Neonatal seizure and short-term outcomes in hospitalized neonates

Original Article

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Abstract

Background: Neonatal seizure is a common problem and associated with a great mortality rate, high risk of chronic neurodevelopmental impairments, also difficult to diagnosis and treatment. The aim of this study was to determine the neurodevelopmental outcome, clinical presentation and etiology of seizures in neonates admitted to Amirkola Children's Hospital (ACH).

Methods: In this cross-sectional study, 42 neonates with the initial diagnosis of seizure, aged less than 28 days, hospitalized in ACH, northern Iran, from April to September 2016 were selected using convenient sampling method. The patients' information was gathered during hospitalization period and 6 months after discharge. Data were analyzed using SPSS 22 through descriptive and chi-square tests.

Results: Among preterm and term neonates with seizures, the main diagnosis in neonates with seizures was idiopathic (38.1%) and hypoxic-ischemic encephalopathy (HIE) (14.3%), hypoglycemia (9.5 %) hypomagnesaemia (7.1%) and opiate withdrawal (4.8%). Twenty-three neonates underwent brain computed tomography (CT) scan and 6 (14.3%) of them had abnormal brain imaging. Seizure control with antiepileptics (P=0.006), metabolic disturbance (P=0.002) and time of drug discontinuation (P<0.001) were significantly associated with adverse neurodevelopmental outcome.

Conclusions: Since idiopathic encephalopathy and HIE were the most common cause of neonatal seizures, it should be attempted to improve care during delivery.

Keywords: Neurodevelopmental outcome, Newborn, Seizures

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Introduction

Seizures as the most common symptom of neurological dysfunction in neonates occur at the first month of life (a time of increased risk) [1, 2]. Seizures are known as paroxysmal brain disorders and presented as behavioral and autonomic activity as well as abnormal motor [3]. The incidence of seizures is about 1 to 3.5 per 1000 live births in neonatal period [4], but its incidence in neonatal intensive care unit (NICU) is as high as 10-25%, where 15% ones die and 35-40% of them have prominent neurological disability [3]. Four recognizable clinical seizure types such as myoclonic, subtle, tonic and clonic are recognized and each of them can be multifocal, focal and generalized [5]. Hypoxic-ischemic encephalopathy (HIE) is the most common cause (50%) of neonatal seizures [5]. HIE is referred to any brain injury influenced by the blood flow to the brain and mixture of inadequate oxygen delivery [6], and to a neonate born with abnormal neurologic function consisting muscle tone, level of consciousness and reflexes [7].

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Other causes comprise central nervous system (CNS) malformations, intracranial hemorrhage, birth trauma, intracranial infections, drug withdrawal, metabolic disorders and less frequent metabolic disorder like inborn error of metabolism (IEM) [6, 8]. The common metabolic disorders were hypomagnesaemia (Mg<1.2 mg/dL), hypernatremia (Na>145-150 mg/dL), hyponatremia (Na<120 mg/dL), hypocalcemia (Ca<7.5-8 mg/dL) and hypoglycemia (glucose level<35-40 mg/dL) [9]. Prolong nothing per oral (NPO) or fasting may lead to metabolic abnormalities. Exact mechanism of fits is not known in hypomagnesaemia, hypoglycemia and hypocalcemia [6, 10]. Proper fluid and electrolyte management can decrease these abnormalities of metabolic disturbance and consequently, the occurrence of seizures can be declined [6].

Neonatal seizure is an emergency, and its early diagnosis and therapy are necessary because any delayed treatment modality results in a long-term disability and unfortunate neurological outcome [3]. Recent studies on animal model indicated that the neonate's CNS, to some extent, could be resistant to long-lasting seizures whereas the frequent short-term seizures could have long-term disability and detrimental effect in these patients [11, 12].

This study was conducted to determine the etiology, clinical type and outcome of seizures in male and female neonates with seizures, hospitalized in NICU.

Methods

This prospective, descriptive and cross-sectional study was performed at the NICU of Amirkola Children's Hospital (ACH) affiliated to Babol University of Medical Sciences, Northern Iran, from April to September 2016. A total of 42 male and female neonates with seizures admitted in NICU through pediatrics emergency room were enrolled in the current study using census sampling method. In addition, all referred neonates from other hospital were included the present study based on inclusion criteria. An informed written consent form was obtained from their parents/attendants.

Data including duration and type of seizures, age of the neonates, maternal drug intake during pregnancy, antenatal history of intrauterine infection and maternal disorders were collected from referring to hospital records. Moreover, the delivery specifics included duration of labor, place of delivery, Apgar score <3 at 1 and 5 minutes of age, mode of delivery and history of resuscitation. Family history of neonatal fits, transfusion, jaundice and deaths was recorded. The feeding history was obtained.

First line investigations including serum sodium, urea/creatinine, magnesium and calcium, blood sugar, complete blood count (CBC) with peripheral smear, cerebrospinal fluid (CSF) for any evidence of infection, hepatic function tests, electroencephalogram (EEG) and cranial ultrasound were done for all of them. Moreover, screening for inborn error of metabolism, blood culture, TORCH antibody titer, computed tomography (CT) scan, reticulocyte count, Coombs test and urine for reducing substances were performed. All mentioned work-ups were conducted on selected cases guided by examination, history and primary work-ups to reach the final diagnosis. Follow-up was done every 3 months by a pediatric neurologist up to six months after discharge from hospital based on Denver Developmental Screening Tests (DDST).

