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ORIGINAL ARTICLE

EPIDEMIOLOGICAL ASPECTS OF REFRACTORY EPILEPSY IN A PEDIATRICS HOSPITAL UNIT

ASPECTOS EPIDEMIOLÓGICOS DA EPILEPSIA REFRATÁRIA EM UMA UNIDADE HOSPITALAR DE PEDIATRIA

ASPECTOS EPIDEMIOLÓGICOS DE LA EPILEPSIA REGRACTARIA EN UNA UNIDAD HOSPITALARIA DE PEDIATRÍA

Gleiciane da Silva Fonseca[1], Deborah Dinorah de Sá Mororó[2], Ylana Karine Fonseca de Medeiros[3], Aurea Nogueira de Melo[4], Juliana Teixeira Jales Menescal Pinto[5]

ABSTRACT

Objective: to know the epidemiological profile of children with refractory epilepsy in a University Hospital. ***Methodology***: descriptive and retrospective study with a quantitative approach, developed from the collection of data from medical records of children under 18 years old, from May 2012 to May 2014. The sample was 82 records. With the aid of the Statistical Package for Social Sciences (SPSS), a descriptive analysis of the data was performed, presented in tables. ***Results***: a variety of etiological factors was found to cause the disease, such as post-anoxic injuries, malformations of the central nervous system trauma and skull-brain injury. ***Conclusion***: the practices focused on attention to prenatal care, childbirth and newborn care can contribute to a reduction of sequelae and complications of the disease. ***Descriptors***: Epidemiological Profile; Epilepsy; Pediatrics.

RESUMO

Objetivo: conhecer o perfil epidemiológico das crianças com epilepsia refratária em um Hospital Universitário. ***Metodologia:*** estudo descritivo e retrospectivo, de abordagem quantitativa, desenvolvido a partir da coleta de dados em prontuários de menores de 18 anos de idade, no período de maio de 2012 a maio de 2014. A amostra foi de 82 prontuários. Com auxílio do programa estatístico *Statistical Package for the Social Sciences* (SPSS®), foi feita a análise descritiva dos dados, apresentados em tabelas. ***Resultados:*** uma variedade de fatores etiológicos foi encontrada como causadores da enfermidade, como as lesões pós-anóxia, as malformações do Sistema Nervoso Central e os Traumas crânio-encefálicos. ***Conclusão:*** as práticas voltadas para uma atenção ao pré-natal, parto e ao recém-nascido poderão contribuir para uma diminuição de sequelas e complicações da doença. ***Descritores:*** Perfil Epidemiológico; Epilepsia; Pediatria.

RESUMEN

Objetivo: conocer el perfil epidemiológico de los niños con epilepsia refractaria en un Hospital Universitario. ***Metodología:*** estudio descriptivo y retrospectivo, de enfoque cuantitativo, desarrollado a partir de la recolección de datos en prontuarios de menores de 18 años de edad, en el período de mayo de 2012 a mayo de 2014. La muestra fue de 82 prontuarios. Con el auxilio del programa estadístico *Statistical Package for the Social Sciences* (SPSS®), fue hecho el análisis descriptiva de los datos, presentados en cuadros. ***Resultados:*** una variedad de factores etiológicos fueron encontrados como causadores de la enfermedad, como las lesiones post-anoxia, las malformaciones del Sistema Nervioso Central y los Traumas cráneo-encefálicos. ***Conclusión:*** las prácticas dirigidas para una atención al prenatal, parto y al recién nacido podrán contribuir para una disminución de secuelas y complicaciones de la enfermedad. ***Descriptores***: Perfil Epidemiológico; Epilepsia; Pediatría.

