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CONCURRENT TREATMENT OF CHILDREN'S EPILEPSY AND DEPRESSION

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Epileptic children suffer from depression, and this condition is not well diagnosed and treated, and this results in poor health. The purpose of this work is to evaluate the rate of depression in children with epilepsy and develop an integrated treatment plan. 156 children (aged 12–17 years) with epilepsy were evaluated for depression using Hamilton depression rating scale and the ICD–10 criteria. The current study establishes a high level of depression in children with epilepsy; 68 % of participants fulfilled the criteria for different degrees of depression. Out of the 106 patients diagnosed with depression, 83 had mild depression, 21 moderate and 2 had severe depression. Wilcoxon test showed significant reduction in depression severity after combined anticonvulsant and antidepressant treatment ($p=0.048$). This is especially important in children as the prevalence of epilepsy and depression is high, and both conditions should be treated concurrently. Depression in children with epilepsy should be diagnosed and treated as soon as possible to enhance neurological and psychiatric prognosis.

Key words: epilepsy, depression, children, concurrent disease, treatment.

С.Е. Алієва

ОДНОЧАСНЕ ЛІКУВАННЯ ДИТЯЧОЇ ЕПІЛЕПСІЇ ТА ДЕПРЕСІЇ

Діти з епілепсією страждають від депресії, і цей стан погано діагностується та лікується, що призводить до погіршення здоров'я. Метою даної є оцінка рівня депресії у дітей з епілепсією і розробка комплексного плану лікування. 156 дітей (віком 12–17 років) з епілепсією було оцінено на предмет депресії з використанням шкали оцінки депресії Гамільтона та критеріїв МКХ-10. Поточне дослідження встановлює високий рівень депресії у дітей із епілепсією; 68 % учасників відповідали критеріям для різних ступенів депресії. Зі 106 пацієнтів з діагнозом депресія у 83 була легка депресія, у 21 – помірною та у 2 – тяжкою. Тест Вілкоксона показав значне зниження тяжкості депресії після комбінованого лікування протисудомними та антидепресантами ($p=0,048$). Це особливо важливо для дітей, оскільки поширеність епілепсії та депресії висока, і обидва стани слід лікувати одночасно. Депресію у дітей з епілепсією слід діагностувати та лікувати якомога раніше, щоб покращити неврологічний та психіатричний прогноз.

Ключові слова: епілепсія, депресія, діти, супутні захворювання, лікування.

Epilepsy is a chronic neurological disorder with recurrent unprovoked seizures and is linked with a range of psychiatric disorders, especially depression. Epilepsy in children presents them with a double jeopardy, that of the neurological disease and the other of mood swings. Depression in this group can lead to learning disability, social withdrawal and poor performance in school [1, 3].

The historical data revealed that epilepsy and depression are related conditions. Hippocrates in his writing of 400 BC has noted that “the melancholics are epileptic and the epileptic are melancholic”. Nevertheless, this ancient insight, the comorbidity of epilepsy and depression in children has not received much clinical attention in the present day [2, 8].

Epilepsy epidemiology differs from one country to another all over the world. Epilepsy in Europe and the United States is estimated to be 40–70 cases per 100,000 population. This rate is even higher in developing countries because of factors such as poor health care, and higher incidence of neurological diseases. Research shows that men are more likely to experience epilepsy than women and older men are more vulnerable to epilepsy than young men. Notably, the prevalence of depression in patients with epilepsy differs, with estimates of 22–58 % based on the type, frequency, and compliance with the antiepileptic drugs used [6, 7, 9].

The effects of uncontrolled depression in epileptic clients are severe. Depression is linked with higher suicide risk, poor seizure outcome, and significant decrease in the quality of life. For example, drug-resistant epilepsy patients claim that depression is a more important determinant of the health-related quality of life than the number of seizures [3, 8, 10].

In the WHO European Region, the cost of epilepsy is estimated at 20 billion euros per year. In this regard, in the WHO European Region, a systematic analysis of the global, regional and national burden of epilepsy and epilepsy incidence for 1990–2016 is presented, which shows that Azerbaijan is the country with the most frequent occurrence of epilepsy in the South Caucasus. This is clearly seen in the number of epilepsy cases, growth rates, mortality and disability-adjusted life years [12].

Since these conditions are common and have significant impact on the development of children, this study was designed to assess the depressive symptoms in children with epilepsy and to establish a therapeutic model for both conditions.

The purpose of the study was to evaluate the association between depression and epilepsy in children and the impact of therapeutic model on symptom severity.

