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Case Report

Clinical Study of Complex Febrile Seizures Associated to Perinatal Pathology

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Abstract

44 infant patients ranging one to seven years old were clinically studied with febrile seizures mainly associated to perinatal hypoxia (9%), hyperactivity and attention deficit (18), aggressiveness (9%), respiratory diseases (11%) strabismus (4%) and mental retardation (4%). EEG recordings showed generalized slow waves (6.9%), paroxysmal activity in frontocentral, parietal and temporal center of both hemispheres (6%). Status epilepticus in one patient. Normal EEGs were observed in six cases (16%). Most patients received Valproic acid (69%). Two patients received Carbamazepine and one patient received a mixture of Valproic acid and Carbamazepine, and the treatment associated with the pathological comorbidity. Five patients did not receive antiepileptic treatment (11%). Comorbidity was associated with perinatal hypoxia, hyperactivity and attention deficit and aggressiveness. The following pathology risks factors were found: pneumonia, tonsillitis, respiratory and gastrointestinal diseases and kidney insufficiency. Four patients exhibit family history of convulsions (9%). We observed some neurologic and neurobehavioral abnormalities such as atonic muscle, languages disorders, hyperactivity and attention deficit, aggressiveness, and psychomotor retardation. In relationship with mother pathology, in our study we found that some mothers exhibited the following pathology during pregnancy: urinary infections, preeclampsia, and dystocic labor. In our study most patients received Valproic acid (69%). Valproate was treatment of choice for symptomatic myoclonic and generalized tonic-clonic seizures., and Carbamazepine initial monotherapy for complex partial seizures.

Keywords: *Complex Febrile Seizures; Perinatal Pathology; Valproic Acid*

Introduction

Asanova and Makshantseva [1] have identified correlation between the severity of cerebral damage and the course of pregnancy and parturition and describe characteristics of the psychomotor development of children with a history of brain damage of varying degree. The Authors made emphasis on the necessity of prolonged observation of children with a history of perinatal encephalopathy.

The American Academy of Pediatrics (AAP) [2] published a clinical practice guideline defining a febrile seizure as "a seizure accompanied by fever (temperature ≥ 100.4°F or 38°C by any method), without central nervous system infection, that occurs in infants and children 6 through 60 months of age". Febrile seizures are further classified as simple or complex[1]. The febrile illness causing the convulsion should

[1]Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures American Academy of Pediatrics (2008) [2].

not be secondary to an intracranial infection (meningitis or encephalitis) or acute electrolyte imbalance. Most cases of febrile convulsion are short lived and self-terminating. However, a few cases of prolonged febrile convulsion may need anticonvulsant medication to stop the seizure. Management is mainly symptomatic, although anticonvulsants may have a role in a small number of children with complex or recurrent febrile convulsion [3]. Children aged from one month to 7 years are analyzed for the following data: type of seizure (simple or complex), clinical manifestation of the convulsion (tonic-clonic, tonic, atonic, partial unilateral), body temperature after convulsion, and the length of convulsion [4]. The predominating perinatal pathological complications were perinatal hypoxia-anoxia and prematurity [5].

There are several types of epileptic seizures and syndromes that are unique to children, including infantile spasms, Lennox-Gastaut syndrome and absence seizures. Febrile seizures and neonatal seizures, while not epilepsy, are relatively common types of seizures in infants and children and are likely markers of risk of later epilepsy. Factors that are known to increase risk of the epilepsies in children include congenital malformations of the central nervous system (CNS), moderate or severe head trauma, CNS infections, certain inherited metabolic conditions, and genetic factors [6].

The main objective of this clinical investigation was to obtain further information on febrile seizures and the relationship with the associated perinatal pathology observed in a developing country.

Materials and Methods

44 infant patients ranging from one to seven years were clinically studied at the Outpatient Clinical Unit of Biological Research Institute at the San Rafael Clinical Home in Maracaibo. Venezuela. This study was carried out according to the Principles of Helsinki Declaration for Research in Human Beings, The American Academy of Pediatrics (AAP) and the European expert opinion, 2007 [7].

