

Characteristics of Paroxysmal Nonepileptic Seizures within Pediatric Population

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Abstract

Introduction: Paroxysmal nonepileptic seizures (PNES) represent suddenly appeared episodes of abnormal movements, sensation and/or cognitive experiences that resemble to epileptic seizures, but they are not the result of pathologic discharge of cortical neurons, and they have their origin in different causes of cerebral dysfunction.

Aim: To explain the terminology, determine the difference in etiology and clinical phenomenology of the disorder.

Material and methods: A retrospective study has included 53 patients of 1 to 67 months old, being hospitalized at the University Children's Hospital, Belgrade.

Results: The most common etiological cause of paroxysmal nonepileptic seizures within the children under 7 years old are affective respiratory crisis, which was also detected in 30,2% patients, followed by gastroesophageal reflux with in 15,1%, hypoglycemia 13,2%, dehydration and electrolyte misbalance 9,4%, benign paroxysmal vertigo 7,5%, abdominal colic, intoxication, postvaccinal reactions in 5,6%. The highest frequency of nonepileptic seizures is during the period from 1 to 5 months of age (30,2%).

Conclusion: The most optimal term for this disorder is paroxysmal nonepileptic seizures, and knowledge of the etiology and symptoms of these disorders are a condition for good differential diagnosis of epilepsy and paroxysmal nonepileptic seizures.

Keywords: *Paroxysmal nonepileptic seizures; Terminology; Etiology*

Introduction

Within the pediatric population, there have often been seizures with numerous symptoms and clinical signs that can look like epileptic seizures. These conditions could also be a consequence of other disorders [1,2].

Paroxysmal nonepileptic seizures (PNES) represent suddenly appeared episodes of abnormal movements, sensation and/or cognitive experiences that resemble to epileptic seizures, but they are not the result of pathologic discharge of cortical neurons, and they have their origin in different causes of cerebral dysfunction. Around 20% of patients sent to neurologists have PNES, with the crises of consciousness and doubts to epileptic seizures [3].

The terminology of this disorder has always been an issue. Since the ancient times, nonepileptic seizures have been recognized as a form of hysteria. From Hippocrates description (400 BC) and Atrous (200 BC), it can be seen that this disorder has been seen as a psychogenic disorder [4]. Many years later, at the end of XIX century, Charcot was the first to describe nonepileptic seizures as a clinical disorder, calling it "hysteria epilepsy" and "epileptic form hysteria" [2]. Earlier terms, as pseudo seizures and hysterical seizures, have been justifiably replaced since their pejorative connotations, implied for symptoms to be false ones, not real [5]. However, today it is known that nonepileptic seizures are not only of psychogenic origin, but they can be the result of some physiological and organic disorders [1,2].

It has been noticed that there have been differences in etiology, clinical image and outcome of PNES when children of different age [6] are to be compared, and also the frequency of some of disorders within PNES is not the same [2].

Early recognition and a suitable treatment of nonepileptic seizures can reduce in largely damage caused by aniatrogenic way. PNES diagnose has been relied on differentiation from epileptic seizures by documenting a typical seizure in video-EEG monitoring [7], i.e. using suggestive provocative methods, if it has been necessary [8]. A precise identification of PNES is necessary, since an early diagnose contributes to better outcome of early application of psychotherapeutic procedures [6]. Opposite of it, a late recognition of PNES, besides a bad outcome, leads to necessary application of antiepileptic diagnostic medications for a longer time period and on treatment of PNES, under a wrong diagnose of epilepsy, can be spent to 100-900 millions of dollars [9].

The aim of the work is, with a special emphasis onto the terminology of the very disorder, to determine the difference in etiology and clinical phenomenon of paroxysmal nonepileptic seizures within children up to 7 years old, which would contribute to different diagnoses of epileptic and nonepileptic seizures.