[1]Nurse, Intensive Care Specialist, Resident of Pediatrics, University Hospital Onofre Lopes/HUOL, Federal University OF Rio Grande do Norte/UFRN. Natal (RN), Brazil. E-mail: gleicianefonseca@hotmail.com; [2]Nurse, Epidemiology Specialist for Hospital Services, Master of Nursing, Ph.D., Graduate Nursing Program, Residency Coordinator Multidisciplinary Integrated Health, Federal University of Rio Grande do Norte/UFRN. Natal (RN), Brazil. E-mail: deborahsa1@hotmail.com; [3]Nurse, Intensive Care Specialist, Resident of Pediatrics, University Hospital Onofre Lopes / HUOL, Federal University of Rio Grande do Norte/UFRN. Natal (RN), Brazil. E-mail: ylanamedeiros@gmail.com; [4]Medical Pediatric Neurologist, Specialist in Neurology, Child Neurology and electroencephalogram, Ph.D. Professor in Internal Medicine Neurology (Post-doctoral degree in Clinical Neurophysiology), Department of Pediatrics, Natal (RN), Brazil. E-mail: aureanmelo@yahoo.com.br; [5]Nurse, Professor in Nursing, School of Nursing, Ph.D., Graduate Program in Public Health, Federal University of Rio Grande do Norte/UFRN. Natal (RN), Brazil. Natal (RN), Brazil. E-mail: jujales@hotmail.com

INTRODUCTION

Epilepsy is currently being debated as a public health problem.[1] This is due to its incidence in approximately one percent of the world population[2] as well as the significant impact of the quality of life of affected individuals.

It is a chronic neurological disorder characterized by recurrent seizures due to several etiological factors.[2] It is defined by the occurrence of two or more seizures over 12 months without evidence of fever, alcohol or drug intoxication or abstinence.[2-3] It is from the hyperactivity of neurons and brain circuits that are capable of generating abnormal synchronous electrical discharges. They can be manifested in various ways, from discharges in certain neuronal population; to prolonged outbreaks occurring with isolated epileptic seizures or taking the form of state of evil and/or clinical electrographic.[2]

Children are the most affected with epilepsy[2], in which the prevalence is approximately 5 in 1000, and the highest frequency is in the age group from 0 to 9-year-old.[4] This can be understood by considering that the nervous system of children is still immature, with few reactions inhibitory synapses. At this stage, they are more prone to infections accompanied by hyperthermia and electrolyte disturbances, and, therefore, they are a susceptible group.[5]

Proper treatment with antiepileptic drugs can be successful in approximately 75% of patients. However, it is estimated that 20-30% of children have refractory epilepsy[2,4], also known as unwieldy because seizures are even persistent in the use of potentially effective antiepileptic drugs for that particular epileptic seizures.

In developing countries, some intractable epilepsy in infancy occurs more frequently, particularly in cases where the refractory is associated with the severity of brain lesions early acquired as perinatal infections, such as disorders of the Central Nervous System (CNS).[4]

if some brain areas more susceptible to hypoxia and ischemia recurrent discharges, such as the hippocampus and some neocortical areas, may contribute to the development of cognitive and motor deficits[4], which becomes a problem for patients with refractory epilepsy since they start to suffer beyond neurobiological problems, psychosocial barriers, as well as higher costs in treatment.[1,6]

It is noted that crises can also interfere directly and negatively on social integration, imposing restrictions on family, school, work, leisure and legal aspects, becoming a stigmatized condition.[2,4]

Knowledge of the aspects that run through refractory epilepsy, as well as the main etiologies involved in their emergence, enable the adoption of necessary measures to prevent crises in some cases, and for other causes, investment in the diagnosis and treatment that can contribute to their control.

It is important to note that prevention and treatment of seizures early in the disease in children can minimize the neuropsychological impact and the resulting consequences of refractory epilepsy.[2]

In this perspective, the objective of this study was to know the epidemiological profile of children with refractory epilepsy drug, attended by child neurology of a Hospital of the Federal University of Rio Grande do Norte (UFRN).