Case Reports

- **Case 1:** JC. F. One year and six month old. Patient with perinatal hypoxia, febrile seizures, numerous, atonic muscle twitching, gait disturbances, right strabismus, drooping head and transitory loss of consciousness. Received intramuscular diphenylhydantoin.
- **Case 2:** LG. M. Patient 18 month old with perinatal hypoxia, febrile syndrome associated with pneumonia, urinary tract infection, speech disorders featured by few monosyllables treatment with antibiotic and valproic acid.
- **Case 3:** LG. M. Three years and a half old. Patient presented febrile seizure, Zika syndrome and hyperactivity. Treatment with risperidone.
- **Case 4:** RZ. F. Four years old. Febrile seizure associated to viral infection. Received valproic acid and antipyretic.
- **Case 5:** LA. M. Two years and three months old. Febrile seizure associated to tonsillitis. Received azithromycin.
- **Case 6:** EH. M. Three years old patient with three febrile seizures at 10 months old, one year old and at three years old. Received valproic acid.
- **Case 7:** LA. F. Four years old. Patient hospitalized by 5 days by febrile seizures associated to hyperactivity and attention deficit. Stool examination showed abundant bacterial flora. EEG recording showed generalized slow waves. Received valproic acid.
- **Case 8:** JA. M. Three years old. One febrile seizure. EEG showed generalized slow waves, family history of seizure disorders. Received valproic acid.

- **Case 9:** JF. M. Six years old. Two febrile seizures. One additional without fever. NMR image showed inflammatory maxilloethmoidal sinusopathy. Received diazepam.
- **Case 10:** TO.M. One year old. One febrile seizure with continuous blinking and clenched hands. Received valproic acid.
- **Case 11:** NR. F. One year and six months old. Three febrile seizures, hyperactivated. EEG showed paroxysmal focus featured by generalized polyspikes and polyspikes projected to all brain regions. Received valproic acid.
- **Case 12:** LH. M. Four years old. Two febrile seizures and associated respiratory disease. Receive valproic acid.
- **Case 13:** MC. F. One febrile seizure associated with pneumonia. Normal EEG. Received valproic acid.
- **Case 14:** YO. Three years old. Two febrile seizures. EEG showed paroxysmal focus featured by generalized polyspikes projected to all brain regions. Received valproic acid.
- **Case 15:** ML. M. One year and half old. Two febrile seizures. Perinatal hypoxia and flat food. Received valproic acid.
- **Case 16:** SD. M. One year and 10 months old. Two febrile seizures associated to respiratory disease. Normal. EEG. Received valproic acid.
- **Case 17:** SM. M. Four years old. One febrile seizure. EEG showed paroxistic focus in superior frontal and parietal center regions at right predominance and slow waves at central regions. Kidney lithiasis and cytomegalovirus infection. Received valproic acid.
- **Case 18:** MM. M. Two years old. Mother with epileptic syndrome during pregnancy. One febrile seizure associated to hyperactivity and attention deficit. Normal EEG. Received risperidone.
- **Case 19:** YL. M. 6 years old. Four febrile seizures associated to hyperactivity, attention deficit and aggressiveness. EEC showed paroxistic activity in frontocentral, parietal and temporal center of both hemispheres. Received valproic acid.
- **Case 20:** LM. One year and 8 months old. F. Two febrile seizures and a third convulsive episode without fever. Perinatal. Hypoxia. Received valproic acid and carbamazepine in the third convulsion.
- **Case 21:** YC. F. Five years old. Five febrile seizures for 6 months old. Normal EEG. Received valproic acid.
- **Case 22:** GA. M. 6 years old. Two febrile seizures and viral infection associated skin exanthematic process and renal insufficiency. Received valproic acid.
- **Case 23:** VA. M. Three years old. Four febrile seizures. Mother with preeclampsia. Severe perinatal hypoxia, hyperactivity and attention deficit, aggressiveness, psychomotor retardation and strabismus. Receive diazepam and valproic acid.
- **Case 24:** SE. M. Four years old. One febrile seizure. Patient has not convulsed for a year and a half. Received valproic acid. Treatment suspended by stabilized. Free seizure syndrome.
- **Case 25:** SM. M. Three years old. Two febrile seizures. Loss of sphincter control. Received valproic acid.
- **Case 26:** JG. M. Six years old. Three febrile seizures. Hyperactivity. Normal EEG. Received valproic acid.