Materials and Methods

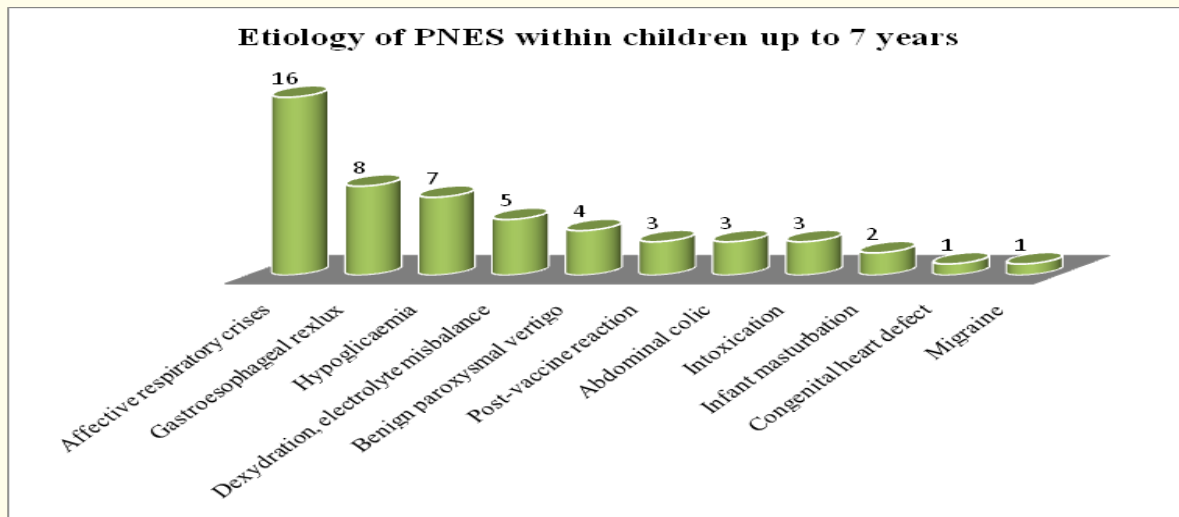
By a retrospective study, it has been included 53 patients in the work being examined, treated and medically followed for at least six months in Department of Neurology of the University Children's Hospital in Belgrade, in the period from the beginning of 2008. Until the end of 2010, whose problems have been initially understood as neurological dysfunction, where it has not been determined the existence of PNES epilepsy. The etiology has been examined related to the gender and age. There has been 29 boys in the group (55%) and 24 girls (45%). According to the age, they have been divided into patients up to 2 years old (62.3%) and patients from 2 to 7 years (37.7%). The youngest patient had 1 year and the oldest has been 67 months old. The average age has been 20 ± 1 months.

It has been analyzed the clinical picture, neurological medical finding and the results of laboratory analyses within all patients. It has been done video (vEEG) or holter-EEG (hEEG) to all patients. During the examination, patients who have been confirmed the epilepsy during diagnostic procedures have not been included, either the patients who have been diagnosed with febrile convulsions.

The methods of descriptive statistics have been applied. The results have been graphically shown in column diagrams and frequency histograms.

