

Iatrogenic depression with Antiepileptic Drug Therapy in Patients with Partial Seizures

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Short Communication

Seizures are defined to be transient paroxysms of uncontrolled neuronal discharge leading to a clinical behavioral disorder.

Partial seizures, according to Browne and Holmes [1] are classified to simple (focal) and complex (temporal lobe or psychomotor) types. The focal type is characterized by motor, sensory and psychic symptoms. As it is focal, the symptoms depend on the location of the abnormal electrical discharge, however, the consciousness is not impaired. On the other hand, the complex type may begin without any warning or as focal type with impaired consciousness. It is also characterized by automatism and is followed by a period of confusion.

Gamma amino butyric acid (GABA) and glutamate play an important role in its pathogenesis. Impairment of the inhibitory effect of GABA occurs in different forms including: defective GABA_A receptor inhibition- Defective GABA_B receptor inhibition or defective intracellular Na⁺-Ca⁺⁺ exchange. Additionally, glutamate can increase the excitation via increased activation of NMDA receptors- increased synchrony between neurons via recurrent excitatory collaterals.

Generally, the antiepileptic drugs act either via GABA-mimetic action, or an inhibition of glutamate neurotransmission or an inhibition of T-type Ca⁺⁺ channels or an inhibition of Na⁺ channels

In partial seizures, we have first and second lines drugs acting via one or more of the above mechanisms of actions. They are:

First Line Drugs: Levetiracetam, Carbamazepine, Oxcarbazepine, Lamotrigine

Second Line Drugs: Lacosamide, Pregabalin

On the other hand, depression in children and adolescents with partial epilepsy is common. It worsen the quality of life in these epileptic patients even if they were well treated with the recommended line of therapy of these type of seizures. Several studies determined the neurobiological, social, and drug-induced (iatrogenic) factors that enhance the development of this depressive disorder and hence affect the response to the anti-epileptic treatment. A case report of a patient with partial epilepsy, secondary to a neonatal stroke, suffered from a depressive disorder when he received levetiracetam (LEV) as a treatment of the partial seizures [2-3]. The authors reported that there is a possible incidence of iatrogenic effect of LEV in the occurrence of depressed mood in this epileptic case. However, dose adjustment of LEV showed a marked reduction of the high incidence of depression comorbidity in pediatric epileptic patients.

So the dose adjustment and the frequent therapeutic drug monitoring of any selected drug from the two lines of therapy in partial seizure with depressed mood are mandatory to achieve both the efficacy and safety of these anti-epileptic drugs and to reduce the incidence of depression or the augmentation of the clinical severity of the disease in such patients.

If the patient is a woman in child bearing period, the physician selects either Oxcarbazepine or Levetiracetam. In elderly patient,

Levetiracetam is used. Again dose adjustment and close therapeutic drug monitoring are essential to be done in these special populations. The clinician should take care from carbamazepine, being an enzyme inducer, it would be used very cautiously with the co-administration of anti-depressant drugs. Dose adjustment is mandatory in such cases to avoid serious adverse effects.

Another case report in 2013 reported that levetiracetam (LEV) can induce serious psychiatric adverse effects including de novo psychosis, affective disorder, and aggression. LEV-induced suicidal behavior has been reported infrequently with a past history of affective disorders [4-7]. The authors report an apparent dose/concentration-dependent LEV-induced de novo major depression with near fatal suicide attempt in a patient without prior history of affective disorder. So these adverse effects necessitate a perfect psychiatric evaluation with a good estimation of benefit/risk effect of LEV on already existing affective disorders, impulsive-aggressive behaviors in patients with partial seizures. Assessment of risk factors for suicidal behaviors is indicated in patients with epilepsy and treated with LEV.

The main issue in treatment of partial seizures with depressed mood is to provide physician and patient counselling about this co-morbid diseases and the precautions in administration of the recommended anti-epileptic drugs regarding: proper diagnosis- therapeutic drug monitoring- preferable monotherapy of partial seizures using the appropriate drug to the clinical condition of the depressed patient- Small dose of co-administered SSRIs and long duration of administration together with the selected antiepileptic drugs- Gradual withdrawal and take care of special population esp. pregnant females.

Studies are now planned to explore in which degree these lines of drug therapy in this case of co-morbidity could enhance the potential therapeutic benefit in the drug therapy of depressed patients with partial seizures and how to avoid the occurrence of serious adverse effects by using the possible small therapeutic doses. The results will be very interesting since a future perspective in treatment of depression with partial seizures with minimum adverse effects or drug interactions could become reality.

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