



Prognosis of Epilepsies and Epileptic Syndromes in Children: A Narrative Review

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ABSTRACT

Epilepsies and epileptic syndromes are among the most common chronic neurological disorders in neonates, infants, and children. Remission occurs in 70% of epileptic children, while other cases experience frequent seizures and become refractory to various treatment modalities. Refractory seizures have a significant adverse impact on the quality of life of epileptic children and their families. Prognosis of epilepsies is determined based on the risk of seizure or convulsion recurrence. Some of the most important risk factors for recurrence are the age at seizure presentation, neurodevelopment of the child, etiology of seizures, seizure frequency before anticonvulsant withdrawal, response to antiepileptic medications, type of epileptic syndromes, and electroencephalography of the patient. Recognition of the risk factors for seizure recurrence results in the optimal management of the treatment protocols, thereby reducing the adverse effects of epileptic seizures on patients and their families. The present study aimed to provide a narrative review of the most important risk factors for the recurrence of epilepsies in children by two child neurologists.

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Introduction

Epilepsies and epileptic syndromes are among the most common neurological disorders in children (1), which may occur since birth and continue throughout life. Fortunately, 70% of these disorders are responsive to conventional anticonvulsive medications, whereas 25-30% of epilepsies are irresponsive to various treatment modalities and have a significant adverse impact on the quality of life of epileptic children and their families (2).

Prognosis of epilepsies and epileptic syndromes is determined based on the risk of seizure or convulsion recurrence, as well as the risk of sudden death (3). The most important aim of seizure treatment is the prevention of seizure recurrence; as such, recognition of the risk factors for the recurrence and impact of epileptic seizures results in the optimal management of the treatment pro-

ocols, thereby improving the quality of life of patients.

Previous studies have extensively explored the important risk factors for seizure recurrence, some of which include the etiology of seizures, age at seizure presentation, initial response to appropriate anticonvulsive agents, neurodevelopment of the child, epileptic syndromes, electroencephalography (EEG) of the patient, and frequency of seizures before anticonvulsive medication withdrawal (4-8).

The present study aimed to provide a narrative review of the risk factors for the recurrence of epileptic seizures using an age-based approach and discuss the most important risk factors in various age groups in children from birth until adolescence.

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Literature Review

The literature search was performed by two child neurologists in order to determine the main prognostic factors in epileptic children. The objective of the research was to provide a narrative review, and the most relevant articles were identified in relation to the subject matter of the study. It should be noted that this was not a systematic review or meta-analysis, and our target audience are the general adult neurologists and child neurologists who are familiar with this issue.

Neonatal period

Seizures are the most prevalent neurological disorders in neonates. The brain of term and preterm neonates is highly susceptible to various insults and seizures, which are considered to be the most common cerebral manifestations in this age group (9-12). Etiologies of seizures are the main risk factors for seizure recurrence in term and preterm neonates, which vary greatly in different cases, including etiologies with excellent prognosis (e.g., hypocalcemia and hypoglycemia) and etiologies with poor prognosis (e.g., early infantile epileptic encephalopathy with burst-suppression, also known as the Ohtahara syndrome) (13-18).

Hypocalcemia and hypoglycemia are highly common in neonates, especially those with diabetic mothers. These etiologies have excellent prognosis, and no further anticonvulsive prophylaxis is needed after the treatment of hypocalcemia and hypoglycemia. Unfortunately, prolonged neonatal hypoglycemia may lead to severe insults to the brain, resulting in irresponsive seizures in neonates. Moreover, severe hypoglycemia is associated with refractory seizures in neonates and infants (11).

Structural brain disorders in neonates are among the important causes of seizures. Seizures in neonates with structural brain disorders, such as pachygyria and lissencephaly, are irresponsive to anticonvulsive agents and require long-term prophylactic treatments after seizure control only if they are successfully overcome by conventional anticonvulsive medications. Many neonates with complex structural brain disorders require other seizure-controlling modalities, such as a ketogenic diet. In addition, these neonates often have low life expectancy, and many of them die during infancy due to other complications, such as frequent pneumonia (11,12).

