

## Çocuklarda postüral ortostatik taşikardi sendromu, uygunsuz sinüs taşikardisi ve vazovagal senkop tanı ve tedavisindeki deneyimlerimiz

### Our experience in the diagnosis and treatment of postural orthostatic tachycardia syndrome, vasovagal syncope, and inappropriate sinus tachycardia in children

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#### ÖZET

**Amaç:** Kliniğimize senkop, presenkop, baş dönmesi ve çarpıntı yakınmaları ile başvuran olguların tanı ve tedavilerindeki deneyimlerimizi paylaşmayı amaçladık. **Çalışma planı:** Çalışmamıza 2014–2016 yılları arasında çocuk kardiyoloji polikliniğimize çarpıntı, senkop, presenkop ve baş dönmesi yakınmaları ile başvuran olgular alındı. Olguların detaylı öyküleri, fizik bulguları, laboratuvar incelemeleri ve EKG sonuçları kaydedildi. Gerekli görülen hastalara eğik masa testi, 24 saatlik ritim Holter monitörizasyonu, uzun süreli olay kaydedici ve efor testi uygulandı. Bu veriler ışığında olgulara vazovagal senkop, postüral ortostatik taşikardi sendromu (POTS) ve uygunsuz sinüs taşikardisi tanıları konuldu. Olguların tedavi yaklaşımları değerlendirildi. **Bulgular:** Otuz hastaya vazovagal senkop, 7 hastaya POTS, 2 olguya uygunsuz sinüs taşikardisi tanıları konuldu. POTS tanısı konan olgularımızdan birine Raynaud fenomeni, birine hipertrofik kardiyomiyopati, birine ise homosistinüri eşlik etmekteydi. Vazovagal senkop tanısı konan olguların yakınmaları önlemler ile geriledi. POTS tanısı konan iki olguya ve uygunsuz sinüs taşikardisi tanısı konan iki olguya farmakolojik tedavi başlandı.

**Sonuç:** Senkop, presenkop, baş dönmesi ve çarpıntı gibi yakınmalarla polikliniğe başvuran hastalarda tanıda vazovagal senkop dışında, nadir de olsa postüral ortostatik taşikardi sendromu ve uygunsuz sinüs taşikardisi gibi kardiyovasküler otonomik bozukluklar akılda tutulmalıdır.

#### ABSTRACT

**Objectives:** The aim of this study was to share our experience in the diagnosis and treatment of patients who presented at our clinic with syncope, pre-syncope, dizziness, and palpitations.

**Study design:** Patients who were treated at pediatric cardiology clinic for complaints of syncope, dizziness, and palpitations between 2014 and 2016 were enrolled in the study. Detailed history of the patients, physical examination findings, laboratory and electrocardiogram results were recorded. Tilt-table test, 24-hour Holter rhythm monitoring, and exercise test were performed, as required. Patients were diagnosed as vasovagal syncope, postural orthostatic tachycardia syndrome (POTS), or inappropriate sinus tachycardia syndrome based on these findings. Treatment of the patients was evaluated.

**Results:** Thirty patients were diagnosed as vasovagal syncope, 7 patients as POTS, and 2 as inappropriate sinus tachycardia. POTS accompanied Raynaud's phenomenon in 1 patient, hypertrophic cardiomyopathy in 1 patient, and homocystinuria in another patient. Complaints of patients with vasovagal syncope improved with non-medical therapy. Medical treatment was administered to the patients with diagnosis of POTS and inappropriate sinus tachycardia.

**Conclusion:** In patients with complaints of syncope, pre-syncope, dizziness, and palpitations without structural heart disease or non-rhythm problems, cardiovascular autonomic disorders, such as POTS and inappropriate sinus tachycardia should be kept in mind, as well as vasovagal syncope.

