Neurology Asia 2013; 18 (Supplement 1) : 35 – 37

Psychiatric comorbidity in patients with epilepsy

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Abstract

People with epilepsy have a higher risk of developing psychiatric problems than the general population. The degree of affective symptoms such as depression and anxiety was affected by seizure control and epileptic syndromes. The higher degree of depression symptoms was more likely to elicit the suicidal ideation, psychosocial problems, adverse events of antiepileptic drugs, and poor quality of life. Antiepileptic drugs also provoke various psychiatric problems in people with epilepsy due to their specific action mechanisms on epilepsy. Carbamazepine, valproate, and lamotrigine can be used as a mood stabilizer, whereas phenobarbital, vigabatrin, topiramate, and levetiracetam may cautiously apply to PWE with psychiatric comorbidity.

INTRODUCTION

The comorbid psychiatric disorders in people with epilepsy (PWE) have been neglected for a long time. For this reason, there are few population-based studies evaluating the prevalence of psychiatric problems in PWE. Recently, a Canadian population-based study demonstrated a 17.4% lifetime prevalence of major depressive disorders (MDD) in PWE versus 10.7% in the general population.[1] Furthermore, it also manifested a 2.4 times higher prevalence of lifetime anxiety disorders and 2.2 times higher prevalence of suicidal thoughts in PWE versus the general population. The purpose of this article is to clarify the relationship between epilepsy and psychiatric problems and to suggest practical strategies for their identification by clinicians.

PATHOGENIC MECHANISMS SHARED BY DEPRESSION, ANXIETY, AND EPILEPSY

An abnormal secretion of serotonin (5-HT) in the central nervous system explains the common pathogenic mechanisms shared by depression, anxiety, and epilepsy. The role of 5-HT in human epilepsy has been identified with PET study. Reduced 5-HT_{1A} binding in mesial temporal structures ipsilateral to the seizure focus was demonstrated in people with temporal lobe epilepsy (TLE).[2] Moreover, an inverse correlation between increased severity of depression symptoms and 5-HT_{1A} receptor binding at the hippocampus ipsilateral to the seizure focus was found.[3] Serotonin's anxiolytic effects may be related to an inhibition of noradrenergic activation through raphe nuclei projections to the locus ceruleus. For example, a lower binding of 5-HT_{1A} in the anterior and posterior cingulated and raphe was manifested in patients with panic disorder, compared with controls.[4]

ARE PSYCHIATRIC COMORBIDITIES HIGHER IN A SPECIFIC EPILEPTIC SYNDROME?

In a Brazilian study, 248 patients with refractory TLE and 124 juvenile myoclonic epilepsy (JME) patients were reviewed and compared. There was a high prevalence of psychiatric disorders in both groups of epilepsy patients, present in 41% of TLE-mesial temporal sclerosis and in 47% of JME patients versus 6% of the general PWE.[5] I also studied PWE who were receiving antiepileptic drugs (AEDs) visiting my epilepsy clinic to evaluate the relationship between psychiatric symptoms and specific epilepsy syndromes. I did not find any higher degree of affective symptoms among different epileptic syndromes, whereas I found the degree of affective symptoms was significantly correlated with the unresponsiveness of AEDs. On the other hand, newly diagnosed TLE or JME patients demonstrated a higher degree of affective symptoms than those with other epileptic syndrome or healthy controls.

WHAT ARE THE IMPACT OF PSYCHIATRIC SYMPTOMS ON PWE?

When I studied 342 PWE received AEDs in my clinic, I found the frequency of depression, anxiety, and suicidal ideation in PWE to be significantly

Address correspondence to: Sung-Pa Park, *Department of Neurology, School of Medicine, Kyungpook National University, Daegu, Korea,* 700-422. Tel: +82-53-420-5769; Fax: +82-53-422-4265; e-mail: sppark@mail.knu.ac.kr

increased in people with uncontrolled epilepsy than those with well-controlled epilepsy. The higher degree of depression symptoms was more likely to elicit the suicidal ideation, which was also demonstrated in the study evaluating predictors of suicidal ideation in PWE living in Korea.[6] People who were unemployed, of lower income, did not have driving license, had felt stigma were associated with the presence of depression symptoms. People with depression or anxiety had a higher degree of adverse events of AEDs than those without depression or anxiety, which was evaluated by the Liverpool Adverse Event Profile questionnaires. All of these problems related to affective symptoms impaired the patient's quality of life (QOL). Depression or anxiety was more critical to determine QOL in PWE than seizure freedom, whereby the QOL of people with drug-refractory epilepsy without affective symptoms was significantly better than that of people with well-controlled epilepsy with affective symptoms.[7] Furthermore, depression symptoms are more important in determining QOL than adverse events of AEDs in well-controlled epilepsy.[8]

WHAT ABOUT THE IMPACT OF AEDS ON PSYCHIATRIC SYMPTOMS?

The use of AEDs is associated with several psychiatric problems due to the mechanisms of action underlying their antiepileptic activity. AEDs can be divided into two categories according to their psychotropic properties: i) sedating or GABA (γ-aminobutyric acid)ergic drugs and ii) activating or antiglutamatergic drugs.[9] This classification is straightforward, but can only partly explain the psychiatric adverse events of AEDs, which are also associated with indirect mechanisms due to their interaction with the underlying epileptic process. Carbamazepine, valproate, and lamotrigine can be used as a mood stabilizer, whereas phenobarbital, vigabatrin, topiramate, and levetiracetam may be cautiously given to PWE with psychiatric comorbidity.

HOW COULD CLINICIANS SCREEN PSYCHIATRIC PROBLEMS?

In a study of people with chronic epilepsy, 43% with a current MDD, 68% with a minor depressive disorder, and 38% with a history of a lifetime episode of MDDs were unrecognized and untreated.[10] In a busy clinical setting, clinicians frequently neglect to ask the psychiatric symptoms and it is hard to conduct time-consuming psychometric tests. Recently, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) was developed in the USA as a validated screening tool for depression in PWE that consists of a brief, 6-item questionnaire.[11] It takes less than 3 minutes to complete and a score of >15 is suggestive of a MDDs. To screen anxiety disorders, the Patient's Health Questionnaire-Generalized Anxiety Disorder–7 (GAD-7), which is a 7-item self-rating scale developed to screen for GAD, can be used.[12] It takes less than 3 minutes to complete and a score of >10 is suggestive of GAD.

CONCLUSIONS

PWE are more likely to have psychiatric problems than the general population. Since psychiatric symptoms are associated with poor seizure control, suicidal ideation, abnormal psychosocial states, adverse events of AEDs and impaired QOL, clinicians who deal with PWE should screen for psychiatric symptoms and treat them appropriately.

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