Epileptic syndromes with excellent and poor prognosis are prevalent conditions in neonates. Some of the epileptic syndromes with the poorest prognosis include the Ohtahara syndrome and early myoclonic encephalopathy. These syndromes present with short tonic spasms and myoclonic seizures, which are normally irresponsive

to anticonvulsive medications, even the adrenocorticotrophic hormone. Neonates with these syndromes have poor neurological development, and those who survive develop other refractory epileptic syndromes, such as West syndrome (13, 19-24).

Epileptic syndromes with excellent prognosis include benign familial and benign idiopathic neonatal seizures. The mothers of these neonates have been shown to have an unremarkable pregnancy and delivery. Neonates with these syndromes develop various seizure types, especially focal clonic and tonic seizures, and have normal EEG developmental indicators. Furthermore, their seizures respond well to anticonvulsant medications. Despite the excellent long-term prognosis, a small number of these neonates develop seizures during infancy and childhood (25-28).

Other etiologies have been reported in the neonatal period with variable impacts on the prognosis of epilepsies and seizures. Hypoxic-ischemic encephalopathy (HIE) is one of the main etiologies in this regard, which could be mild, moderate or severe. Neonates with mild and moderate HIE have a relatively good prognosis, while those with severe HIE develop severe cerebral palsy and refractory seizures (9-12,29).

Neonatal sepsis and meningitis are among the etiologies for epilepsies in children. According to the child neurology and epilepsy literature, neonatal meningitis is a remote symptomatic etiology. In other words, these neonates are at the risk of developing epilepsies in the future, while the prognosis depends on the extent of their brain damage (9-12,29).

Pyridoxine deficiency and pyridoxine decency are other etiologies for epilepsy and epileptic spasms in neonates. These neonates experience severe seizures (e.g., epileptic spasms) since birth through infancy. With early diagnosis and treatment with high doses of pyridoxine, these neonates could often have normal development. Although the prognosis for epilepsy might be acceptable in such cases, poor prognosis is likely in the neonates that do not receive treatment; therefore, early diagnosis is of paramount importance in this regard (9-12,29).

Infancy

The risk factors for seizure recurrence in infancy are very similar to those of the neonatal period and should be addressed as such in the case of the infants with seizures. Infancy is typically associated with the development of specific epileptic syndromes, the most important of which are febrile seizures and febrile convulsions (29,30).

Febrile convulsions are the most frequent seizures with excellent prognosis in children. The

clinical course of febrile convulsions has been extensively studied, and many experts believe that these seizures are benign without the need for prolonged prophylaxis (31-34). Nevertheless, it should be noted that various epileptic syndromes with excellent and poor prognosis (e.g., Dravet syndrome) could begin as febrile seizures. Therefore, febrile seizures, particularly the prolonged types, which persist for more than 15 minutes before discontinuation require special attention (35,36).

Syndromic approach is the most effective method in the treatment of the infants and children with seizures and epilepsies. In this approach, factors such as seizure semiology, seizure etiology, and EEG of an epileptic syndrome could be diagnosed based on the age of the patients. Many epileptic syndromes have a predefined clinical course and prognosis. In the syndromic approach, the clinician could recognize the clinical course required for the patient and develop the most effective care plan accordingly (37-41).

Epileptic spasms (West syndrome) are one of the most important epileptic syndromes with poor prognosis. This syndrome is characterized by epileptic spasms, developmental regression or retardation, and an interictal EEG of hypsarrhythmia. West syndrome is irresponsive to many conventional anticonvulsive agents, and in the majority of infants, it is refractory to even three appropriately selected anticonvulsive medications. Many infants with the West syndrome need a ketogenic diet for seizure control and develop poorly nonetheless. Furthermore, they may become autistic even after seizure control. Unfortunately, many infants with the West syndrome develop another refractory epileptic syndrome after infancy, manifesting the characteristics of seizures such as the Lennox-Gastaut syndrome (42-46).

Poor prognosis is not reported in all the epileptic syndromes of infancy. For instance, benign myoclonic epilepsy in infants is an epileptic syndrome characterized by frequent myoclonic jerks during infancy and generalized multiple spikes in the EEG. These infants develop normally and have an excellent response to valproate therapy (40,41).