Materials and methods. The study was carried out on the basis of the Department of Neurology of Azerbaijan Medical University. The work was approved by Local Ethical Committee of Azerbaijan Medical University. Informed consent was obtained from children's legal representatives.

The study included 156 people (aged 12–17 years) with various forms of epilepsy, who were examined for depressive disorders at the Children's Neurological Hospital in Baku in the period 2018–2022. The severity of depression was studied using the Hamilton scale and ICD–10. Among the examined, 132 boys and 24 girls. During the study, 63 children were diagnosed with focal epilepsy G40.0, and 93 children with generalized epilepsy G 40.3. Patients were examined in the interictal period. The mean age of the children involved was 14.0 ± 0.5 years. Inclusion criteria: The age limit of the examined patients was from 12 to 18 years. Exclusion criteria: patients under 12 years old, 18 years old and older.

Anamnesis was collected from the patients and a neurological examination was performed. A patient examination card developed for our study was filled out for each child. This questionnaire recorded the patient's demographic indicators, medical history, and epilepsy indicators. The Hamilton Depression Scale was used to identify different degrees of depression in children with epilepsy. The patients were examined using 16–channel electroencephalographic examination, with electrodes arranged 10/20 according to the international system, using the Neuron-Spectrum Digital EEG System.

The clinical characteristics of the children under observation are presented in Table 1.

Table 1

Clinical characteristics of enrolled children

Clinical characteristics	Abs. (%)
Gender distribution	
Boys	132 (85 %)
Girls	24 (15 %)
Epilepsy type (ICD–10 code)	
Generalized idiopathic epilepsy (G40.3)	93 (60 %)
Focal epilepsy (G 40.0)	63 (40 %)

All participants were on anticonvulsants based on their type of epilepsy and antidepressants where needed. The first choice of an antidepressant was venlafaxine, serotonin–norepinephrine reuptake inhibitors (SNRI), although there is controversy about its use in patients with epilepsy because of concerns about the seizure threshold.

The treatment efficacy was analyzed using the Wilcoxon signed rank test which is a non-parametric statistical test that is used when the data involve related samples. The differences were considered significant at $p < 0.05$.

Results of the study and their discussion. The duration of the epilepsy ranged from 1 to 15 years (5.0 ± 0.3 years). The onset of the disease was observed at the age of 1 to 16 years, on average, it was more often observed at the age of 9.0 ± 0.3 years.

Depression was found in 106 of the 156 patients (68 %). Diagnosis of depression in ICD–10: Depressive episodes (F32.0–32.2). Of these, 83 (78 %) reported mild depression, 21 (20 %) moderate depression, and 2 (2 %) severe depression. Table 2 shows the distribution of depression by type of epilepsy.

The Wilcoxon test also showed significant changes in depression severity after treatment with venlafaxine and anticonvulsants ($p = 0.048$).

The results of this study support the previous reports of high depression rate in children with epilepsy as observed globally in cases of epilepsy–depression co-morbidity.

Distribution of depression in children with epilepsy

Indices	
The Hamilton scale in points (n=156)	
Normal range (0–7 points)	50
Depression	106
Distribution of depression severity (n=106)	
Mild depression	83
Moderate depression	21
Severe depression	2
Association between Epilepsy type and Depression (n=156)	
Depression in Generalized idiopathic epilepsy (G40.3)	93
Depression in Focal epilepsy (G 40.0)	63

The mechanism of epilepsy and depression is still unknown, but there are some theories that connect these two diseases with common neurobiology. For example, it is postulated that the serotonergic and noradrenergic dysfunctions may play a role in the generation of seizures and mood disorders.

In addition, structural changes in the brain, especially in the hippocampus and the prefrontal cortex, are also associated with both disorders, but the exact nature of these relations requires further investigation.

Venlafaxine as a therapeutic intervention in this study yielded positive outcome. Although there are arguments that venlafaxine may reduce the seizure threshold, the findings of the present study show that the advantages of depression treatment surpass the risks when adequate antiseizure medications are used.

These findings have implications for clinical practice. First, the high level of depression in children with epilepsy points to the necessity of compulsory psychological examination of such patients. Second, the data indicate that the combination of psychiatric care into management of epilepsy may enhance not only the mental health but also seizure prognosis since epilepsy and psychiatric disorders are reciprocally associated.