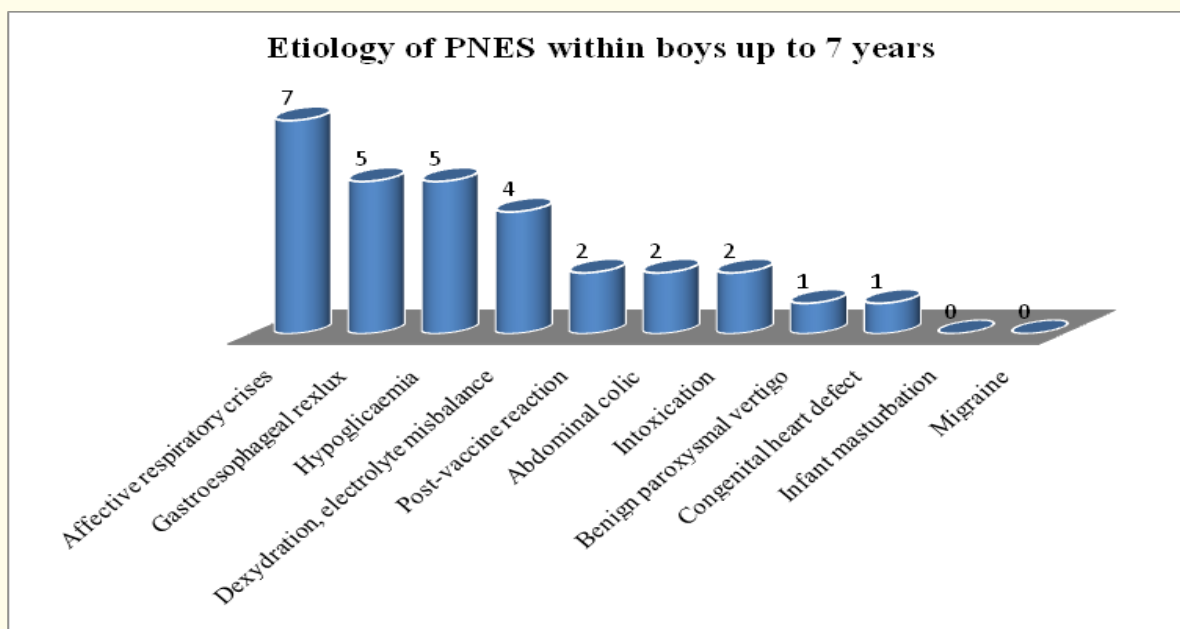
Results

The analyze show that affective respiratory crises are the most often etiology cause of paroxysmal nonepileptic seizures within children up to 7 years. They have caused PNES with 30.2% (16 patients), with a note that with 3.8% (2) have been together with the Sudden Infant Death Syndrome-SIDS/Acute Life Threatening Event-ALTE. The second place in etiology has been taken by Sandifer's syndrome, where gastroesophageal reflux has caused PNES within 15.1% of patients (8), and right behind it, in the third place are hypoglycemia's. The low value of glucose in blood is responsible for 13.2% (7) cases of PNES. Dehydration and electrolyte imbalance have brought to PNES with 9.4% (5), and benign paroxysmal vertigo with 7.5% of patients (4). Abdominal colic has been confirmed in 5.6% (3), and also intoxication in 5.6% (3), as well as post-vaccine reactions in 5.6% (3). Two of three cases of intoxication have been verified (-valproic acid and -xilometazoline). Infant masturbation has been diagnosed in 3,8% of patients (2). Migraine and congenital heart defect have caused in 1.9% of cases paroxysmal nonepileptic seizures (1). Benign paroxysmal torticollis has not caused in any case a particular PNES, but it has participated in 3.8% of patients (2) in etiology mutually with gastroesophageal reflux and benign paroxysmal vertigo (Graph 1).



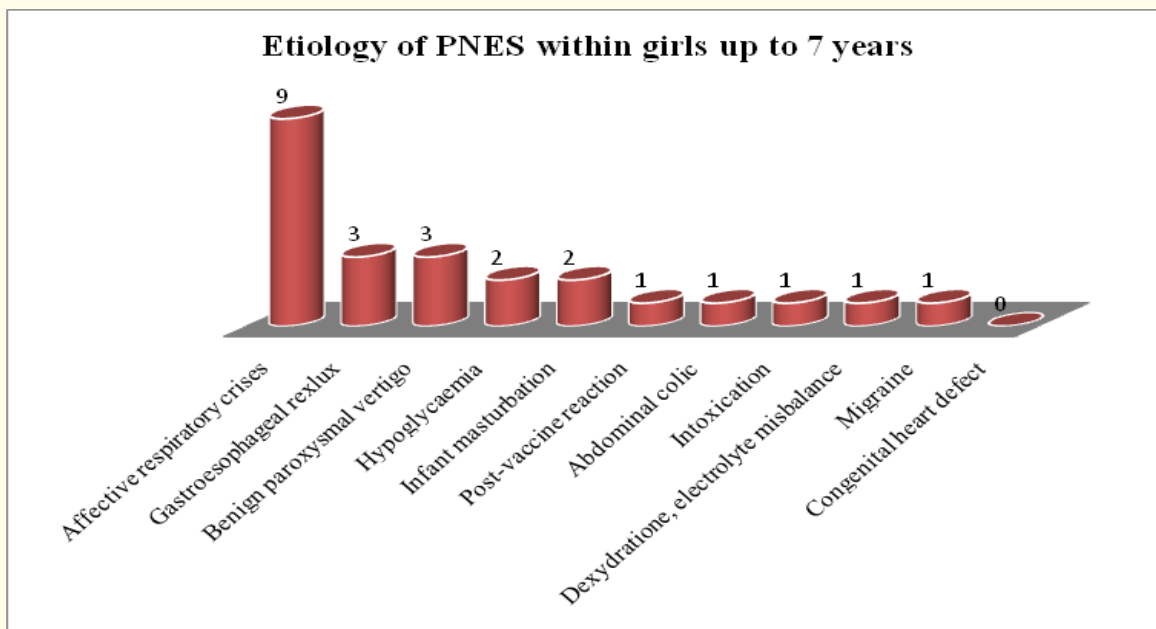
Graph 1: Etiology of PNEN within children up to 7 years.

