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Dr. Víctor Soriano
In Memoriam

ORIGINAL

Non-epileptic paroxysmal disorders of childhood and adolescence

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ABSTRACT

Introduction: non-epileptic paroxysmal disorders constitute a heterogeneous group of polymorphic situations from a semiological Paint of view that are very frequent in pediatric ages.
Objective: to clinically and epidemiologically characterize pediatric patients with non-epileptic paroxysmal disorders admitted to the" Pepe Portilla "Provincial Pediatric Teaching Hospital of Pinar del Río in the years 2022 and 2023.
Method: observational, descriptive, cross-sectional study. Universe: 282 patients diagnosed with paroxysmal nonepileptic disorder. A simple of 237 patients was selected using simple randon sampling. Descriptive and inferential statistics were used.
Results: the female sex predominated in 57,8 %. The age groups of 1 to 3 years and 10 to 12 years represented 19,8 % and 18,6 % of the cases studied. A personal history of paroxysmal nonepileptic disorder was found in 12,2 %females and 9,7 % of males. A family history of paroxysmal nonepileptic disorder was identified. Epileptics seizures occurred in 12,2 % of girls and 9,7 % of boys. Vasovagal syncope accounted for 29,1 % of the patients studied.
Conclusions: It was evident that paroxysmal nonepileptic disorders of childhood constitute a clinical challenge for the pediatrician with a significant social impact.

Keywords: Paroxysmal Non- Epileptic Disorder; Children; Neurology; Syncope.

INTRODUCTION

Non-epileptic paroxysmal disorders (NEPDs) constitute a heterogeneous group of highly polymorphic situations from a semiological point of view in which intermittent attacks of very diverse clinical pictures occur that can mimic an epileptic seizure and are caused by physiological, psychological, and sometimes unknown processes. NEPDs are defined as episodes that mimic an epileptic seizure but are not. They generally occur abruptly and are short-lived, caused by cerebral dysfunction of various origins and, unlike epilepsy, are not due to excessive neuronal discharge.[1,2,3]

An epileptic seizure is defined as a clinical event, whether motor, behavioral, sensory, or perceptual, resulting directly from a change in brain electrical activity. The difference is very subtle and sometimes difficult to detect, hence the ease with which the two disorders can be confused·Treatises on epilepsy are numerous, but very few analyze TPNE. The list of NPETs that can mimic an epileptic seizure is enormous.[2]

The incidence in childhood is 10 times higher than that of paroxysmal epileptic disorders. Treatment options are limited, and most NPEs have a favorable outcome.[1,2,3]

The concern they cause in the patient and, especially, in family members who have witnessed the episode, is enormous. Even greater distress is caused by failing to diagnose them or mislabeling them as epilepsy when in fact they are not. Subjecting them to antiepileptic medication when they do not need it, to many unnecessary complementary tests, or to the limitations of epilepsy when they do not require them. All of this is part of the common mistakes that can be made when childhood NEPS are not analyzed in depth or are unknown. Paradoxically, it is less common for an epileptic disorder to be misdiagnosed as a non-epileptic paroxysmal disorder.[2,3]

Fifteen percent of children under the age of 15 have experienced some type of paroxysmal disorder. Many of these disorders are age-dependent and, in most cases, tend to disappear without sequelae in the early years of life.[2,3]

Paroxysmal events are a frequent reason for consultation, both in emergency departments and in outpatient clinics; they are mostly characterized by the sudden onset of neurological symptoms, in the form of motor disturbances, changes in tone, posture, eye movements, fluctuation or decrease in level of

consciousness, and behavioral disturbances. Sometimes, one of the differential diagnoses is the presence of an epileptic seizure or a non-epileptic paroxysmal disorder.[3]

In most cases, a thorough interview and physical examination will be sufficient to make an accurate diagnosis, with emphasis on a detailed description of the episode and possible precipitating factors. Most PNETs are benign, with typical ages of presentation and transient, requiring no treatment or additional studies. However, there are some cases that may be related to serious diseases.[4,5,6,7]

Despite this clinical need, there are few contemporary epidemiological studies that comprehensively characterize the clinical presentation, associated factors, and outcomes of PNEs in pediatric hospital populations, particularly in the Cuban context. Most of the evidence comes from different clinical realities and health systems, which limits the generalization of their findings and the optimization of local protocols.

Therefore, this study aims to clinically and epidemiologically characterize patients with TPNE admitted to the Pepe Portilla Provincial Teaching Pediatric Hospital in Pinar del Río between January 2022 and December 2023. As the first study of its kind in the province, its results seek to fill a critical knowledge gap by providing highly relevant local data that will enable the refinement of the diagnostic process, the optimization of resource use, and, ultimately, the improvement of the quality of care provided to these patients and their families.