METHOD

Article elaborated from the research << **Epidemiology of refractory epilepsy in a hospital pediatric** >> presented in the Multidisciplinary Residency Program in Child Health, Federal University of Rio Grande do Norte/UFRN. Natal, RN, Brazil. 2015.

Descriptive and retrospective study with a quantitative approach, developed in the child neurology clinic of the University Hospital Onofre Lopes (HUOL/UFRN). The institution has an ambulatory monitoring service and hospitalization to children with refractory epilepsy, with reference in pediatric neurology in the state.

The inclusion criteria used were the medical records of patients with refractory epilepsy drug, aged 0-18 years old; accompanied by child neurology from May 2012 to May 2014. The records that had no charts of admission filled from the neurologist and those who were not in the hospital file in the period of data collection were excluded.

The sample was composed of 82 records, which is approximately 60% of the total population of patients seen in the period. For data collection, a printed organized by researchers was used from the hospitalization form used by the pediatric neurology team, composed of sociodemographic, family, obstetric and neonatal history; and clinical characteristics of the disease.

The research was developed by the ethical standards set in Resolution 466/12 of the National Health Council. The project was

approved by the Research Ethics Committee of HUOL by the General Certificate for Ethics Assessment (CAAE) 30172114.1.0000.5292 and under the Protocol 638,470/2014.

With the aid of the Statistical Package for Social Sciences (SPSS), a descriptive analysis of the data with absolute and relative frequencies was performed.

RESULTS AND DISCUSSION

After mapping the information of 82 records, it was possible to condense and build categories for analysis: sociodemographic characteristics and etiological factors related to epilepsy refractoriness.

There is some difficulty attributed to the epilepsy study due to the variability of brain pathologies related to its emergence. However, it was possible to associate the results of this study to other made in this area.

Regarding the sociodemographic characteristics, it was shown that 45 (54.9%) patients were male, a fact that has also been described in other studies[7], which stated that there are specific differences in the development of neural networks of each sex and these differences allow increased epilepsy susceptibility to male.[8]

Most children, 73 (89%) were in the life cycle of 0-12 years old, which can be attributed to neuro-maturational and physiological factors from the brain in development for this age group. Also, 52.4% of patients were residents from the countryside, but 55.7% were born in the capital.

In this study, it was possible to observe the presence of various etiologies. In some cases, there was more than one factor correlated as a cause for the onset of epilepsy. Many seizures are presented in the form of West Syndrome, which is characterized by the triad involving hypsarrhythmia as EEG standard, developmental delay, and epileptic spasms.[9] Tables 1 and 2 show etiological factors according to the type of epileptic crisis.

Table 1. Etiological factors and seizures patterns. Natal (RN), May 2012 to 2014, Brazil.

Prenatal Factors	Seizures patterns			
	Focal n (%)	Generalized n (%)	West n (%)	Total n
CSN Malformation	3 (21.4)	6 (42.9)	5 (35.7)	14
Inborn errors of metabolism	-	2 (33.3)	4 (66.7)	6
Prematurity	-	1 (50.00	1 (50.0)	2
Sturge-Weber Syndrome	3 (100.0)	-	-	3
Tuberous sclerosis	1 (33.3)	1 (33.3)	1 (33.3)	3
Post-infectious	1 (50,0)	1 (50.0)	-	2
Cyst of the choroid plexus	-	-	1 (100.0)	1
Moyamoya Disease	-	1 (100.0)	-	1

Table 2. Etiology and seizures patterns. Natal (RN), May 2012 to 2014, Brazil.

Postnatal Factors	Seizures patterns			
	Focal n (%)	Generalized n (%)	West n (%)	Total n
Post-anoxic injury	4 (20)	8 (40)	8 (40)	20
TBI	1 (10)	8 (80)	1 (10)	10
Post infectious	1 (100.0)	-	-	1
Hydrocephalus	1 (50.0)	-	1 (50.0)	2
Acute hypoxia after coughing	-	1 (100.0)	-	1
Lupus encephalopathy	-	1 (100.0)	-	1

There was a predominance of etiologic factors acquired in the postnatal period, with post-anoxic injury highlighted. The second most found among the etiologic factors were malformations of the CNS, such as prenatal causes; followed by the TBI, which are among the postnatal causes.

