

Chapter 15

Psychotic Symptoms of Epilepsy

CQ 15-1

What kinds of psychosis accompany epilepsy and what are their treatments?

Summary

- (1) The majority of psychoses associated with epilepsy are interictal psychoses including alternative psychosis and postictal psychosis.
- (2) For treatment of psychosis, use antipsychotic drugs according to symptoms as for schizophrenia, and if some antiepileptic drugs are suspected to be the cause, consider dose reduction and discontinuation.
- (3) After remission of psychotic symptoms, taper the antipsychotic agents carefully. In patients with a long duration of psychotic symptoms, taper gradually from 1–2 months after complete remission.
- (4) For postictal psychosis, administer benzodiazepine or a sedating antipsychotic drug to induce sleep during the lucid interval after seizure clustering or during the manic state just before emergence of psychotic symptoms.

Comment

- (1) Psychosis (psychotic disorder or psychiatric symptoms) is a state of obviously abnormal behaviors such as delusions, pronounced hallucinations with lack of insight, or disorganized languages, disorganized behavior, and catatonic behavior. In a meta-analysis¹, the frequency of psychosis associated with epilepsy was 5.6% (95% CI: 4.8–6.4%, odds ratio 7.8) among all patients with epilepsy, and 7% (95% CI: 4.9–9.1%) among patients with temporal lobe epilepsy. The frequency of interictal psychosis was 5.2% (95% CI: 3.3–7.2%) and that of postictal psychosis was 2% (95% CI: 1.2–2.8%). Preictal psychosis and ictal psychosis are rare.

Interictal psychosis² is delusional psychosis with strong emotional change, sometimes accompanied by first-rank symptoms typical of schizophrenia such as feeling of being manipulated, but unlike schizophrenia, emotions are preserved.

Alternative psychosis² is a subtype of interictal psychosis with various emotional symptoms and delusions occurring when seizures are controlled. The EEG often shows forced normalization (paradoxical normalization), but EEG examination is not a requisite for the diagnosis. Alternative psychosis sometimes occurs when seizures disappear following epilepsy surgery³.

Postictal psychosis² occurs after seizure clustering (rarely after a single seizure). After a lucid interval of 24 to 48 hours, visual hallucination, auditory hallucination, or delusion occurs within one week. Various hallucination-delusion states accompanied by emotional changes last from a few days to a few weeks (usually 1–2 weeks).

- (2) For the treatment of psychosis, antipsychotic agents are used as for schizophrenia⁴. Many antiepileptic drugs induce hepatic metabolic enzymes and attenuate the effects of antipsychotic agents. Therefore, high-dose antipsychotics may be needed⁵. If antiepileptic drugs are suspected to have induced psychotic symptoms, consider dose reduction and discontinuation of the antiepileptic drugs^{4,5}.
- (3) After remission of psychotic symptoms, reduce the doses of antipsychotic agents carefully. In patients with prolonged psychotic symptoms, reduce doses gradually from 1–2 months after complete remission⁵.
- (4) During the lucid interval after seizure clustering or during the manic state, administration of benzodiazepine or a sedating antipsychotic drug to induce sleep may prevent the postictal psychosis or mitigate psychotic symptoms⁴.

■ References

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- 2) Krishnamoorthy ES, Trimble MR, Blumer D. The classification of neuropsychiatric disorders in epilepsy: a proposal by the ILAE Commission on Psychobiology of Epilepsy. *Epilepsy Behav*. 2007; 10(3): 349-353.
- 3) González Mingot C, Gil Villar MP, Calvo Medel D, et al. Epileptic peri-ictal psychosis, a reversible cause of psychosis. *Neurologia*. 2013; 28(2): 81-87.
- 4) Matsuura M, Fujiwara T, Ikeda A, et al. Diagnosis and treatment guideline for psychotic complications of adult epilepsy. *Tenkan Kenkyu*. 2006; 24(2): 74-77 (in Japanese).
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■ Search formula and secondary reference sources

epilepsy [majr] AND mental disorders [majr] AND therapy [sh] Filters: Clinical Trial; Meta-Analysis; Multicenter Study; Randomized Controlled Trial; Publication

PubMed = 86

How to manage depression and suicide-related behaviors associated with epilepsy?

