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Etiology and Neuruological Evaluation of Non-Cardiogenic Syncope in Children

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Aim: The aim of this study was to evaluate the clinical characteristics, etiology, and the value of neurologic investigations in the diagnosis of syncope in children.
Material and Method : The records of 218 patients (124 female, 94 male; mean age: 12.8 ± 4.1) admitted to our pediatric neurology outpatient clinic between January 2016 and December 2018 were retrospectively reviewed for age, sex, number of syncopal events, history of syncope, results of neurological diagnostic tests. Patients with known epilepsy, no eyewitness during syncope, and patients with structural heart disease or arrhythmia on cardiologic examination were excluded.
Results: Eighty six (39.4%) patients had one syncopal event, 80 (36.7%) patients had two, 31 (14.2%) patients had three and 21 (9.6%) patients had more than three syncopal attacks. Prodromal findings before syncope were present in 80 % of patients, urinary incontinence during syncope were present in 6%, motor findings were present in 18.3%, postsyncopal findings were present in 14.2%. Twenty-one (9.6%) patients had a family history of epilepsy. Electroencephalography (EEG) was performed in all patients and revealed epileptic discharges in 19 (8.7%) of them. Neuroimaging studies were performed in 97 (44.4%) patients and revealed incidental white-matter lesions in 10(10.3%), mega sisterna magna in 6(6.1%), asymmetry of the lateral ventricles in 5(5.1%), temporal lobe arachnoid cyst in 2(2%), hydrocephalus in 1 (1%), dysgenesis of corpus callosum in 1 (1%), eosinophilic granuloma in 1 (1%) and leukodystrophy in 1 (1%). The etiology was neurally mediated syncope in 181 patients (83%), convulsive/epileptic syncope in 19 patients (8.7%), psychogenic pseudosyncope in 16 patients (7.3%), metabolic in 1 patient (1%), drug induced syncope in 1 patient (1%).
Neurally- mediated syncope (NMS) was further grouped as vasovagal (n=172), reflex-anoxic (breath holding) (n=6), situational(post micturition syncope , n=6). It was seen that 79.7% of vasovagal syncopes were caused by postural orthostatic condition and 20.3% were caused by pain stimulation.
Conclusion: The history and comprehensive physical examination in children are in fact largely sufficient in the differential diagnosis of non-cardiogenic syncope. Although the contribution of neuroimaging to the etiology and diagnosis is very limited, electroencephalography may be helpful in diagnosis and treatment management in selected cases.

Key Words: *Child, Non-Cardiogenic Syncope , Neuruological Evaluation*

Çocuklarda Non-Kardiyojenik Senkopların Etiyolojisi ve Nörolojik Değerlendirmesi

Amaç: Dr.Sami Ulus Kadın Doğum,Çocuk Sağlığı ve Hastalıkları Eğitim Araştırma Hastanesi Çocuk Nöroloji Kliniğine Ocak 2016- Aralık 2018 tarihleri arasında senkop nedeniyle yönlendirilen hastaların dosya kayıt bilgileri geriye yönelik olarak değerlendirilerek yapılan nörolojik incelemelerin tanısal değerinin belirlenmesi amaçlandı.

Yöntem: Hastaların yaş, cinsiyet, öykü, elektroensefalografi, nörogörüntüleme bulguları geriye dönük olarak incelendi. Bilinen epilepsi tanısı olan hastalar, senkop esnasında görgü tanığı olmayanlar ve kardiyolojik incelemede yapısal kalp hastalığı veya aritmi saptanan hastalar değerlendirme dışı bırakıldı.
Bulgular: Yaşları 1 yaş-17,9 yaş (124 kız, 94 erkek, ortalama yaş; 12,8 ± 4,1) olan 218 çocuk hasta değerlendirildi. Senkop öncesi prodromal bulgular hastaların %79.8'inde, senkop esnasında idrar inkontinası %6'sında, motor bulgular % 18.3'ünde, postsenkopal bulgular % 14.2'sinde mevcuttu. Yirmibir(%9.6) hastada ailede epilepsi öyküsü vardı. Hastaların tamamına elektroensefalografi (EEG) incelemesi yapıldı ve bunların 19'unda (%8.7) epileptik aktivite görüldü. Nörogörüntüleme yapılan 97 (%44.4) hastanın 10'nunda(%10.3) rastlantısal nonspesifik beyaz cevher lezyonları, 6'sında (%6.1) mega sisterna magna, 5'inde(%5.1) lateral ventriküllerde asimetri, 2'sinde(%2) posterior terminal miyelizinasyon bulguları, 2'sinde(%2) temporal yerleşimli araknoid kist, 1'inde(%1) hidrosefali, 1'inde(%1) korpus kallozum disgenezisi, 1'inde(%1) eozinofilik granülom, 1'inde(%1) lökodistrofi saptandı. Senkop nedenleri sırasıyla nöral aracılı senkop (n=181), konvülzif senkop (n=19), psikojenik pseudosenkop (n=16), metabolik senkop (n=1), ilaç-madde kullanımı ilişki (n=1) senkop olarak belirlendi. Nöral aracılı senkoplar kendi içinde vazovagal senkop (n=172), refleks-anoksik (katılma nöbeti) senkop (n=6), miksiyon ilişkili durumsal senkop (n=6) olarak gruplandırıldı. Vazovagal senkopların %79.7'sinin postural ortostatik durum ile, %20.3'ünün ağrı-acı uyarısı ile meydana geldiği görüldü.

