are characterized by a protracted and even chronic course with rare clear intervals, which allowed Kanner [2] to speak of a disorder similar to dysthymia. The author found a similar disorder in at least 70% of patients with epilepsy and depression who needed psychopharmacotherapy [3]. Many authors in this regard believe that epilepsy has dysthymic or dysphoric disorders, although systematic studies that could confirm the specificity of this syndrome, empirically isolated for epilepsy, have not been performed [4]. It is believed that depressive symptoms in temporal epilepsy are accompanied by a dysfunction of the frontal lobes (hypofrontality state) [5], which can be judged by the impairment of tests for the so-called executive functions. In turn, this occurs more often when the focus is located in the left temporal region. Based on this, it is believed that depressive disorder is more likely a clinical manifestation of the remote effect of dysfunction of the left-sided temporal focus within the neural networks than the result of a local effect within the mediotemporal structures of the brain [2]. At the same time, there is data showing that depression can also occur with right-sided temporal foci [3]. This is usually observed in paleocortical (mediobasal) temporal epilepsy. Thus, in this form, the side of focus does not play a role at all for the occurrence of depressive symptoms [4].

Anxiety disorders, including anxiety itself, panic attacks and phobic symptoms, can occur in the interictal period in both temporal and idiopathic generalized epilepsy [5]. It is believed that anxiety disorders are more common in temporal epilepsy with a focus on the left than with a focus in the right hemisphere [3]. It is important that the whole variety of anxiety disorders in epilepsy in their phenomenological manifestations are practically no different from anxiety disorders in individuals without epilepsy, which introduces certain difficulties in their diagnosis. Unlike depression, anxiety disorders more often occur when the focus of epileptic activity is localized in the left hemisphere. In one of our studies, it was shown that the risk of developing anxiety symptoms is 3.3 times higher than the risk of developing depressive symptoms with left-sided temporal localization [1]. It should also be emphasized that, along with the localization and lateralization of the focus, the risk factors for developing affective and anxiety symptoms also include the factor of the dominant hand (motor asymmetry), and personality characteristics of the premorbid period are also important [2]. In this case, the factor of left-handedness interacted with the presence of alexithymia, which was accompanied by the appearance of pronounced affective and anxiety symptoms in patients with epilepsy. On the other hand, patients with the dominant right hand may also develop depressive and anxious symptoms, provided that they combine the presence of alexithymia and a right-sided focus of epileptic activity. In other words, the alexithymia factor



is of fundamental importance in terms of the risk of developing affective symptoms, but only under the condition of interaction with the factor of left-handedness and (or) right-sided focus, whereas the absence of alexithymia in any case indicates a low risk of developing affective and anxiety disorders. It is important that classical personality characteristics of the premorbid period, such as neuroticism and esoteric tendencies, increased the risk of developing depression in right-handed patients with left-sided localization of the temporal focus. In this context, such an interaction of right-handedness and left-sided focus represents a kind of mirror image of the neurobiological interaction of alexithymia, left-handedness and right-sided focus, although in each of these cases the risk of developing affective and anxiety symptoms is high [3].

Extraversion and frustration tolerance among all premorbid personality characteristics had a preventive effect in terms of the emergence of affective and anxiety symptoms, i.e. had a favorable prognostic value [4].

It should be noted that both affective and anxiety states in patients with epilepsy are characterized by rather pronounced disorders in the mnemonic-intellectual sphere, which is manifested in the form of memory impairment (mainly autobiographical) and attention.

It is fundamentally important that with left-sided temporal focus, mainly verbal memory is impaired, whereas with right-sided focus, spatial, visual and geographic memory is impaired [5]. Attention is the basis of cognitive activity and often suffers in epilepsy. This is especially noticeable in children with epilepsy, who develop attention deficit syndrome [2]. AEDs themselves can impair both memory and attention [3]. Long-term and persistent AED therapy aimed at eliminating seizures is a necessary condition for sufficient social adaptation and rehabilitation of patients with epilepsy. At the same time, some AEDs themselves can aggravate cognitive impairment and affective symptoms in epilepsy. These include barbiturates and phenytoin (PNT) [4]. In this case, psychomotor retardation occurs, the ability to concentrate and learn new material decreases, memory is impaired, and the IQ index decreases [1]. The data on other classical AEDs, such as carbamazepine (CBZ) and valproates (VPA), are less clear-cut, although it is indicated that they can also lead to similar disorders [3]. It is important to emphasize that in epilepsy there is a relationship between affective and cognitive disorders [4]. In this context, these two groups of disorders can be considered as external manifestations of one more general neuropsychological syndrome in the form of a disorder of the functions of the frontal lobes of the brain in both cases [3]. This is supported by the data that in depressive disorders, patients perform tests of attention, vigilance and executive functions much worse than controls [4]. On the other hand, with a disorder of the frontal lobes, that is, with the development of the so-called syndrome of impaired executive functions, patients develop obvious depressive symptoms. In half of the cases, this condition meets the diagnostic criteria for a major depressive episode [3]. All this, ultimately, speaks of the commonality of pathogenetic links between depressive symptoms and a decrease in executive functions, which can be legitimately associated with disturbances in the functioning of the frontal lobes in epilepsy.

In connection with the above, it becomes clear that the use of AEDs for the treatment of epilepsy is a task that is not limited to eliminating seizures of a specific type. It is also important to select a drug that, in addition to eliminating seizures, will not aggravate the



manifestations of the mnestic-intellectual defect and contribute to the emergence of an affective disorder, or, on the contrary, will reduce the severity of affective depressive symptoms. The spectrum of psychotropic activity and mechanisms of action as criteria for choosing an AED. Analysis of literature data, however, shows that the spectrum of psychotropic activity of a particular AED has never been considered a fundamental criterion in choosing a specific drug for the treatment of epilepsy. In this context, the treatment of epilepsy, as well as other neuropsychiatric disorders, remains the main method of "trial and error", which today cannot satisfy either the needs of patients or the requests of epileptologists [4].

CONCLUSION

It should also be borne in mind that such AEDs as barbiturates, phenytoin and carbamazepine are strong inducers of liver enzymes. Due to their effect on the P-450 system (mainly on the isoenzymes CYP1A2 and CYP3A4), the plasma concentration of antidepressants decreases, which may lead to their insufficient effectiveness in eliminating depression [5]. Thus, SSRIs and, in particular, citalopram remain the drugs of choice in the treatment of a group of affective and anxiety disorders in epilepsy.

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