The analyze of PNES etiology within 29 boys being up to 7 years old has shown that affective respiratory crises have been presented within 24.1% of cases (7), gastroesophageal reflux within 17.2% (5), both as hypoglycemia in 17.2%. Dehydration and electrolyte misbalance within 13.8% (4), post-vaccine reaction in 6.9% (2), abdominal colic in 6.9% (2) and intoxication within 6.9% of patients (2). Benign paroxysmal vertigo has been currently presented 3.4% of patients (1), just as congenital heart defect in 3.4% (Graph 2).



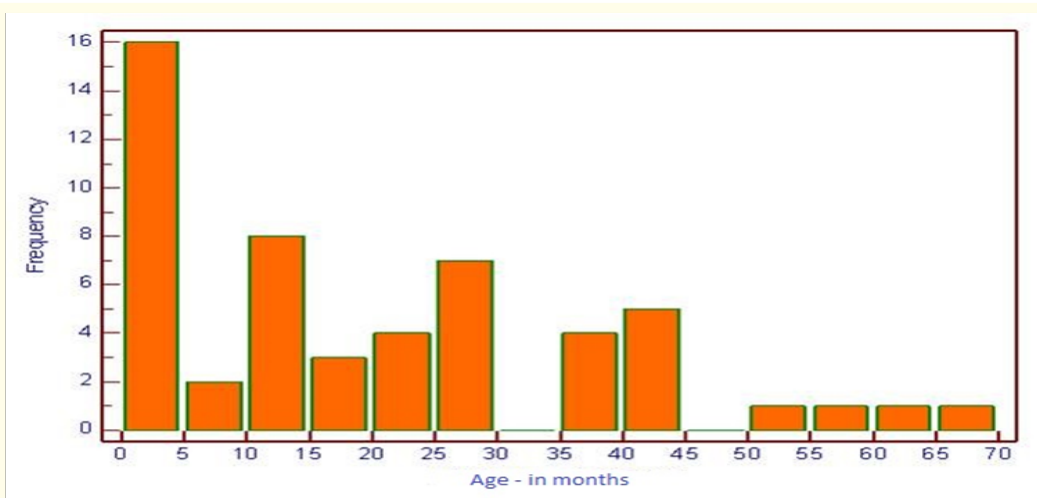
Graph 2: Etiology of PNES within boys up to 7 years.

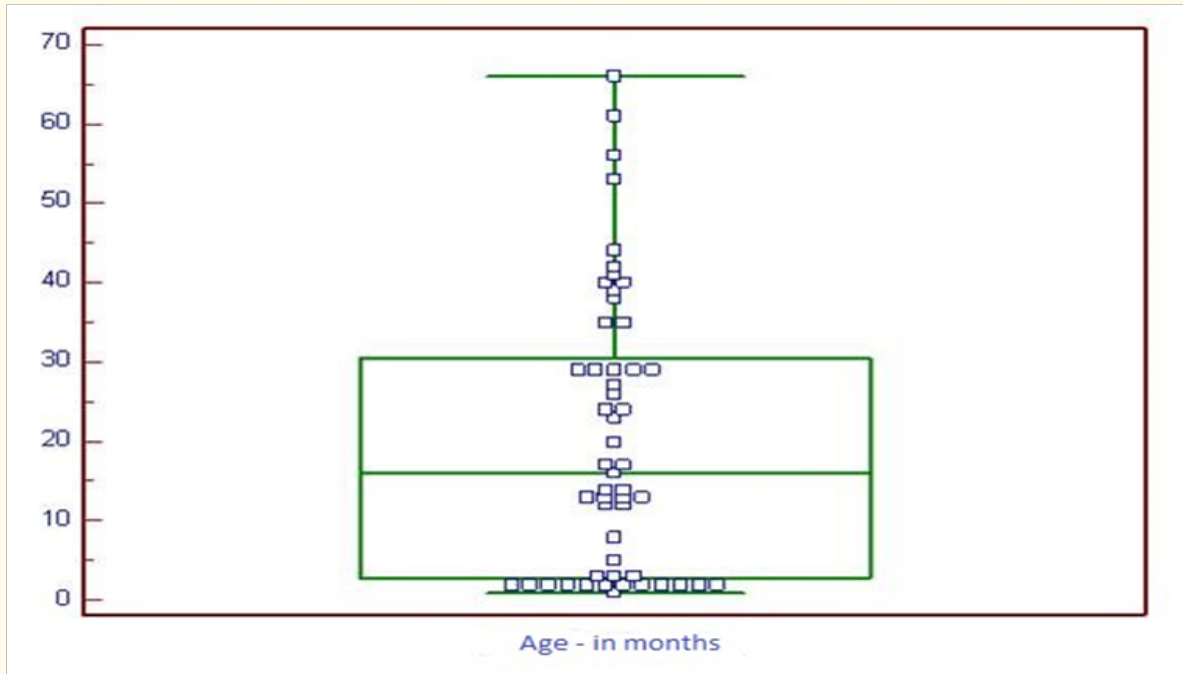
The analyze of PNES etiology within 24 girls being up to 7 years old has shown that affective respiratory crises have been definitely in the first place. They have been diagnosed in 37.5% of cases (9). The second place share gastroesophageal reflux (12.5%) and benign paroxysmal vertigo (12.5%), being presented with 3 girls. Hypoglycemia has been discovered in 8.3% of the examinees (2), and infant masturbation in 8.3%, as well. Dehydration and electrolyte imbalance (4.2%), intoxication (4.2%), post-vaccine reaction (4.2%), abdominal colic (4.2%) and migraine (4.2%) have been presented in one patient (Graph 3).