METHOD

An observational, descriptive, cross-sectional study was conducted during the period from January 2022 to December 2023 at the Pepe Portilla Provincial Teaching Pediatric Hospital in Pinar del Río.

The universe consisted of 282 patients admitted with a diagnosis of non-epileptic paroxysmal disorder at the Pepe Portilla Provincial Teaching Pediatric Hospital in the province of Pinar del Río. The sample consisted of 237 patients admitted with a diagnosis of non-epileptic paroxysmal disorder, aged between one month and 18 years, admitted to the miscellaneous wards of the Pepe Portilla Provincial Teaching Pediatric Hospital in Pinar del Río, for which simple random sampling was used.

Patients aged between one month and 18 years of age were included, regardless of sex, Cuban nationality, residents of the province of Pinar del Río, admitted with a diagnosis of non-epileptic paroxysmal disorder to the hospital wards of the hospital and whose parents or guardians consented to take part in the study. Patients who did not meet one or more inclusion criteria were excluded.

The variables studied were age, sex, personal medical history, family medical history, and clinical classification of non-epileptic paroxysmal disorders.

A structured survey was administered to the patient's parents or guardians after obtaining their informed consent. The patient's individual pediatric hospital medical history was also used to obtain information.

The information obtained was stored in a database. Descriptive statistics were used for data analysis.

This research complied with the principles and recommendations for biomedical research involving human subjects adopted at the Eighteenth World Medical Assembly in Helsinki in 1964, where a series of principles and recommendations for physicians conducting research were adopted. These were subsequently revised by the 29th Assembly in Tokyo, the 35th Assembly in Vienna, and ratified at the 41st World Assembly held in Hong Kong in 1991.

RESULTS

The distribution of patients by year of study according to sex with TPNE shown in table 1 illustrates that the sample selected in the study showed a predominance of females, representing 57,8 % of the cases studied.

Table 1. Distribution of patients with PNET treated at the Pepe Portilla Provincial Teaching Pediatric Hospital by sex and year of admission

Sex	Year 2022		Year 2023		Total (n=237)	
	No.	%	No.	%	No.	%
Female	62	60,2	75	55,9	137	57,8
Male	41	39,8	59	44,1	100	42,2
Total	103	100	134	100	237	100

The 1-3 age group was found to be predominant, accounting for 19,8 % of the cases studied, followed by the 10-12 age group, accounting for 18,6 % (table 2).

Previous episodes of paroxysmal non-epileptic disorders (female: 12,2 %; male: 5,9 %) and epilepsy (female: 10,1 %; male: 7,1 %) were the most common personal medical histories among the patients studied (table 3).

Table 2. Distribution of the sample studied according to sex and age group

Sex	1m-11m		1st-3rd		4th-6th		7th-9th		10th-12th		13th-15th		16th-18th	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Female	15	6,3	23	9,7	19	8,0	21	8,9	18	7,6	29	12,2	12	5,1
Male	10	4,2	24	10,1	12	5,1	11	4,6	26	11	11	4,6	6	2,5
Total	25	10,5	47	19,8	31	13,1	32	13,5	44	18,6	40	16,9	18	7,6

Table 3. Prenatal, perinatal, and postnatal history of patients with PNET by sex

Personal medical history	Female (n=137)		Male (n=100)	
	No	%	No	%
High-risk pregnancy	15	6,3	10	4,2
Prematurity	12	5,1	8	3,3
Epilepsy	24	10,1	17	7,1
Genetic Disease	8	3,3	6	2,5
Previous episodes of TPNE	29	12,2	14	5,9
Static injuries to the central nervous system	5	2,1	3	1,3
Anemia	11	4,6	9	3,8
Neuropsychiatric disease	1	0,4	0	0
Cardiovascular Disease	2	0,8	0	0
Medication Ingestion	7	3,0	5	2,1
Central nervous system infection	9	3,8	11	4,6

The family medical history of patients with TPNE is shown in table 4. The most prevalent family medical histories in the study were a history of PNES in 12,2 % of females and 9,7 % of males, and epilepsy in 8,9 % of girls and 6,8 % of boys. Statistically significant results ($p<0,05$) showed an association between sex and family medical history in this study.

Table 5 shows the clinical classification of PNETs in the sample studied. Vasovagal syncope and hiccup spasms were predominant in 29,1 % and 15 % of the cases studied, respectively.