The literature shows that seizures are divided according to etiology in crypto-genetic without apparent clear cause; in idiopathic, which are genetic in origin; and symptomatic epilepsies caused by certain diseases genetically, prenatal and postnatal aggression on the nervous system, brain malformations, nervous system infections, inborn errors of metabolism among others.[3]

Within the etiological causes of epilepsy in newborns and infants, there are the hypoxic-

ischemic lesions, bleeding, and strokes, cortical dysgenesis, the neurocutaneous syndromes such as tuberous sclerosis, the chromosomal disorders such as Down syndrome and others.[10]

In developing countries, it is indicated a high incidence of epilepsy rate attributable to parasitic causes (mainly neuro-cysticercosis); intracranial viral or bacterial infections; traumatic brain injury (TBI) and cerebrovascular diseases. However, it is known that genetic factors, risk factors related to the environment and the study methodology influence the search result.[3,7]

As for the post-anoxic injury, physiologically, uterine contractions produce some decrease in blood flow in the vessels leading to the placenta. When brief, this process is well tolerated, but when prolonged it may produce mild or severe brain abnormalities that can be fatal or reversible, or even with sequelae.[11]

Associated with this factor, there are others that can cause decreased blood flow to the fetus, as the placental or cord malformation, the presence of uterine tumors, some maternal factors (primiparity, hypertension, diabetes, anemia, malnutrition, poisoning), the placenta displacement, placenta Previa, preterm or post-maturity, birth defects, respiratory disorders of fetus, birth length, presentation and perinatal maneuvers and anemic anoxia postpartum.[11]

Regarding the TBI, it is observed that it most often occurs in children under one-year-old, while older children are more affected by upper and lower limb trauma. The main determinants of TBI in children are falls, followed by running over or car accidents.[12] In this way, the preventive measures need to be presented as relevant as a result of the consequences that can cause in children.

Post-infectious causes are considered still common in developing countries due to prevention failures in health systems[13], which account for 28% of deaths in children under five years old[14]. This study may be highlighting three cases, two due to congenital syphilis and visceral post-leishmaniosis and recurrent infections.

Heredity was strongly evidenced in this study. Out of the evaluated children, 51 (62.2%) had relatives with seizures, highlighting the following degrees of kinship: cousins (42%), uncles (30%), siblings (22%) and second-degree relatives (22%).

It is believed that subtle changes in gene expression can determine the formation of neural circuits more likely to develop seizures and thus be transmitted from generation to generation.[15]

♦ Background of pregnancy, obstetric and neonatal for refractory epilepsy

It was observed that from the pregnancies of children with refractory epilepsy, 73 (89%) had prenatal follow-up; with 69 (84.1%) children born at term gestation time; 46 (56.1%) by vaginal delivery, 34 (41.5%) by cesarean section and 2 (2.4%) at Forceps. At birth, 52 (74.3%) children were crying, and 11 (19.6%) had lower Apgar score than or equal to 7 at 5 minutes of life. (Table 3)

Table 3. Obstetric and neonatal history for refractory epilepsy. Natal (RN), May 2012 to 2014, Brazil.

	n	%
Gestational age		
Preterm	13	15,9
At term	69	84,1
Post-term	-	-
Prenatal		
Yes	73	89,0
No	9	11,0
Type of delivery		
Vaginal	46	56,1
Cesarean	34	41,5
Forceps	2	2,4
Crying at birth		
Yes	52	74,3
No	18	25,7
Apgar		
>7 at 5’	45	80,4
< OU = 7 no 5’	11	19,6

Although the data show that most of the pregnancies had to monitor in prenatal, pregnancy at term and the newborn crying at birth, it is wondered the quality of health care in prenatal care, childbirth and the care of newborn in the delivery room, since sequels were observed resulting from the type of

assistance offered to the mother/son in childbirth.