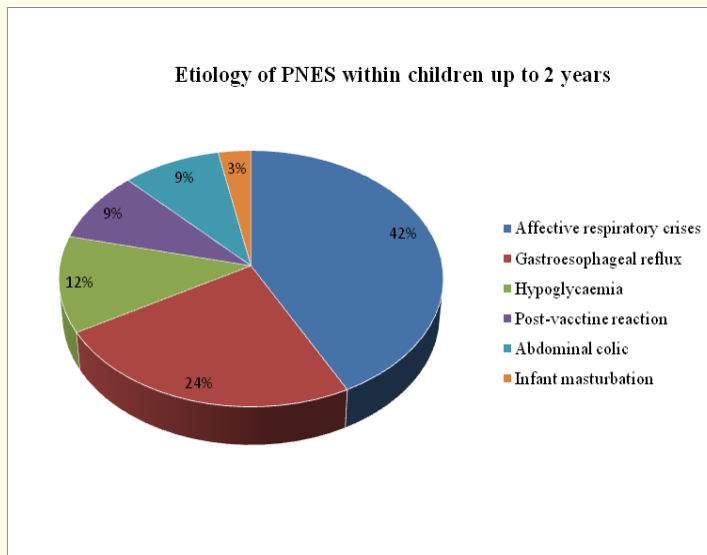
Graph 3: Etiology of PNES within girls up to 7 years.

By analyze of PNES distribution compared to the age, it has been noticed that the frequency of nonepileptic seizures has been the highest in the period from 1 to 5 months of life. In this group there has been even 30.3% of patients being that age (16). The frequency of PNES in the period from 5 to 45 months has been gradually reduced, with less or more deviations, so as the frequency of seizures from 45 to 72 months has been the smallest in this group (Histogram 1. Box and Whisker plot 1).

