



## Examining the etiology and types of neonatal seizure (A review)

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### Abstract

**Introduction:** There are five main types of neonatal seizures: minor subunit seizures, clonic seizures, tonic seizures, spasms, focal clonic or tonic seizures, and myoclonic seizures associated with aligotr graphic disorder (epileptic seizures). While kinetic automatism, septic seizures, clonic tonic and multifocal myoclonic seizures are not usually associated with EEG discharges, therefore, these seizures are considered to be more indicative of the phenomenon of release; these disorders are abnormal movements caused by brain damage rather than actual epileptic seizures.

**Methods:** Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus and Google scholar) and national (SID, Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned.

**Discussion:** With a frequency of 50-60%, hypoxic ischemic encephalopathy is the most common cause of neonatal seizures. Seizures resulting from this encephalopathy occur within the first 12 hours of birth. vascular events include intracranial and ischemic hemorrhage, accounting for 10 to 20 percent of cases of seizure. Bacterial and non-bacterial infections account for 5 to 10% of cases of neonatal seizures and Brain malformations cause 5 to 10 percent of cases of neonatal seizures.

**Keywords:** etiology, seizures, neonatal seizure

### Introduction

There are five main types of neonatal seizures: minor subunit seizures, clonic seizures, tonic seizures, spasms, focal clonic or tonic seizures, and myoclonic seizures associated with aligotr graphic disorder (epileptic seizures)<sup>[1]</sup>. While kinetic automatism, septic seizures, clonic tonic and multifocal myoclonic seizures are not usually associated with EEG discharges, therefore, these seizures are considered to be more indicative of the phenomenon of release; these disorders are abnormal movements caused by brain damage rather than actual epileptic seizures<sup>[2,3]</sup>.

### Methods

#### Search strategy

Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus and Google scholar) and national (SID, Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. The specific search strategies were created by a Health Sciences Librarian with expertise in systematic review search using the MESH terms and free terms according to the PRESS standard. After the MEDLINE strategy was finalized, it was adapted to search in other databases. Accordingly, PROSPERO was searched for ongoing or recently related completed systematic reviews. The key words used in the search strategy were "etiology, seizures, neonatal seizure" and Iran which were combined with Boolean operators including AND, OR, and NOT.

### Study selection

Results of the Literature review were exported to Endnote. Prior to the formal screening process, a calibration exercise was undertaken to pilot and refine the screening. Formal screening process of titles and abstracts were conducted by two researchers according to the eligibility criteria, and consensus method was used for solving controversies among the two researchers. The full text was obtained for all titles that met the inclusion criteria. Additional information was retrieved from the study authors in order to resolve queries regarding the eligibility criteria. The reasons for the exclusion criteria were recorded. Neither of the review authors was blinded to the journal titles, the study authors or institutions.

### Discussion

#### Subtle seizures

Subtle seizures include perianal disturbances, nystagmus, blinking, oral movements, abnormal movements of the organs (movements like weeping, swimming, biking, walking and walking), heart rate changes, high blood pressure and mirror attacks. Subtle seizures are more common in preterm infants than term neonates<sup>[4]</sup>.

#### Clonic seizures

Clonic seizures can be focal or multifocal. Multifocal clonic seizures affect various parts of the body and have displacing nature. This displacement follows a non-Jacksonian process. For example, the contraction of the left arm can be accompanied by a right leg contraction. Clonic seizures that are two-sided, symmetrical, and synchronous are not common

in infancy, as the connections between neurons and demyelization are not complete at this age<sup>[5]</sup>.

### **Tonic seizures**

Tonic seizures can be focal or generalized (more commonly). Focal tonic seizures include a change in the condition of an organ or a change in the position of the trunk or neck in an unconventional form, often accompanied by continuous horizontal deviation of the eyes. Tonic generalized seizures include bilateral tonic enhancement or upper limb tonic flexion, often with tonic enhancement of the lower limbs<sup>[6]</sup>.

### **Spasms**

Spasms are sudden cranial contractions lasting 1-2 seconds; these disorders are differentiated from generalized tonic attacks through their shorter duration and the fact that spasms are usually present in an EEG with a single, very minor general discharge.<sup>[7]</sup>

### **Myoclonic seizures**

Myoclonic seizures are divided into focal, multifocal, and generic types. Myoclonic seizures can be distinguished from clonic seizures through fast contractions (less than 50 milliseconds) and lack of rhythmic seizures. Focal myoclonic seizures specifically affect the flexor muscles of the upper extremities and sometimes with seizure activity in the EEG. Multifocal myoclonic movements include asymmetrical contractions of various parts of the body which are not usually associated with seizure discharge in the EEG. Generalized myoclonic seizures are bilateral contractions with upper limb, and sometimes lower limbs, flexion. These types of myoclonic seizures are associated with EEG disorders more than other forms<sup>[8,9]</sup>.

### **Seizure versus jitteriness**

Jitteriness is considered as a quick motor activity like a tremor or chill that stops with bending or holding the limb. But seizure generally does not stop by touching or moving. Unlike most seizures, jitteriness is usually caused by an actuator. Seizures are often associated with deviation of the eye and autoimmune changes, as opposed to jitteriness<sup>[10]</sup>.

### **Etiology of seizures during infancy**

With a frequency of 50-60%, hypoxic ischemic encephalopathy is the most common cause of neonatal seizures. Seizures resulting from this encephalopathy occur within the first 12 hours of birth<sup>[11]</sup>.