Summary

- (1) Treat epilepsy-associated depression with individualized psychotherapy and antidepressants.
- (2) The first-line antidepressants are new antidepressants such as SSRI and SNRI.
- (3) After recovery from the first episode of depression, carefully taper and discontinue antidepressant. After recovery from the second or subsequent depression episode, continue antidepressant even after recovery.
- (4) For patients with a history of depression, when tapering antiepileptic drugs which also have mood-stabilizing effect, carefully taper those drugs.
- (5) Antiepileptic drugs may increase suicide-related behaviors. Provide information to patients and their families regarding the negative psychotropic effects of antiepileptic drugs. Consult with experts in mental health for high risk patients.

Comment

- (1) In a meta-analysis of epilepsy and depression¹⁾, the overall prevalence of active (current or in the past year) depression was 23.1% (95% CI: 20.6–28.3%), with an odds ratio of 2.77 (95% CI: 2.09–3.67). The lifetime prevalence was 13.0% (95% CI: 5.1–33.1%) with an odds ratio of 2.20 (95% CI: 1.07–4.51).

Treatments include individualized supportive psychotherapy, psychoeducation, cognitive behavioral therapy (CBT), and antidepressants²⁾. According to systematic reviews^{3,4)}, antidepressants and CBT are effective. Especially, CBT tailored to individual patient is useful.

- (2) The first-line antidepressants are new antidepressant that are less likely to exacerbate seizures, such as a selective serotonin reuptake inhibitor (SSRI) and serotonin–noradrenaline reuptake inhibitor (SNRI). Start with a low dose to reduce adverse effects and increase until the therapeutic effect appears.

Among SSRIs, enzyme inhibitors such as fluvoxamine may increase serum concentrations of antiepileptic drugs.

When lithium carbonate is used in combination with antiepileptic drugs, adverse effects such as seizure exacerbation and neurotoxicity may occur. Pay special attention to encephalopathy when combined with carbamazepine.

- (3) For the first depression episode, continue antidepressants for around 6 months even after recovery. From the second or subsequent depression episode, continue antidepressants for around 2 years after recovery.
- (4) In patients with a history of mood disorder, carefully taper antiepileptic drugs with mood-stabilizing effect (carbamazepine, oxcarbazepine, valproate, and lamotrigine) when tapering those drugs.
- (5) Provide information to patients and families regarding the negative psychotropic effect of antiepileptic drugs. Especially, pay attention to suicidal ideation in patients with a history of mental disorders.

In patients with a history of suicidal ideation, avoid antiepileptic drugs that induce depression. In patients with a history of episodic behavioral disorders, pay attention to the manifestation of depression in association with a seizure-free state, and consult a mental health expert for patients at high risk of these symptoms²⁾.

A systematic review reported no sufficient evidence for a significant association between antiepileptic drugs and suicide-related behaviors⁵⁾. However, expert consensus from the ILEA Task Force on Therapeutic Strategies proposed the followings.⁶⁾ (1) Although some antiepileptic drugs may induce psychiatric symptoms and lead to suicidal tendency, its rate is very low and the actual suicidal risk is yet to be established. (2) Suicide in epilepsy is multifactorial. Even in patients with some suicide risk factors, treatment should not be withdrawn. (3) When starting or switching antiepileptic drugs, we (attending doctors) should tell patients to report any mode changes and suicidal ideation when they appear. (4) In clinical trials, information on psychiatric adverse effects caused by antiepileptic drugs should be collected, including family and past history of psychiatric disorders, past history of suicidal behaviors, and screening result using a suicide scale.

■ References

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- 2) Kerr MP, Mensah S, Besag F, et al. International consensus clinical practice statements for the treatment of neuropsychiatric conditions associated with epilepsy. *Epilepsia*. 2011; 52(11): 2133-2138.
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■ Search formula and secondary reference sources

epilepsy AND (mental disorders OR depression OR mood OR suicide) Cochrane = 303

epilepsy [majr] AND (depress* OR suicide) Filters: Clinical Trial; Meta-Analysis; Multicenter Study; Randomized Controlled Trial; Publication date from 2008/01/01 to 2015/12/31; English; Japanese

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