Sonuç: Çocuklarda ayrıntılı fizik muayene ve öykü esasında non-kardiyojenik senkopların ayırıcı tanısının yapılmasında büyük ölçüde yeterlidir. Nörogörüntülemenin etiyoloji ve tanı tespitine katkısı oldukça sınırlı olmakla birlikte seçilmiş vakalarda elektroensefalografi tanıda ve tedavi yönetiminde fayda sağlayabilir.

***Anahtar kelimeler**: Çocuk, Non-kardiyojenik Senkop, Nörolojik Değerlendirme*

Introduction: Syncope is defined as a sudden, self-limited loss of consciousness and postural tone followed by spontaneous and complete recovery without any neurological sequelae(1). It is one of the most common paroxysmal disorders in children and adolescents, and approximately 30-50% of children have experienced at least one syncope in their lives till the adolescent period. The common unifying mechanism is transient global hypoperfusion of the brain. The three major causes of syncope in children are neurally mediated syncope, cardiovascular syncope and other non-cardiovascular causes. The most common cause of syncope in adults is cardiac causes, whereas neural mediated syncopes are the most common cause of syncope in childhood. Neuronal mediated syncope is often confused with epileptic seizures in children. On the other hand, seizures can mimic syncope in upto 5% of cases(2). It should be kept in mind that syncope is not a disease itself but a symptom of an underlying disorder.Hence, all children with syncope require assessment to exclude an underlying life-threatening cardiac or non-cardiac disorder. The etiology and classification of childhood syncope are summarized in Table 1. The aim of this study was to evaluate the clinical characteristics, etiology, and the value of neurologic investigations in the diagnosis of syncope in children.

Material and Method : The records of 218 patients (124 female, 94 male; mean age: 12.8 ± 4.1) admitted to our pediatric neurology outpatient clinic between January 2016 and December 2018 were retrospectively reviewed for age, sex, number of syncopal events, history of syncope, results of neurological diagnostic tests. Patients with known epilepsy, no eyewitness during

syncope, and patients with structural heart disease or arrhythmia on cardiologic examination were excluded. The nausea, epigastric discomfort, visual blurring, dizziness, sweating, hyperventilation, pallor, cold skin were defined as prodromal symptoms. Tonic spasms of muscles, focal or generalized clonic contractions, uprolling of eyes and involuntary micturition were defined as seizure- like activity.

Results: A total of 218 patients (124 female, 94 male; mean age: 12.8 ± 4.1) were included in the study. Eighty six (39.4%) patients had one syncopal event, 80 (36.7%) patients had two, 31 (14.2%) patients had three and 21 (9.6%) patients had more than three syncopal attacks. Prodromal findings before syncope were present in 80 % of patients, urinary incontinence during syncope were present in 6%, motor findings were present in 18.3%, postsyncopal findings were present in 14.2%. Twenty-one (9.6%) patients had a family history of epilepsy. Demographic and clinical characteristics are summarized in Table 2. Electroencephalography (EEG) was performed in all patients and revealed epileptic discharges in 19 (8.7%) of them. Sixty-three percent of these epileptic discharges were generalized epileptiform activity and 37% were focal epileptiform activity. Seventeen of 19 patients with epileptic discharge in EEG were diagnosed with epilepsy and antiepileptic drug treatment was initiated. Neuroimaging studies were performed in 97 (44.4%) patients and revealed nonspecific white-matter lesions in 10(10.3%), mega sisterna magna in 6(6.1%), asymmetry of the lateral ventricles in 5(5.1%), temporal lobe arachnoid cyst in 2(2%), hydrocephalus in 1 (1%), dysgenesis of corpus callosum in 1 (1%), eosinophilic granuloma in 1 (1%) and leukodystrophy in 1 (1%). The etiology was neurally mediated syncope in 181 (83%) patients, convulsive/epileptic syncope in 19(8.7%) patients , psychogenic pseudosyncope in 16 (7.3%) patients , metabolic in 1(1%) patient , drug induced syncope in 1 (1%) patient. Neurally- mediated syncope was further grouped as vasovagal (n=172), reflex-anoxic (breath holding) (n=6), situational (post micturition syncope , n=3) (Table3) . It was observed that 79.7% of vasovagal syncopes were caused by postural orthostatic condition and 20.3% were caused by pain stimulation. Younger children were more likely to have a breath-holding spells ($P < .0001$), whereas older children were more likely to have NMS ($P < 0.01$) or a psychogenic cause ($P = 0.04$). Recurrence of the syncopal events and prodromal findings were associated with the neurally mediated syncope ($p= 0.027$, $p<0.01$, respectively). Prolonged upright posture were clearly related to the NMS group($p<0.01$). Seizure- like motor activity was related to the convulsive/epileptic syncope($p<0.01$).