### **Vascular events**

These events include intracranial and ischemic hemorrhage, accounting for 10 to 20 percent of cases of seizure. Three types of bleeding can be identified: primary hemorrhagic hemorrhage, hemorrhage of the germinal-intrauterine matrix and subdural bleeding. Patients with arterial stroke or venous sinus thrombosis can manifest symptoms of seizures and the only way to diagnose these two is through imaging. If MR or CT is not requested, venous thrombosis is quite difficult to detect<sup>[12]</sup>.

### **Intracranial infections**

Bacterial and non-bacterial infections, including bacterial

meningitis, torch infections (toxoplasmosis, other infections, tuberculosis, cytomegalovirus, herpes simplex virus), especially herpes simplex encephalitis, account for 5 to 10% of cases of neonatal seizures,<sup>[13]</sup>.

### **Brain malformations**

Brain malformations cause 5 to 10 percent of cases of neonatal seizures. An example of this is the icidoid syndrome with corpus callosum and severe seizures involving spasticity of the infancy, with epigastric arthritis in the EEG, which is sometimes unilateral at the beginning<sup>[14]</sup>.

### **Metabolic disorders**

These disorders include glucose disorders, magnesium calcium, other electrolytes, amino acids or organic acids, as well as pyridoxine dependence. Hypoglycemia can cause neurological disorders and is very common in low birth weight infants and infants with diabetic or pre-diabetic mothers. The duration of hypoglycemia is quite critical in determining neurological symptoms. Hypoglycemia occurs in two different ages, the first one being 2-3 days after birth, mostly occurring in low birth weight infants; the second peak is more likely to occur later in the infant, and often involves large and infected babies whose milk contains an inappropriate ratio of phosphorus to calcium and phosphorus to magnesium. Hypomagnesium is often accompanied by hypoglycemia. Hyponatremia can cause seizures and is often secondary to the secretion of anti-urogenital hormone<sup>[15]</sup>.

Seizures caused by topical anesthetic poisoning can occur due to neonatal poisoning with topical anesthetic injected into the head of the baby. Neonatal seizures can also be caused by disorders of amino acid metabolism or allergic arthritis. These disorders are usually associated with acidosis or hyperammonia. However, even in the absence of these findings, if it is not possible to determine the cause of seizure quickly, a complete metabolic examination is required to rule out metabolic causes; the mentioned clinical examination includes serum amino acids, acele carnitine, lactate, pyrovalate and ammonia serum, long fatty acids (in terms of infantile adrenal coronary syndrome and zalogroup syndrome, organoleptic evaluation of acids, alpha-amino-adipic acid, aldehyde and sulfosysteine, and CSF examination in terms of glucose, the cellular protein is amino acids, pyruvate, alpha-adipic acid, aldehyde, pyridoxal phosphate MTHF-5 (5-methyltetrahydrofolate), succinyl adenosine, and neurotransmitter metabolites in CSF. The reasons for such an action is that many congenital metabolic disorders, including non-ketotic hyperglycimini, might manifest themselves as neonatal seizures (it's often mistaken for hiccups that are also seen in these patients at first) and only by doing these a clear and definite differentiation is possible. For example, the definitive diagnosis of non-ketotic hyperglycimini requires a measure of the proportion of CSF to Glycine plasma<sup>[16]</sup>.

Extreme dependence on pyridoxine and pyridoxal can cause severe seizures. These seizures, which are often multifocal clonic ones, usually occur during the first hours of life. If treatment is delayed, mental retardation is a very probable consequence<sup>[17]</sup>.

### **Sudden discontinuation of the medication**

Sudden discontinuation of medication causes seizures in those

infants who are born with cesarean section. These drugs include narcotic painkillers, sedative-hypnotizers, and other medications. Seizures caused by drug discontinuation appear in the first 3 days of life <sup>[18]</sup>.

### Neonatal seizure syndromes

Neonatal seizure syndromes include benign idiopathic seizures of the infant (fifth day attacks), which are usually focal seizures that start around the fifth day of life. EEGs occur between specific attacks on the Tetapointalentrantatus (thighs with Sharp 4 to 7 waves); in addition to multi-focal electrographic seizures, EEG suggest that patients have a good response to drugs and have good prognosis. Benign familial seizures of the neonatal autosomal dominate at 2 to 4 days and usually resolve within 2 to 15 weeks. Seizures are a distortion of the eye, clonic contractions, tonic status, clonic contractions, and sometimes motor automata. EEGs are usually normal between attacks. These seizures have been shown to be due to mutations in the KCNQ2 and KCNQ3 genes. Approximately 16% of patients will develop epilepsy later.

Early myoclonic encephalopathy and early epileptic seizure encephalopathy (Atahara syndrome) <sup>[19]</sup>.

### Other situations

Other situations include benign neonatal myoclonus during sleep and hyperplasia, which is a non-epileptic situation.

Clinically, it is often determined that either these movements are symptoms of seizure or the phenomenon of release is quite difficult to conduct; however, it is caused by incitement and disintegration, with or without altering the condition of the limb that suggests that it is not seizure. It is important to remember that epileptic seizures can also be triggered. Therefore, continuous monitoring of EEG in the patient's bedside helps to differentiate such uncontrollable motions, especially in infants with a history of neurological damage. Accordingly, such monitoring is considered a standard of care in many neonatal care centers (18).

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