In the literature, a study had lower Apgar scores at 5 minutes and more frequent birth trauma and anoxia in vaginal deliveries in which women had a history of cesarean delivery. Fact that also originated longer hospitalization of newborns in the neonatal intensive care unit.[16]

The Apgar score is used in the delivery room to assess the overall condition of the newborn to extra-uterine life and assists in the identification of perinatal asphyxia. The assessment is then made to birth through five signs: breathing and crying; heart beats; skin color; muscle tone and sensory stimuli.[3] It is noteworthy that 11 (19.6%) children had less or equal rate to seven in the fifth minute of life, however, 26 children had no Apgar score recorded in the medical record.

About three decades ago, an epidemiological study found a statistical overrepresentation of epilepsy in the first and the last children of several women. The results corroborated the view of the presence of birth injuries in the development of epilepsy, because while the first-born are more likely to obstetric accidents, the last children end up facing problems concerning uterine mobility, with the corresponding fetal anoxia.[17]

With the advancement of technology and better living conditions of the population in general, epilepsy can be prevented in cases where crises happen both due to infectious diseases, such as unwanted conditions in the period of pregnancy and delivery.[18]

The research also found that 25 (31.6%) women had an infection during pregnancy, especially urinary tract infection; 4 (4.9%) developed diabetes; 15 (18.5%) hypertension, and 9 (11.1%) bleeding at some time during pregnancy. Thus, preventive actions should be carried out through educational activities and effective monitoring of pregnant women in prenatal care to reduce risks from toxic substances, the vertical disease transmission to prepare the mother for the perinatal period, and to receive the child and provide appropriate care.

Besides these, other actions are effective to minimize damage in the newborn. Among them, there is the intrauterine transport for more prepared centers in neonatal intensive care and the availability of trained personnel to that sequels reduced and hence to an improvement of the epileptic frame.[18]

The Ministry of Health (MOH) is investing in programs such as the Stork Network to improve care for women of childbearing age, which offers a set of actions aimed at ensuring quality care, safe and humane, from planning family until the first two years of the child´s life, contributing to the accessibility to health services, resoluteness and safe transportation of the mother and newborn.[19]

In addition to these actions, WHO launched the care guidelines manual to people with cerebral palsy to provide guidance to multidisciplinary teams for the care of these people, at different points of care of the health network and throughout the life cycle.[20]

This care is essential for a safer labor and childbirth and to reduce risks to the newborn and the child´s development, which in turn could contribute to improving the quality of lives of people with epilepsy.

♦ General aspects and clinical manifestations of refractory epilepsy

The onset of epileptic seizures in the studied population usually occurred in phases of newborns (0-28 days), nursling (1-12 months) and toddle (1 to 3 years), as seen in Table 4.

Table 4. Clinical aspects and seizures patterns. Natal (RN), May 2012 to 2014, Brazil.

Clinical Aspects	Seizures patterns			
	Focal n (%)	Generalized n (%)	West n (%)	Total n
Age of onset of seizures				
Newborn (0 to 28 days)	3 (23.1)	4 (30.8)	6 (46.1)	13
Infant (1 to 12 months)	13 (35.1)	11 (29.8)	13 (35.1)	37
***Toddle* (1 to 3 years old)**	2 (14.2)	9 (64.3)	3 (21.4)	14
Kindergarten (3 to 6 years old)	1 (12.5)	7 (87.5)	-	8
School (6 to 12 years old)	3 (50.0)	3 (50.0)	-	6
Adolescents (12 to 18 years old)	-	1 (100.0)	-	1
Therapeutic drug				
Monotherapy	9 (27.3)	17 (51.5)	7 (21.2)	33
Polytherapy	13 (28.3)	18 (39.1)	15 (32.6)	46

The clinical presentation of refractory epilepsy is variable. Some children may have frank encephalopathy from birth, or show no abnormalities at first and then evolve rapidly CNS deteriorating.[21] In some cases, seizures may appear in the first six hours of life and then relapse at six months, and in others, depending on the cause, can occur at any time of life.[20]

In this study, the neurological examination, mostly showed normal patterns (65%), however, these changes are described in Table 5.