The data were analyzed using SPSS 22. Descriptive and analytical (Chi-square test) statistics were used for proper parameters.

Results

During 6-month period, 42 patients (48% females, 52% males) with presentation of seizure were admitted to ACH. Their average age and gestational age was 3±1.50 days and 40 weeks, respectively. Among them, 28 (66.7%) and 35 (83.3%) neonates had normal electrolyte balance and metabolic profile, respectively.

Fifteen (35.7%) neonates had abnormal neurologic deficit which was highly correlated with inborn error of metabolism as a cause of seizure. The most common neurologic finding was swallowing problem (9 neonates=21.4%).

Sixteen (38.1%) and 6 neonates had idiopathic seizure and HIE (the cause of seizure), respectively. Among 42 neonates with seizure, 28 and 14 ones were controlled with one antiepileptic drug and two antiepileptic drugs, respectively. Totally, 27 and 15 neonates had normal and abnormal growth rate, respectively. Regarding timing of drug discontinuation, 10 (23.8%) patients discontinued antiepileptic drug

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before discharge and 20 (47.6%) ones continued 3-month treatment after discharge. No relapse was reported after antiepileptic treatment discontinuation (table 1).

Twenty-three neonates underwent brain CT scan and 6 (14.3%) of them had abnormal brain imaging. One neonate based on sonographic findings had grade 2 intraventricular hemorrhage. Regarding EEG and venous blood gas (VBG), 6 (14.3%) and 7 (16.7%) newborns had abnormal results, respectively (table 2).

All four patients with transient hypoglycemia had normal neurodevelopment. Among 3 patients with maple syrup disorder, only one had normal development (table 3).

There was no significant correlation between electrolyte imbalance and neonatal development (P=0.23). During discharge, antiepileptics were discontinued in 23.8% of neonates and continued in 47.6% till 3 months later at follow-up visit.

Table 1: Prevalence of seizure etiology in hospitalized neonates

Etiology of Seizure	Frequency	Percentage
Idiopathic	16	38.1
HIE	6	14.3
Transient Hypoglycemia	4	9.5
Hypomagnesaemia	3	7.1
Maple syrup disease	3	7.1
Hypocalcemia	2	4.8
Opiate withdrawal	2	4.8
Infection	1	2.4
Intraventricular Hemorrhage	1	2.4
Congenital metabolic disorders	1	2.4
Methylmalonic Acidemia	1	2.4
Hyperglycinemia	1	2.4
Toxicity	1	2.4

Table 2: Relationship between seizure outcome and different diagnostic tools

Cause of Seizure	Normal development (N=27)	Abnormal development (N=15)	P-value
Sonographic findings			
Normal	25(64.1)	14(35.9)	0.99
Abnormal	1(50)	1(50)	
Grade 2 IVH	1(100)	-	
Brain CT scan			
Not requested	17(89.5)	2(10.5)	<0.0001
Normal	9(60)	6(40)	
Abnormal	-	6(100)	
unstable	-	1(100)	
Not Consent	1(100)	-	
EEG			
Normal	20(6.5)	11(35.5)	0.61
Abnormal	4(66.7)	2(33.3)	
Unstable	1(33.3)	2(66.7)	
Not Consent	2(100)	-	
VBG			
Normal	23(56.7)	12(34.3)	0.68
Abnormal	4(57.1)	3(42.9)	

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Table 3: Relationship between seizure outcome and etiological factors

Cause of Seizure	Normal development (N=27)	Abnormal development (N=15)	P-value
HIE	2 (33.3%)	4 (66.7%)	0.04
Infection	-	1 (100%)	
IVH	1 (100%)	-	
Hypoglycemia	4 (100%)	-	
Urea cycle defect	-	1 (100%)	
Idiopathic	11 (68.8%)	5 (31.3%)	
Opiate withdrawal	2 (100%)	-	
PKU	-	1 (100%)	
Methylmalonic acidemia	-	1 (100%)	
Hyperglycemia	-	1 (100%)	
Hypocalcemia	3 (100%)	-	
Hypomagnesemia	2 (100%)	-	
Maple syrup disease	1 (33.3%)	2 (66.7%)	

Discussion:

Among the etiological factors, the idiopathic was the most common finding and HIE (14.3%) was the second common cause. This finding is comparable to several studies [10, 13, 14].

In the present study, there were infections in 24.5% of cases. Two studies also reported the infections in 28.2% and 28.7% of neonates, respectively [15, 3], which are similar to our finding. However, a study by Legido et al. showed that 17.2% of neonates had infections so that this difference could be due to the high incidence of infection in our culture.

In the current study, the intracranial hemorrhage was observed only in one neonate, which was lower than that in several studies [3, 16, 17, 18] and this difference could be because of lower rate of preterm neonates in our investigation. To our best knowledge, the intracranial hemorrhage occurs more frequently in preterm than term neonates.