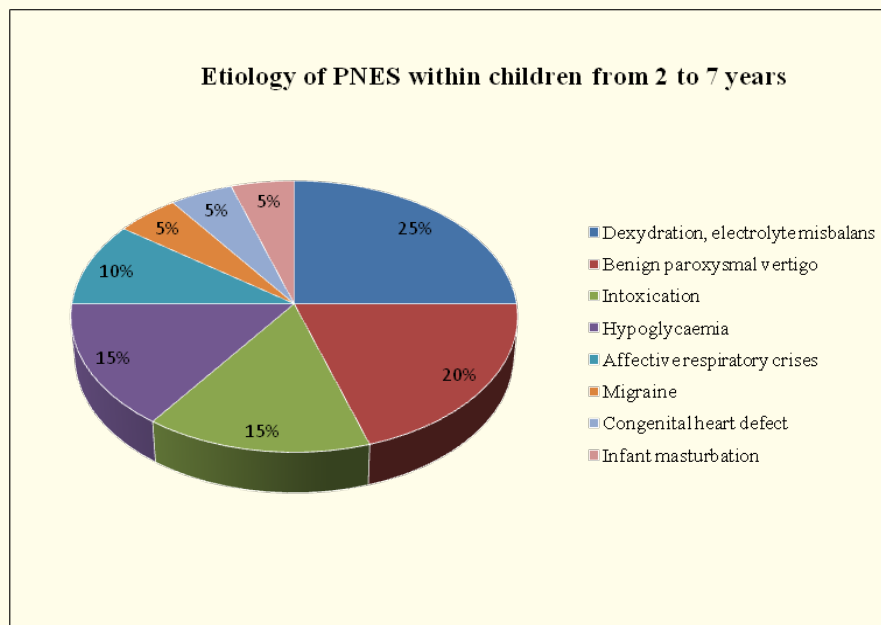




Byanalyze of PNES etiology distribution compared to the age, it has been noticed the difference in etiology within children up to 2 years and children from 2 to 7 years of life. Children being younger than two years (33 children, 62,3% of the total sample), PNES has been caused in 48% of cases by the affective respiratory crises (14 children); in 24% of the cases the reason has been gastroesophageal reflux (8 children). Older children from 2 to 7 years (20 children, 37,7% of the total sample), dehydration and electrolyte misbalance have surpassed (5 children, 25%), benign paroxysmal vertigo (4 children, 20%), intoxication (3 children, 15%) andhypoglycemia (3 children, 15%). The other etiology factors have been presented in a smaller part (Graphs 4. and 5).



Graph 4: Etiology of PNES within children up to 2 years.



Graph 5: Etiology of PNES within children from 2 to 7 years.

Discussion

In 1966th Dr. Steven Schachter [10] made a survey among American epileptologists regarding what term would be the most appropriate for this kind of disorder. Among several pejorative and inadequate terms as: “hysterion-epilepsy”, “hystericalseizures”, “pseudo-epileptic seizures”, “non-epileptic pseudo-seizures”, the majority responded that the most optimal term would be “nonepileptic seizures”. All previous terms had significantly humiliating connotation, and they had been incorrectly related to the pathophysiology of the disorder itself. The precision and width of the term “nonepileptic seizures” allowed to be included in one term both psychogenic and organic disorders of behavior [11]. The term “psychogenic seizures” is a narrow term and represents a sub-set of nonepileptic seizures, emphasizing their psychological origin. Since this term can be misinterpreted and think on epileptic seizures caused by psychological factors, it has been found a solution by an agreement and adoption of the term “psychogenic nonepileptic seizures” [12].

Mistakes in diagnoses of nonepileptic seizures conditions can have a line of harmful consequences for a child, firstly, unnecessary taking of antiepileptic medications for several months or years. Concerned parents shall often limit “a child with epilepsy” in numerous activities and unnecessarily bind one’s real abilities and creativity. Therefore, it is very important from an expert medical view that in cases when there is a dilemma whether it is a word on epileptic or nonepileptic seizures, these conditions to be diagnosed as “unclear-unclassified-paroxysmal seizures”. Clinical following and a repeated clinical estimation after a certain time, shall allow a correct diagnoses, where a haste and wrong epilepsy diagnoses shall be avoided [13]. Around 10% of children in population have nonepileptic seizures that are multiply often compared to epileptic ones [14]. Even 20-25% of psycho-neurologically normal children and even 60% of children with mental retardation being sent to evaluation of paroxysmal disorders, have PNES [15].

To have an adequate diagnosis of differential epileptic seizures and nonepileptic ones, it is needed to know well the etiology and clinical phenomena of seizures. In an adopted Table I, it has been given etiological classification of nonepileptic seizures [2,16].

Physiological and organ disorders within children are very often a cause of nonepileptic seizures. On the other side, with elderly ones in the etiology of PNES, we meet psychogenic and cardiovascular disorders [17]. The group of 53 patients being analyzed, consisted of children age up to 7 years, and according to it, physiological and organ disorders have been dominant ones.