The seriousness of the mental diseases problem in children is beyond doubt. The period from childhood to early adulthood involves increased susceptibility to the onset of mental disorders, with implications for policy making that may be better appreciated by disaggregated analyses of narrow age groups. Kieling C, et al, studying data from the 2019 Global Burden of Disease revealed that globally in 2019, 293 million of 2516 million individuals aged 5 to 24 years had at least 1 mental disorder. The mean prevalence was 11.63 % for mental disorders. For the narrower age groups, the prevalence of mental disorders was 6.80 % for 5 to 9 years old patients, 12.40 %—for aged 10 to 14 years, 13.96 % for aged 15 to 19 years, and 13.63 % for aged 20 to 24 years. The authors concluded that stratified age groups should be used to study mental disorders from childhood to early adulthood, as age-disaggregated data are important for understanding vulnerability and effective prevention and intervention initiatives [4]. This is why our research and the proposed therapeutic tactics should be perceived as a contribution to the overall task of combating these disorders.

The International League Against Epilepsy Guidelines Task Force, composed of 14 international members, uses international epilepsy clinical care guidelines, assess their quality, and determine gaps in areas of need of development. According to its report anxiety and depressive disorders and symptoms are significantly higher in youth with epilepsy compared to young persons without epilepsy. There is also evidence that certain anxiety disorders are particularly elevated, perhaps reflecting the special impact of epilepsy on youth psychopathology. Scott AJ, et al, who presented systematic review, noted that research is needed to understand the risk factors associated with anxiety and depressive disorders in epilepsy, and better understand how these symptoms change across development [11]. These conclusions are concordant with our recommendations related to treatment and prevention exacerbation in children with problems mentioned above.

The 68 % prevalence rate noted in our study is within the range of prevalence rates reported in other studies that range from 22 % to 58 % depending on the study population and the diagnostic criteria used.

So, LaGrant B, et al performed survey to detected national prevalence of depression and anxiety among children with epilepsy and the role of demographic factors and comorbidities. They also compare the rates of depression and anxiety in pediatric epilepsy to those of other chronic health conditions in childhood. The authors observed 283,000 children between 5 and 17 years of age who have epilepsy in the United States. Among these children, 25 % have depression and/or anxiety [6]. In our study the percent of epileptic children was 68 %, which is significantly higher. However, we did not assess the role of other

risk factors, this might be the purpose for further researches. Therefore, physicians should consider the various factors that are related to depression and anxiety in children with epilepsy so that at-risk children can be screened and managed appropriately.

According to other work, which was performed in United States, and included 500 children with epilepsy aged 6 to 9 years in was shown that 67 (13.4 %) of children with epilepsy had criteria for depression [13].

The prevalence of depression in the study of Kwong et al in Hong Kong, which enrolled 140 children with epilepsy between the ages of 10 and 18 years, was 22.1 %. This study found that factors such as medical comorbidities, female sex, frequent seizures, and younger age of seizure onset predicted depression [5].

In the similar study, conducted by Yang C, et al in China, the results also were different. In their work aimed to assess the depression status of children with epilepsy and factors related to depression the prevalence of symptoms of depression among these children was 16.9 %. Factors found to be associated with depressive symptoms in children with epilepsy in multivariate analyses were medical comorbidities, adverse reactions to medication and negative attitudes towards seizures [13].

According to Besag F, et al report, depression in children manifests as mood swings, impulsivity, poor self-esteem, self-harm and suicide, and abdominal pain, which can have undesirable consequences to both the patient and the family. They found that the prevalence of depression in children with epilepsy is 7 % to 29 %. In addition, the chance of having depression in children with epilepsy is 5 times greater than in children without epilepsy. In this study also was noted that there are many factors that may cause depression in children with epilepsy (include sex, frequent seizures, comorbidities, seizure onset, and types of antiepileptic drugs) [1].

Conclusion

The current study establishes a high level of depression in children with epilepsy; 68 % of participants fulfilled the criteria for different degrees of depression. The addition of anticonvulsant and antidepressant medications, particularly venlafaxine, was related to significant changes in depression severity, indicating that the administration of multiple forms of treatment is effective in enhancing the quality of life of this high-risk group. The Wilcoxon test showed significant changes in depression severity after treatment with venlafaxine and anticonvulsants ($p=0.048$).

More study is required to determine the possible outcomes of treating depression in epileptic teenagers in terms of frequency and quality of life or seizures. Furthermore, subsequent research should examine the role of risk factors such as comorbidities, adverse reactions to medication etc. and assess effectiveness of other types of antidepressants to determine the best therapy for these patients.

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