Discussion : Syncope is a common event in the pediatric population and should be considered as an important health concern(3). Syncope is seen in 15–25% of children and adolescents with a female preponderance. Neurally mediated syncope is the most frequent cause of pediatric syncope and occurs in 64-75% of all cases. A syncopal event is typically preceded by a 'prodromal phase' characterized by non-specific symptoms such as nausea, epigastric discomfort, visual blurring, dizziness, sweating, hyperventilation, pallor, cold skin or weakness that can last few seconds up to 1–2 min. The loss of consciousness is usually brief, followed by rapid spontaneous recovery without neurologic deficits(4). In our study, neurally mediated syncopes were the most common etiologic cause(83%) and these prodromal findings before syncope were present in 80% of our patients.
It is important to clinically differentiate between an epileptic and a syncopal attack. In general, epileptic attacks may occur irrespective of the sleep-awake state and the position of the patient. Repeated spells of unconsciousness at a rate of several attacks per month are more likely to be epileptic. Syncope, on the other hand, rarely occurs when the patient

is recumbent or asleep and it is commonly situational. Tonic spasms of muscles, focal or generalized clonic contractions, uprolling of eyes and involuntary micturition are common manifestations of epileptic attacks. Whereas these manifestations occur rarely and in later stages of syncope(5). Most of our patients with vasovagal syncope had syncope attacks while standing for a long time and seizure- like motor activities were related to the convulsive/epileptic syncope.

An electroencephalograph may show various types of epileptiform activities in the brain. Several studies have shown that the diagnostic value of EEG is as low as 1.5% in patients presenting with syncope(6,7). However, a study reported that 14.3% of patients were diagnosed with epilepsy(8). In our study, seventeen of 19 patients with epileptic discharge in EEG were diagnosed with epilepsy and antiepileptic drug treatment was initiated. Two other patients with epileptic activity on EEG were clinically diagnosed as vasoovagal syncope and antiepileptic drug treatment was not initiated. Therefore, electroencephalography may be used when there is a strong suspicion of an underlying seizure. Neuroimaging is a widely used method for evaluation in children presenting with syncope. However, the diagnostic value of neuroimaging is very low(9). In our study, nonspecific white matter lesions were mostly observed and these findings were not related to diagnosis.

Conclusions : Syncope is one of the most common paroxysmal disorders in children and adolescents. Neural mediated syncopes are the most common cause of syncope in childhood . The key to diagnosis is detailed history and comprehensive physical examination. However, it is important to evaluate each child since syncope may be the first warning sign of a serious underlying disease. Syncope must also be differentiated from epilepsy, which is an important cause of transient alterations in the level of consciousness. Although the contribution of neuroimaging to the etiology and diagnosis is very limited, electroencephalography may be helpful in diagnosis and treatment management in selected cases.

Table 1. The classification of syncope in childhood

Neurally mediated syncope
1. Neurocardiogenic (vasovagal)
2. Situational syncope
3. Carotid sinus syncope
4. Glossopharyngeal and trigeminal neuralgia syncope
Cardiogenic syncope
Non-cardiogenic syncope
1. Orthostatic hypotensive syncope
2. Postural orthostatic tachycardia syndrome
3. Metabolic reasons of syncope
4. Psychogenic syncope
5. Drug-induced syncope
6. Triggered reflex syncope
8. Hyperventilation-induced syncope
9. Neurologic Syncope
Cerebrovascular diseases
Increased intracranial pressure
Seizure

Table2. Demographic and clinical characteristics of patients

	Number(%)
Sex	
Female	124 (56.9)
Male	94 (43.1)
Age	12.8 ± 4.1 years
Age groups	
1-4	15 (6.9)
5-9	39 (17.9)
10-14	95 (43.6)
>15	69 (31.7)
Number of attacks	
1	86 (39.4)
2	80 (36.7)
3	31 (14.2)
>3	21 (9.6)
Family history of epilepsy	21 (9.6)
Prodromal symptoms	174 (80)
Incontinence	13 (6)
Seizure-like motor activity	40 (18.3)

Table 3. Etiology of syncope

	Number(%)
Neurally mediated syncope	181(83)
Neurocardiogenic (vasovagal)	172(95)
Refleks anoxic syncope	6(3.3)
((Breath-holding spells)	
Situational syncope	3(1.7)
Epileptic syncope	19(8.7)
Psychogenic syncope	16(7.3)
Metabolic syncope	1 (1)
Drug induced syncope	1(1)

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