- **Case 27:** SC. M. Two years old. Two febrile seizures. Associated parasitosis and influenza infection. Received Carbamazepine.
- **Case 28:** MC. F. One year and a half old. One febrile seizure. Hyperactivity and aggressiveness. Received valproic acid.
- **Case 29:** JF. M. One year and a half old. Two febrile seizures. Hyperactivity and aggressiveness. Received valproic acid.
- **Case 30:** JG. M. Six years old. Two febrile seizures. Hyperactivity and attention deficit. EEG showed generalized slow waves irradiated to all brain regions. Received valproic acid.
- **Case 31:** JG. F. One year and 10 months old. Two febrile seizures after brain trauma, associated tonsillectomy. Family history of convulsive syndromes. Received valproic acid.
- **Case 32:** JA. M. Five years old. Three febrile seizures. Family history of convulsive syndromes. Received valproic acid.
- **Case 34:** JM. M. Three years old. Five febrile seizures. Two of them without fever. Aggressiveness. Normal EEG showed acute vertex waves and sleep spindles. Received valproic acid.
- **Case 35:** JP. M. Four years old. Nine febrile seizures. Hyperactivity and attention deficit. EEG showed medium voltage spikes in frontal and temporal regions. Received valproic acid and carbamazepine.
- **Case 36:** ER. M. One year and six months old. Mother with urinary infection during pregnancy. One febrile seizure. Respiratory disease and diarrhea. Received valproic acid.
- **Case 39:** HG. M. Seven years old. M. Mother with urinary infection during pregnancy. One febrile seizure. Parasitosis by *Entamoeba histolytica*. Receive paracetamol, bactrim and metronidazole.
- **Case 40:** EV. F. Four years old. Two febrile seizure. Prematurity, pulmonary immaturity, perinatal hypoxia, psychomotor retardation and equine gait.
- **Case 41:** JG. One year and 10 months old. F. Two febrile seizures. Tonsillitis. Family history of convulsive syndromes.
- **Case 42:** JG. M. Two years old. One febrile seizure. Hyperactivity. Received valproic acid.
- **Case 43:** RG. M. Two years old. Two febrile seizure. Respiratory diseases. Received valproic acid and Bidroxil. 44. LC P. M. Focal convulsive syndrome and status epilepticus. 30 convulsive crisis in the las 48 eight hours. Epilepsy refractory to Carbamazepine and Valproic acid. Received gabapentin, oxicodal ribotrils ND. Pregabalin.
- **Case 44:** M. eleven years old. Generalized convulsive syndrome grand mal type, mother with stress and depression. Dystocia delivery. Neonate with perinatal hypoxia. Received valproic acid and carbamazepine.

Results

44 infant patients ranging one to seven years old were clinically studied with febrile seizures mainly associated to perinatal hypoxia (9%), hyperactivity and attention deficit (18), aggressiveness (9%), respiratory diseases (11%) strabismus (4%) and mental retardation (4%). EEG recordings showed generalized slow waves (6.9%), paroxistic activity in frontocentral, parietal and temporal center of both hemispheres (6%). Status epilepticus in one patient. Normal EEGs were observed in six cases (16%). Most patients received Valproic acid

(69%). Two patients received Carbamazepine and one patient received a mixture of Valproic acid and Carbamazepine, and the treatment associated with the pathological comorbidity. Five patients did not receive antiepileptic treatment (11%). Comorbidity was associated with perinatal hypoxia, hyperactivity and attention deficit and aggressiveness, The following pathology risks factors were found: pneumonia, tonsillitis, respiratory and gastrointestinal diseases, and kidney insufficiency. Four patients exhibit family history of convulsions (9%).