Table 5. Neurological examination. Natal (RN), May 2012 to 2014, Brazil.

Neurologic alterations	Type of epileptic syndrome			
	Focal n (%)	Generalized n (%)	West n (%)	Total n
Skull				
Macrocephaly	2 (33.3)	-	4 (66.7)	6
Microcephaly	-	3 (75.0)	1 (25.0)	4
Typical face	2 (33.3)	2 (33.3)	2 (33.3)	6
Abnormal attitude	2 (22.2)	2 (22.2)	5 (55.6)	9
Altered Hands	2 (40.0)	1 (20.0)	2 (40.0)	5
Altered Feet	1 (14.3)	5 (71.4)	1 (14.3)	7
Altered Column	-	2 (40.0)	3 (60.0)	5
Altered gait	4 (28.6)	7 (50.0)	3 (21.4)	14
Paresis	3 (27.3)	3 (27.3)	5 (45.5)	11
Decreased muscle strength	4 (40.0)	3 (30.0)	3 (30.0)	10
Changed static balance	-	5 (29.4)	12 (70.6)	17
Involuntary motor	-	1 (33.3)	2 (66.7)	3
Altered surface reflections	1 (20.0)	4 (80.0)	-	5
Altered primitive reflexes	2 (28.6)	2 (28.6)	3 (42.9)	7
Meningeal signs	-	-	-	-
Bad school performance	4 (28.6)	9 (64.3)	1 (7.1)	14

It is noted that in the face of seizures difficult to control, where the neuro-psychomotor involution occurs, prevention and treatment of seizures in early onset can minimize the impacts and neuropsychological sequels associated with its recurrence.

Carriers of refractory epilepsy drug, although heterogeneous for the different seizures and etiologies is a group in which almost all the cases involve children who have suffered the adverse effects and summations of several antiepileptic drugs in combination therapy, and are surrounded by serious problems because it is a chronic and debilitating disease.[8]

It was observed that the treatment is usually medication, especially the treatment of associated drugs. In many cases, the frequency of seizures in the treatment can be decreased but not completely controlled. Thus, the emphasis in therapy aimed at the risk-benefit of the combination of drugs, considering that high doses of antiepileptic drugs may also cause damage.[22]

The health professional ability to identify types of seizures and choose the appropriate therapy, considering the clinical benefits and potential side effects, imply the effectiveness of treatment.[23] Therefore, knowing the aspects that permeate refractory epilepsy and availability of other therapies may contribute to a better attention to this group.

FINAL REMARKS

Refractory epilepsy drug is related to a variety of etiologies. Many of these causes are preventable. Thus, the practices focused on family planning, attention to prenatal care, childbirth and newborn care, when having quality, are of fundamental importance to the reduction of epileptic diseases.

Greater attention to children, care for falls and assistance to growth and development can contribute to a reduction of sequels and complications of the disease. It is known that the higher numbers are the epileptic seizures the greater the injury, so it is necessary that health professionals have a different look for this disease. It is stressed the importance of multidisciplinary look at a comprehensive care and not just professionals prepared to meet the aspects that permeate the epilepsies, but the availability of resources and accessibility to other therapies may contribute to a better attention to this group.

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Correspondence Address

Gleiciane da Silva Fonseca
Rua Hilton Guimarães, 01
Bairro Santos Reis
CEP 59141-225 – Parnamirim (RN), Brazil