Childhood

Similar to infancy, epileptic syndromes with poor and excellent prognosis have been described in childhood. For instance, Rolandic epilepsy or benign partial epilepsy of childhood is one of the main syndromes with excellent prognosis, which starts in this age group (40,41). This syndrome is characterized by the focal seizures of the lips (especially during sleep), normal development, and EEG features with centrottemporal spikes (Rolandic spikes). Many experts believe that these sei-

zures do not require treatment, and many children with Rolandic epilepsy have no frequent seizures, with remission occurring even without treatment (47-49).

On the other hand, a subgroup of the children with Rolandic epilepsy has been shown to develop cognitive decline during the course of epilepsy. Moreover, these children have continuous spike and wave during slow wave sleep (CSWS) in sleep EEG. Unfortunately, these patients have a poor prognosis, while a high suspicion index and early treatment with appropriate agents could improve the outcome (50).

Lennox-Gastaut syndrome has been shown to develop during childhood and have a poor prognosis, while it is irresponsive to anticonvulsive medications as well. This syndrome is associated with multiple seizure types (e.g., atypical absences, focal seizures, sleep tonic seizure, and atonic seizures), EEG features, and developmental delay. Many of the children with the Lennox-Gastaut syndrome develop poorly and may become debilitated. In addition, the prognosis of this syndrome for seizure remission is extremely poor (42,43,45).

Adolescence

Juvenile absence epilepsy and juvenile myoclonic epilepsy are the main epileptic syndromes in adolescence with excellent prognosis. Adolescents with these syndromes develop normally, have an acceptable response to appropriately selected anticonvulsive medications, and have acceptable cognitive abilities after seizure control. In juvenile absence epilepsy, anticonvulsive medication withdrawal could be successful, while in juvenile myoclonic epilepsy, patients need lifelong treatment for seizure remission. Unfortunately, a number of the patients with juvenile myoclonic epilepsy develop CSWS and require special treatment.

Other Aspects of Prognosis

In addition to considering epileptic syndromes in the case of young patients, there are other important aspects to be addressed with regard to the risk of seizure recurrence. Some of these aspects are briefly discussed in the following section.

Age at Seizure Presentation

According to the literature, the onset of seizures during adolescence adversely affects prognosis, and these patients are at a high risk of relapses after drug withdrawal (51,52).

Idiopathic and Symptomatic Epilepsies

Children with idiopathic epilepsies have excellent prognosis compared to those with lesional epilepsies and developmental delay (53).

Seizure Type

Some studies have indicated that focal seizures have poor prognosis, while other studies have proposed variable results, showing that generalized seizures have poor prognosis. (54,55). However, almost all the studies in this regard have demonstrated that patients with multiple seizure types often have poor prognosis (56,57).

Response to Anticonvulsants (AEDs)

According to the literature, children with a cluster of seizures after anticonvulsant initiation and those with continuous weekly seizures during the first year of treatment tend to have poor prognosis (58).

Early and Delayed Treatment

Many clinicians believe that early treatment could improve the prognosis of epilepsies, while a study in this regard has denoted that early treatment versus treatment only after a further seizure has a comparable impact on the long-term prognosis of patients (59).

EEG and Seizure Recurrence after AED Withdrawal

A study in this regard investigated the effects of EEG before drug withdrawal in the children with epilepsy. According to the findings, normal EEG without epileptiform discharges is an excellent prognostic factor before medication withdrawal, while the presence of irregular generalized spike waves is considered to be a poor prognostic factor. Relapse rate in the children with normal EEG before withdrawal was reported to be 33%, while it was 67% in the children with abnormal EEG containing irregular generalized spike waves (60).

Prognosis after Epilepsy Surgery

According to previous studies, more than 60% of the epileptic patients who were appropriately selected for surgery became seizure-free after surgery, and their quality of life improved significantly as well (61-63).

Conclusion

According to the results, the prognosis of epilepsies and seizure recurrence in children depend on numerous factors. Some of the most important risk factors in this regard include the etiology of the seizures, neurodevelopment of the patient, and epileptic syndromes. Recognition of the risk factors for seizure recurrence could result in the optimal management of the treatment plan in epileptic patients.

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Conflict of Interest

The authors declare no conflict of interest.

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