We observed some neurologic and neurobehavioral abnormalities such as atonic muscle, languages disorders, hyperactivity and attention deficit, aggressiveness, and psychomotor retardation.

Discussion and Conclusion

In all children examined, convulsive seizures occurred in hyperthermia largely in early childhood. Apparently, in the majority of cases, perinatal injury alone was insufficient to precipitate seizures. However, the combined perinatal brain injury and an infectious disease form favourable conditions for the appearance of recurrent convulsive conditions in children. Therefore, to prevent them we applied Valproic acid and Carbamazepine considering importance the prophylaxis of both perinatal pathology and infectious diseases. According to Bondyrev and Mamed'iarov [8] the patients with convulsive conditions should be given combined treatment including anticonvulsants, anti-inflammatory, antibacterial, detoxication and other drugs.

In 44 cases herein studied we have observed five cases with perinatal hypoxia (9%). Calderón-Gonzales., *et al*. [5] reported in 44.8% of cases with perinatal history of high risk. Acute somatic pathology such as acute respiratory diseases, pneumonia, intestinal infections dominated was reported by Bondyrev and Mamed'iarov [8].

In episodes of feverish convulsions. we observed associated viral illness in a three cases (7%) and bacterial diseases in two cases (4%).

Iakunin., *et al*. (1980) stressed the importance of the premorbid background for the formation of the character and the course of the convulsive seizures in children, and for the formation of epileptiform syndrome.

Ellenberg., *et al*. [9] reported neurological abnormality in the first year of life before any seizure and the presence of minor motor seizures, were associated with an increased rate of mental retardation and cerebral palsy.

Our study support the Bondyrev and Mamed'iarov [8] findings that in the majority of cases, perinatal injury alone was insufficient to precipitate seizures. However, the combined perinatal brain injury and an infectious disease form favourable conditions for the appearance of convulsive conditions in children. The predictors of recurrent febrile seizures include younger age, lower threshold of temperature, onset within one hour of fever and positive family history [10].

According to Mustafic., *et al*. [4] we studied the following data: type of seizure: simple or complex, clinical manifestation of the convulsion (tonic-clonic, tonic, atonic, partial unilateral, body temperature after convulsion, and the length of convulsion. Normal EEG findings were recorded in four cases (9%),

Martin-Fernández., *et al*. [11] postulated that those patients who suffered from convulsions from an early age, who had convulsions of a partial--complex type, which lasted over 20 minutes and repeated frequently--were seen to be the most likely to develop epilepsy. The existence of family history of febrile seizures or epilepsy increase the risk of recurrent febrile seizures. The existence of family history of febrile seizures or congenital epilepsy increase the risk of recurrent febrile seizures.

Those patients who suffered from convulsions from an early age, who had convulsions of a partial--complex type, which lasted over 20 minutes and repeated frequently--were seen to be the most likely to develop epilepsy.

In relationship with mother pathology, in our study we found that some mothers exhibited the following pathology during pregnancy: urinary infections, preeclampsia, and dystocic labor. According to Arpino., *et al*. [12] neonatal seizures were found to be associated with maternal disease in the 2 years before pregnancy, mother's weight gain > 14 kg during pregnancy, placental pathology, preeclampsia, low birth weight, low gestational age, and jaundice in the first 3 days of life. Scher., *et al*. [13] studied the relationship of intrapartum and neonatal factors, such as labor duration, fetal heart rate abnormalities, cord blood gas values to assess the relationship between seizure timing and intrapartum/neonatal factors. Seizures were noted earlier for the encephalopathic group than for the non-encephalopathic group.

Febrile seizures and neonatal seizures are relatively common types of seizures in infants and children and are likely markers of risk of later epilepsy [6]. Development from febrile convulsions into nonfebrile convulsions was detected, Similar observations were earlier reported by Tsuboi and Endo [14].