Table 4. Family medical history of patients with PNES according to sex

History	Female (n=137)		Male (n=100)	
	No	%	No	%
Family history of PNET	29	12,2	23	9,7
Epilepsy	21	8,9	16	6,8
Sudden death	4	1,7	5	2,1
CNS injury	6	2,5	4	1,7
Neuropsychiatric disease	7	3,0	8	3,4
Cardiovascular disease	15	6,3	11	4,6
Febrile crisis	16	6,8	12	5,1
Neurocutaneous disease	1	0,4	2	0,8
Migraine	10	4,2	6	2,5

Table 5. Clinical classification of PNETs in the study sample according to sex

Paroxysmal disorder	Female (n=137)		Male (n=100)		Total	
	No	%	No	%	No	%
Sobbing spasm	19	8,0	17	7,2	36	15,2
Vasovagal syncope	40	16,9	29	12,2	69	29,1
Night terrors	6	2,5	2	0,8	8	3,4
Tics	15	6,3	10	4,2	25	10,6
Shivering	6	2,5	3	1,3	9	3,8
Benign sleep myoclonus	9	3,8	5	2,1	14	5,9
Psychogenic crisis	10	4,2	6	2,5	16	6,8
Medications	6	2,5	5	2,1	11	4,6
Infant colic	8	3,4	7	3,0	15	6,3
Migraine	11	4,6	10	4,2	21	8,9
Cyclic vomiting	7	3,0	6	2,5	13	5,5

DISCUSSION

Non-epileptic paroxysmal disorders are a heterogeneous group of disorders that, due to their clinical semiology, can present as a neurological emergency when confused with epileptic seizures. They are very common in childhood. It is important to be familiar with them in order to identify them and take a rational approach.[6]

Fifteen percent of children under the age of 15 will suffer from paroxysmal disorders, distributed approximately as follows: 10 % non-epileptic paroxysmal disorders; 3-4 % febrile seizures; and 1-1,5 % epileptic seizures, half of which are single and half of which are recurrent.[8]

There are many classifications of non-epileptic paroxysmal disorders, which are classically divided into: cerebral hypoxia, sleep-related, extrapyramidal, psychiatric,

and a miscellaneous group. [2,7,9]This classification was used in this study.

The Cuban Statistical Yearbook showed a predominance of the female population in 2023 in the country, with an average population of 5 181 896 inhabitants.[10,11] A similar pattern for this demographic variable was evident in this research, with a predominance of females in hospital admissions for non-epileptic paroxysmal disorders. There are no statistical reports on the behavior of this disorder in this publication.

The 52nd edition of Cuba's Statistical Yearbook on Health presented indicators on the health status of the Cuban population for consultation and official reference. This document showed that the average population and population density by age group and province in 2023 in Pinar del Río in the pediatric age groups showed a predominance of the 10-14 age group with 29 571 inhabitants and the 15-19 age group with 28 942 inhabitants,[10] results that differ from those found in this study in relation to hospitalization for TPNE according to age groups.

A thorough and well-structured medical history allows the epileptic or non-epileptic nature of the paroxysmal phenomenon to be correctly defined in the vast majority of children.[8,9,11] The anamnesis of the paroxysmal episode must be thorough and detailed because, in general, the medical history leads to the diagnosis of these entities.[12]

In the literature reviewed, several authors agree on the existence of a personal history of some type of non-epileptic paroxysmal disorder in pediatric patients diagnosed with NPET and/or comorbidity, which is evident in the present study.[13,14] More frequently in patients with neurological deficits, in addition to having a higher incidence of epilepsy, they may also manifest paroxysmal disorders of a non-epileptic nature. Paradoxically, it is less common for an epileptic disorder to be misdiagnosed as a non-epileptic paroxysmal disorder.[2,15]

The prevalence of tic disorders comorbid with attention deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) in particular refers to rates of 0,3 % and 1,1 % respectively for Tourette's syndrome and 0,5 % and 1,1 % for tic disorder.[12]

In the study on the prevalence of sleep disorders in children with epilepsy conducted at the Niño Jesús University Hospital, PhD candidate Marta Furones García concluded that children with epilepsy and another comorbid neurological condition, especially ADHD and intellectual disability (ID), are more likely to have sleep disorders.[14]

Prenatal and perinatal factors also play an important role in tic disorders, as they can act as mediators in the clinical expression of symptoms, especially when combined with stress during pregnancy, the role of sex hormones, and postnatal stress factors. Factors such as exposure of the nervous system to high levels of dihydrotestosterone or other sex hormones during intrauterine development, the correlation between androgen levels during the prenatal stage and the severity of the clinical picture of tics, maternal illness during pregnancy, smoking, stress, perinatal hypoxia, and abnormal early experiences can act as risk factors, increasing the likelihood of developing the disorder. In addition, prematurity and low birth weight are involved, especially if accompanied by ischemic lesions of the brain parenchyma. Another risk factor is having a low Apgar score at 5 minutes and the mother requiring a greater number of visits and follow-up by the physician during the prenatal stage.[16,17]

Studies of twins and family members point to the existence of a genetic vulnerability to tic disorders. In Gilles de la Tourette syndrome (GTS), there is a family history of the syndrome or multiple chronic tics, with a correspondence rate of between 65 % and 90 %.[16,17,18]

The most common NPEs described in the scientific literature are hiccup spasms in childhood and syncope in adolescence.[1,2,4] Similar results were found in this study.