Affective respiratory crises have been the most presented etiology factor of PNES in the group. They have caused paroxysmal nonepileptic seizures within 30.2% of patients. Around 20-30% of parents of those children also had affective respiratory crises [18]. Breathing always stops in expiratory ones. There are different dark blue, cyanotic and pale, acyanotic crises. The cyanotic ones are three times more often and they appear after anger, frustration or fear; a child starts to cry and scream. The one becomes blue, weak and loses consciousness. The seizure lasts for a few seconds and after it, the child becomes conscious and behaves well, the one is tired and falls into sleep fast [19]. Pale, acyanotic crises become since sudden, unpleasant irritation, it often hurts, without previous crying. The one is pale, stiffed, opisthotonus and colic spasms of arms can also appear, and stiffeyeballs. The condition lasts for several seconds and the child sleeps after it and wakes up without any obstacles [20]. In two patients (3.8%), affective respiratory crises have been associated with a syndrome of avoid death. This syndrome is characterized by breathing disorder (apnea), change of skin color (cyanosis and pale), muscle hypotonic, suffocation, increased saliva, conscious disorder and bradycardia [21,22]. In the second place in PNEN etiology within 53 children up to 7 years old, it has been found Sandifer's syndrome where gastroesophageal reflux has caused seizures in 8 patients (15.1%). Gastroesophageal reflux (GER) is a disorder of lower esophageal sphincter of infants and small children that allows returning of a gastric content into an esophagus. It has been manifested most often clinically in a form of vomiting or food pouring without steams (1). Children with GER are in most cases sent to a gastroenterologist, but in more difficult cases since additional syndromes, they are sent to a neuropediatrics, under suspicion of seizures or a syndrome of avoided infant death. Acausal-consequence connection of gastroesophageal reflux and the syndrome of avoided infant death is not clear yet, and published GER frequencies up to now in apnea are very variable, from low [23-25] to high ones [26]. GER in infants in the first months of a life has been followed often by over crying "with no reason" [27,28]. Association of GER, hiatus hernia and torticollis makes Sandifer's syndrome, followed by a line of other paroxysmal changes: irritation and attacks of dystonic body movements and extremities [29]. Torticollis, but without shortening of sternocleidomastoid muscle in this syndrome, has been present since one's birth.

Hypoglycemia crises have been present in 7 patients (13.2%). The level of glucoses in blood is low enough for defining of hypoglycemia, it can be different for persons of different ages, in different circumstances, and thus it is sometimes a subject of controversy. The majority of healthy adult persons keep the glucoses level above 4.0 mmol/l, and one can develop the symptoms of hypoglycemia when glucoses falls under 4 mmol/l [30]. Normal glucoses scope in blood with children is an issue. Since there is knowledge that the brain of an infant and a small child can use alternative sources of energy, the glucoses level for defining hypoglycemia should be lower than in adults [31]. The experts are still discussing on the significance and risk of such level. In diagnoses purpose, hypoglycemia in children has been defined as a condition that has been followed by concentration of glucoses in blood 2.2 mmol/l and less [32]. Glycemia under given values can cause PNES.

Dehydration and electrolyte misbalance in infants and small children appear most often since the abundance of vomiting or hyperventilation. Metabolic alkalosis leads to the reduction of the level of ionic calcium in blood appearing then, and it results in carpopedal spasm and positive Chvostek's sign (but it can also be present in healthy children) [33]. Laryngospasm can also appear and consciousness has been kept [34]. This condition has been the cause of PNES in 5 patients or in total of 9.4%.

Benign paroxysmal vertigo (BPV) appears both with boys and girls from 1st to 5th year of their life. The seizures appear suddenly, without provocations. A child is terrified and the one describes that the environment spins around him/her and has a feeling of falling down [35]. The consciousness has been kept, but pale can appear, vomiting and sweating. The number of seizures has been varied up to 5 in a month, and they last for several seconds to 5 minutes [16,33]. Since the child falls, this condition looks like an epileptic seizure. In the examined group, BPV has caused nonepileptic seizures in 4 patients (7.5%).

Abdominal colic and constipation have been in the base of PNES diagnoses in 3 cases (5.6%). This condition can be associated with stereotype movements of the child (1), where epileptic seizures have been stimulated.

Nonepileptic seizures appeared after intoxication and they are most often motoric [36], and they manifest clinically most often by intensified tonus, hyperextension of a head and opisthotonus, with consciousness. Oculogyric crises are frequent [37]. These conditions have been caused by psychotropic medications, such as phenothiazine, butirofenon, metoclopramide and similar, and in the examined group,

two cases of intoxication out of three have been solved (5.6%). The causes have been valproin acid and xilometazoline. Post-vaccination reactions have been responsible for PNES appearing, also in three patients (5.6%). For one post-vaccination reaction, it can be said to appear after DTP vaccine, with a certainty from anamnesis data, while the other two cannot be precisely brought to a certain vaccine. Until now, there are no precise and valid scientific proofs that would tightly connect paroxysmal nonepileptic seizures with application of any of the vaccines, while on the other side, application of a new combination vaccine against measles, mumps, rubella and varicella can lead to febrile convulsions [38].

