The first seizure: risk of recurrence and when to initiate treatment

Unprovoked seizures are defined as events occurring in the absence of an acute systemic or cerebral insult. They are distinct from acute symptomatic seizures, which are triggered by reversible conditions such as infections, electrolyte imbalances, or substance withdrawal, and in which recurrence can be considered a rare event.[1]

A first unprovoked seizure is a pivotal clinical event,[1,2] yet often surrounded by uncertainty regarding the risk of recurrence and the right moment for treatment initiation.[3] For healthcare professionals, timely and evidence-informed decision-making is essential for preventing further seizures, especially as unprovoked seizures may carry high risk of relapse which can lead to the diagnosis of epilepsy .[1] The International League Against Epilepsy (ILAE) classifies seizures by the location of onset in the brain and subcategorises them based on the presence of motor symptoms and loss of awareness.[2,4]

Recurrence risk after a first seizure

The likelihood of seizure recurrence after the first unprovoked event varies based on different clinical factors. Several studies and the American Academy of Neurology (AAN) guideline on management of an unprovoked first seizure in adults suggest that the highest overall risk of recurrence occurs within the first two years and ranges between 21% and 45% in the absence of major risk factors.[1,3,5]

However, certain diagnostic findings can increase this number beyond 60%. This meets the extended ILAE epilepsy definition “epilepsy can be diagnosed after a first unprovoked seizure, if the recurrence risk is estimated to be >60% over the course of 10 years”, which highlights an opportunity to consider initiating antiseizure medication (ASM) to these patients.[3,5-7]

Risk predictors of seizure relapse

Among the high-risk clinical variables, interictal epileptiform discharges (IEDs) (abnormal electrical waves that occur in the brain between seizures) on electroencephalography (EEG) stands out as one of the most consistently associated predictors of relapse.[1,5,7,8] The presence of IEDs may indicate recurrence probabilities as high as 77% in adults and 66% in children.9 Similarly, brain imaging evidencing remote brain injury or lesion, significantly increases the risk of a second unprovoked seizure.[1,5,7] A nocturnal seizure (experienced during sleep time) is also associated with higher risk of recurrence, with estimates reaching 75% within 2 years and 68.1% over 5 years.[1]

The patient's clinical history also plays an important role on risk recurrence. Some individuals may not remember or recognize previous events, but they have been related to a higher likelihood of experiencing further seizures.[1] Conversely, a positive family seizure history, seizure type, age or sex have not been fully correlated with higher risk of relapse.[1,5]

Benefits and limitations of early antiseizure treatment

The decision to start ASM after a first seizure depends on whether the anticipated benefits of ASM administration outweighs the risks and should be done based on patient's risk of relapse. Immediate ASM initiation has shown an absolute reduction in seizure recurrence of 35% in the short-term (2-year) prognosis, but had no impact on quality of life.[5] Both adult and elderly patients have reduced the risk of recurrence with this measure.[1,10] However, evidence suggests that early ASM administration does not alter long-term outcomes in terms of seizure remission beyond three years.[2,5]

Guideline-based decision-making

Considering these findings, current guidelines recommend an individualized approach.[5,7] Treatment is generally advised when the recurrence risk exceeds 60% (based on the high-risk factors previously mentioned), but when the risk is lower, shared decision-making becomes vital. The decision to prescribe antiseizure medication (ASMs) after a first-time seizure should be guided by the risk of recurrence based on clinical history and comprehensive work-up including electroencephalography and magnetic resonance imaging. Patients should be informed about the short-term/long-term evidence, the potential ASM administration side effects (affecting 7-31% of patients, most of them mild) and how the pathology and medication may impact their daily life.[5,7]

The management of a patient after a first unprovoked seizure is about balancing risk, evidence, and patient preferences. Prompt evaluation and a nuanced discussion of risks and benefits are key to define the first steps after this potentially life-changing event.

References

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