In our study most patients received Valproic acid (69%). Valproate was treatment of choice for symptomatic myoclonic and generalized tonic-clonic seizures., and Carbamazepine initial monotherapy for complex partial seizures [7].

Capovilla., *et al*. [15] stressed the benign prognosis of the majority of cases and the risk factors for recurrence of febrile seizures and appearance of epilepsy later on. The recurrence of febrile seizures and appearance of epilepsy later on can not be estimated in the present study since some patients did not attend a rigorous medical consultation.

As suggested by Paul., *et al*. [3] in most cases of recurrent seizures we applied epileptic treatment, mainly valproic acid and a mixture of valproic acid and carbamazepine to stop the seizures. Recently, Li., *et al*. [16] reported that antiepileptic drugs are effective in preventing the recurrence of complicated febrile seizures (CFS), and the main mechanism may be related in mouse experimental findings to the targeted regulation of BCL-2 on the apoptosis of the hippocampus in the nervous system [17].

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Bibliography

1. Asanova LM and Makshantseva NV. "Late sequelae of intrauterine and birth-related lesions of the brain". *Zh Nevropatol Psikhiatr Im S S Korsakova* 87.10 (1987): 1550-1554.

2. Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures American Academy of Pediatrics. "Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures". *Pediatrics* 121.6 (2008): 1281-1286.

3. Paul SP., *et al*. "Recognition and management of febrile convulsion in children". *Nursing Standard* 29.52 (2015): 36-43.

4. Mustafić N., *et al*. "Clinical characteristics at onset of first febrile convulsions". *Acta Medica Croatica* 62.5 (2008): 511-515.

5. Calderón-González R., *et al*. "Febrile convulsion. A clinical study of 303 patients". *Boletín Médico del Hospital Infantil de México* 47.1 (1990): 7-13.

6. Cowan LD. "The epidemiology of the epilepsies in children. Review". *Mental Retardation and Developmental Disabilities Research Reviews* 8.3 (2002): 171-181.

7. Wheless JW., *et al*. "Treatment of pediatric epilepsy: European expert opinion". *Epileptic Disorders* 9.4 (2007): 353-412.

8. Bondyrev AJ and Mamed'iarov AM. "Convulsive conditions in somatic pathology of infectious etiology in children with perinatal brain injury". *Zh Nevropatol Psikhiatr Im S S Korsakova* 91.6 (1991): 16-18.

9. Ellenberg JH., *et al*. "Age at onset of seizures in young children". *Annals of Neurology* 15.2 (1984): 127-134.

10. Rajadhyakshav S and Shah KN. "Controversies in febrile seizures". *Indian Journal of Pediatrics* 67.1 (2000): S71-S79.

11. Martín-Fernández JJ., *et al*. "Risk factors in recurrent febrile seizures". *Revue Neurologique Journals* 24.136 (1996): 1520-1524.

12. Arpino C., *et al*. "Prenatal and perinatal determinants of neonatal seizures occurring in the first week of life". *Journal of Child Neurology* 16.9 (2001): 651-656.

13. Scher MS., *et al*. "Timing of neonatal seizures and intrapartum obstetrical factors". *Journal of Child Neurology* 23.6 (2008): 640-643.

14. Tsuboi T and Endo S. "Febrile convulsions followed by nonfebrile convulsions. A clinical, electroencephalographic and follow-up study". *Neuropadiatrie* 8.3 (1977): 209-223.

15. Capovilla G., *et al*. "Recommendations for the management of "febrile seizures": Ad Hoc Task Force of LICE Guidelines Commission". *Review Epilepsia* 50.1 (2009): 2-6.

16. Li B., *et al*. "The effect of complicated febrile convulsion on hippocampal function and its antiepileptic treatment significance". *Translational Pediatrics* 10.2 (2021): 394-405.

17. Graves RC., *et al*. "Febrile seizures: risks, evaluation, and prognosis". *American Family Physician* 85.2 (2012): 149-153.

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