Infant masturbation is a very interesting problem being dealt by scientists a hundred years ago. Masturbation or sexual self-satisfaction appears in all ages, but it is seldom in small children, especially within infants. A British pediatrician, defined masturbation as a form of physiological behavior in 1915 [39], even in puritan England when this appearance was considered a sexual disorder. Bakwin [40] published in 1952 the first three cases of masturbation in three girl infants. Twenty years later, the same author published his results of a prospective study of his two “female patients”, where there was a spontaneous stoppage of masturbation episodes before their fifth year. He described infant masturbation as rubbing of his legs with hands or rubbing his body to an object that was followed by moaning, redness in face and this brought to a condition that could be orgasm, where relaxation followed, pale, sweating and sometimes deep sleep [41]. By further investigation of this problem, it has come to a discovery of a line of other clinical characteristics and appearances. They are fixation or deviation of a look into a point, absence, coital pelvis movements, preference of different positions (laying, sitting, standing in a lap/arm of an adult person). Some children have masturbation seizures at certain time (e.g. before sleeping), while others have regardless of the day time. Seizure lasting varies up to several minutes and frequency of certain ones up to a dozen a day. Knowing and recognizing of these frequent signs by pediatrics in a primary health protection, but also a specialist neuropsychiatry where these children are usually sent to, shall help in a regular diagnosing and it shall exclude a need for voluminous unnecessary clinic examinations [42]. Infant masturbation in the group being examined has been diagnosed in two girls (3.8%), while within the boys has not, and this is appropriate to current knowledge on this condition [43,44].

Migraine in older children is a relatively frequent cause of PNES and in the examined group only one patient has been diagnosed in it (1.9%). The diagnosis is usually easily made, with anamnesis assistance on migraine diagnoses in certain intervals. There is an aura preceding the pediatric migraine consisted of visual, sensor and motor symptoms, with or without vomiting or stomach pain [16].

Congenital heart defects seldom lead to paroxysmal nonepileptic seizures and pathophysies similar to other cardiovascular disorders (Table I). One patient (1.9%) has had this disorder.

Physiological and Organic Disorders	Psychogenic Disorders
Cardiovascular disorders	Converse disorders
<ul style="list-style-type: none"> • Syncope 	
<ul style="list-style-type: none"> • Affective respiratory crises 	Dissociative disorders
<ul style="list-style-type: none"> • Apnea 	
	Anxiety disorders
Paroxysmal movement disorders	
<ul style="list-style-type: none"> • Spasm and tremor 	Posttraumatic Stress Syndrome
<ul style="list-style-type: none"> • Paroxysmal choreoathetosis 	
<ul style="list-style-type: none"> • Benign myoclonus 	Somatisation disorders
<ul style="list-style-type: none"> • Spasms nutans 	
<ul style="list-style-type: none"> • Benign paroxysmal torticollis 	Psychoses
<ul style="list-style-type: none"> • Pills poisoning 	
<ul style="list-style-type: none"> • Tic disorders 	Munchausen Syndrome

• Sandifer Syndrome	
• Stress seizures	and other similar disorders
• Stereotype movements	
• Infant masturbation	
• Disorders of motet intestine and constipation	
Disorders related to sleeping (Parasomnia)	
Migraine and migraine equivalents	
Benign paroxysmal vertigo	

Table 1: Etiology of PNES within children up to 7 years.

Benign paroxysmal torticollis has been detected in two patients, but together with gastroesophaegal reflux in one case, and in the other with benign paroxysmal vertigo. It has been followed by a line of clinical changes: sleeping state, rolling or deviation of eyeballs in the beginning of seizures, aggressiveness, painful crying, strong sweating, headache, dizziness, and ataxia, refusal to walk or walk skidding [45-47].

Conclusion

The most acceptable name for this kind of disorder is “paroxysmal nonepileptic seizures”. This term does not limit in etiology either, symptoms and it does not contain any pejorative characterization. PNES etiology in children up to 7 years is very complex, but there are some conditions that cause nonepileptic seizures more frequently and they are: affective respiratory crises, as the most often state, then gastroesophageal reflux and hypoglycemia crises. Knowing of these entire etiology factors well, the ones that lead to PNES can contribute to differential diagnoses of epilepsy and nonepileptic seizures, where the unwanted effects are prevented in patients and family, and they also reduce the costs of health institutions.

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