The result coincides with authors such as Anna Duat Rodríguez, who reports that the most frequent non-epileptic paroxysmal disorders are sob spasms in childhood and syncope in adolescence. It is important to be aware of them in order to identify them and take a rational approach.[6]

Episodes of breath-holding spells usually appear between 6 and 18 months of age and may persist longer or begin earlier. There are two types: pale and cyanotic. Pale breath-holding spells are vasovagal syncope caused by a neurologically mediated cardioinhibitory mechanism, triggered by painful situations, often by mild head trauma, especially in the occipital region, which causes an unpleasant surprise (panic). The episode can be confused with an epileptic seizure if it is not detected that it was preceded by trauma and if it is also followed by myoclonus. Recovery takes place within a short time. The episodes subside with age, although they can progress to vasovagal syncope.[7]

Cyanotic sobbing spasms are much more common than pale ones, and mixed forms exist. It is common to find family members with similar symptoms.[2]

Syncope is one of the most common causes of transient loss of consciousness and is one of the main reasons for visits to emergency services.[20] The causes vary depending on the person, hence the importance of individualizing each patient. A hereditary component has been estimated in 20 % of cases. This is observed in children, where one-third have a family history of syncope, while in the adult population, most cases do not have this history. Some children have associated iron deficiency anemia, the relationship of which to the disorder is unclear.[7,19,21,22] These results coincide with our study, which shows the presence of a family history of syncope as well as the presence of anemia in several patients.

Gómez Martin et al. in their article Neurological emergencies in pediatrics in relation to the etiologies associated with syncope report that autonomic forms, especially vasovagal syncope, account for up to 80 % of cases in this population.[23] This is consistent with the results of this study.

Vasovagal syncope results from a combination of excessive vagal tone, abnormal catecholamine response to stress, and increased venous content due to prolonged standing. More common in schoolchildren and adolescents, it can be frequent and, in general, familial.[2,3,4,15]

Currently, syncope accounts for 3 % of all pediatric emergency room visits and 1 % of all hospitalizations. Approximately 10 % of syncope cases are referred to a

specialist. This pathology has a bimodal peak incidence occurring between the ages of 10 and 30, with syncope mediated by neural mechanisms being the main cause.[21]

Syncope occurs at least once in 15 % to 50 % of children before the end of adolescence. It is most prevalent between the ages of 12 and 19 and is more common in females. The average age of onset of symptoms is 14 to 19 years, 14 in women and 12 in men. In an emergency department, syncope occurred in 0,4 % of consultations (0-16 years), predominantly in girls and at an average age of 10,8 years.[7]

The current study found similar results in relation to the behavior of the demographic variables of age and sex in syncope.

The recurrence of a syncope episode in the general population is estimated to be 1 in 6 000, with syncopal events in the previous year being reliable predictors.[21] This study did not evaluate the recurrence of these events.

Cardiac syncope can occur in any position, including lying down or sleeping, and especially during periods of intense exercise, emotion, or excitement.[1,15,21,22] It is important to investigate the family history of: death in young people, sudden unexplained death, or personal history of heart disease or arrhythmias. Loss of consciousness and seizures triggered by fear or shock, particularly if they occur during exercise, are highly suggestive of long QT syndrome. When accompanied by congenital deafness, they are part of Jervell and Lange-Nielson syndrome (autosomal recessive) or Romano Ward syndrome (autosomal dominant with incomplete penetrance). In cases of syncope in children and adolescents, where the criteria for neural mediation are clearly not met or there are doubts, a cardiological study should be performed, given the possibility of sudden death.[15,19,21,22,24,25] There were no patients with cardiac syncope in the sample studied.

CONCLUSIONS

The diagnosis of non-epileptic paroxysmal disorders in childhood is a clinical challenge for pediatricians due to their semiological heterogeneity, as they are a frequent cause of morbidity in infants and adolescents. This research showed the predominance of vasovagal syncope and breath-holding spells in our setting, with females having the highest incidence of the disorder with a family history of events of this nature. Non-epileptic paroxysmal disorders in childhood have a significant social impact.

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CONFLICT OF INTEREST

The authors declare that they have no financial or non-financial conflicts of interest.

AUTHOR CONTRIBUTION

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