The most common metabolic disturbance was hypoglycemia, which is concordant with the observations of Fiaz et al. [3]. In the current study, 15 neonates developed abnormal neurologic deficit which was highly correlated with inborn error of metabolism as a cause of seizure. The most common neurologic finding was swallowing problem. In the present and other studies, the most common etiology of seizure was idiopathic and the same frequency of Maple syrup urine disease was found in neonates [11].

There was no correlation between these metabolic disturbances and neurodevelopmental outcomes

Although metabolic abnormalities were observed in 16.7 % of newborns in the running study.

In another study, all 120 neonates underwent EEG which was abnormal in 26 (21.6%) cases [17]. According to Scher et al., the neonates had more complications and illustrated high frequency of abnormal EEG, which could be because of genetic, environmental and maternal status in pregnancy period [17].

In conclusion, idiopathic causes and birth asphyxia were the foremost etiology identified in most neonatal seizures in this cross-sectional study. However, to establish the exact cause of seizures, more extensive work-up and investigations are needed to better understand, prevent and treat the neonatal seizures in Northern Iran**.**

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References:

1. Brunquell PJ, Glennon CM, DiMario Jr FJ, et al. Prediction of outcome based on clinical seizure type in newborn infants. J Pediatrs 2002; 140(6): 707-12.
2. Lai YH, Ho CS, Chiu NC, et al. Prognostic factors of developmental outcome in neonatal seizures in term infants. Pediatrs & Neonatol 2013; 54(3): 166-72.
3. Sankar R, Koh S, Wu J, Menkes JH. Paroxysmal disorders, In: Menkes JH, Sarnat HB, Maria BL. (eds). Child neurology. 7th ed. Philadelphia: Lippincott Williams and Wilkins. 2005; pp: 857-942.
4. Shellhaas RA, Glass HC, Chang T. Neonatal Seizures, In: Swaiman KF, Ashwal S, Ferriero DM, et al. (eds). Swaiman's Pediatric Neurology: Principles and Practice. 6th ed. Elsevier. 2017; pp: 87-106.
5. Carrascosa M, Martínez-Gutiérrez A, Onsurbe I, et al. [Neonatal convulsions in health care. II. Prognostic factors]. Revista neurologia 1996; 24(136): 1516-9.
6. Dehdashtian M, Momen A, Ziae T, Moradkhani S. Evaluation of seizure etiology in convulsive neonates admitted to Imam Khomeini and Abozar hospitals of Ahvaz 2004-2007. Jundishapur Sci Med J 2009; 8(2): 163-7.
7. Krüger E, Kritzinger A, Pottas L. Breastfeeding and swallowing in a neonate with mild hypoxic-ischaemic encephalopathy. South African J Communication Disorder 2017; 64(1):1-7.
8. Chan DWS, Tan ES, Cleary MA. Neonatal seizures: when to consider and how to investigate for an inborn error of metabolism. Proceedings of Singapore Healthcare. 2010;19(2):112-23.
9. Martin RJ, Fanaroff AA, Walsh MC. Fanaroff and Martin's Neonatal-Perinatal Medicine E-Book: Diseases of the Fetus and Infant. 10th ed. Elsevier Health Sciences; 2014.
10. Ronen GM, Penney S, Andrews W. The epidemiology of clinical neonatal seizures in Newfoundland: a population-based study. J Pediatrs 1999; 134(1):71-5.
11. Wallois F, Patil A, Kongolo G, et al. Haemodynamic changes during seizure-like activity in a neonate: a simultaneous AC EEG-SPIR and high-resolution DC EEG recording. Neurophysiolog Clin Neurophysiolog 2009; 39(4-5): 217-27.
12. Pisani F, Facini C, Pelosi A, et al. Neonatal seizures in preterm newborns: a predictive model for outcome. Europ J Paediatr Neurolog 2016; 20(2): 243-51.
13. Ashrafzadeh F, Mahmoodi E, Hydarian F, Kharazmi A. Outcome of term neonates with identified seizures. Horizon Med Sci 2006; 11(4): 37-41.
14. Clancy RR. The newborn drug development initiative workshop: summary proceedings from the neurology group on neonatal seizures. Clin Therap 2006; 28(9): 1342-52.
15. Abbaskhanian A, Mohammadi M, Farhadi R, Khademloo M. Prevalence and associated factors of neonatal seizure in neonates admitted in neonatal ward of Bu-Ali Sina and Imam Khomeini hospitals, Sari, Iran. J Mazandaran Uni Med Sci 2014; 23(2): 89-94.
16. Nunes ML, da Costa JC. Sleep and epilepsy in neonates. Sleep med 2010; 11(7): 665-73.
17. Scher MS, Alvin J, Gaus L, et al. Uncoupling of EEG-clinical neonatal seizures after antiepileptic drug use. Pediatr Neurolog 2003; 28(4): 277-80.
18. Shellhaas RA, Chang T, Wusthoff CJ, et al. Treatment duration after acute symptomatic seizures in neonates: a multicenter cohort study. J Pediatrs 2017; 181: 298-301. e1.

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