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Following, murmurs, main reasons for application to the outpatient clinics of pediatric cardiology are palpitation, syncope/dizziness.<sup>[1,2]</sup> In some patients who presented with these complaints, making a diagnosis can be extremely difficult.<sup>[3-5]</sup> In addition to frequently seen vasovagal syncope, more rarely encountered autonomic dysfunctions as postural orthostatic tachycardia syndrome (POTS), and inappropriate sinus tachycardia should be remembered in the differential diagnosis.<sup>[6]</sup> In pediatric patients, multiple number of studies are available on vasovagal syncope, while limited number of investigations are available on the diagnosis, treatment, and follow-up of the cases with inappropriate sinus tachycardia, and POTS. In the year 2015, World Heart Rhythm Society made recommendations on diagnosis, and treatment of these three diseases in children, adolescents, and adults.<sup>[6]</sup>

In this study we have presented our experience in the diagnosis, and treatment of the cases diagnosed as inappropriate sinus tachycardia syndrome, POTS and vasovagal syncope.

## PATIENTS AND METHOD

Patients who consulted outpatient clinics of pediatric cardiology between the year 2014, and 2016, with complaints of palpitation, syncope, presyncope, and dizziness were included in our study. The patients were invited to attend ambulatory controls in outpatient clinics one by one by phone calls. The information of the patients who couldn't come to polyclinics was questioned on phone, and recorded in their files.

Syncope is defined as transient loss of consciousness characterized by sudden, short-lived, postural tonus loss.<sup>[6]</sup> Presyncope is defined as the presence of sudden, transient blackout, dizziness, nausea without associated transitory loss of consciousness. Detailed history, results of physical examination, laboratory tests, electrocardiographic (EKG) analysis of the cases were recorded. In case of need tilt-table test, 24-hour Holter rhythm monitoring, and long-term event recorder, and stress test were applied. Echocardiographic assessments of all cases were performed. For treadmill stress test Bruce protocol was used.<sup>[7]</sup> Before tilt-table test, the patients were laid supine for 20 minutes to rest, and electrocardiographic monitorization, and arterial blood pressure (ABP) measurements were performed. Then the table was inclined at 70° and for 40 minutes the patients were observed. Meanwhile continuous EKG monitorization, and at 3-minute-intervals ABP measurements were performed.

## Abbreviations

ANA Antinuclear antibody

Anti-ds Anti-double strain

POTS Postural orthostatic tachycardia syndrome

RNP Ribonucleoprotein

The complaints of the patients were recorded. When patients had complaints, then the test was terminated within 19 seconds and the table was leveled. Types of vasovagal syncope were classified as follows: At the time of fainting peak heart rate decreased, but not dropped below 40 bpm in mixed type (Type 1), in cardioinhibitory type without asystole (Type 2A) peak heart rate dropped below 40 bpm for longer than 10 seconds associated with asystole for less than 3 seconds. In cardioinhibitory type with asystole (Type 2B) asystolic episodes last longer than 3 seconds. In vasopressor type at the time of fainting, peak heart rate does not drop more than 10 % of the maximum peak heart rate (Type 3) (vasovagal syncope).<sup>[8]</sup> At the tilt-table test greater than 30 bpm increase in heart rate or heart rate exceeding 120 bpm within 10 minutes after rotating the table from horizontal to vertical position established the diagnosis of postural orthostatic tachycardia syndrome.<sup>[6]</sup> Detailed patient history, and average heart rate exceeding 90 bpm during 24-hour Holter rhythm monitorization suggested inappropriate sinus tachycardia syndrome.<sup>[6]</sup> The patients with inappropriate sinus tachycardia syndrome underwent treadmill stress test, and if any abnormal increase in sinus rate with minimal effort was observed. Orthostatic hypotension was defined as a drop of 20 mmHg in systolic, and 10 mm Hg in diastolic blood pressure within 3 minutes after the child assumed standing position from a supine position.<sup>[6]</sup> Medical treatment was administered in case of need. The patients with the diagnosis of vasovagal syncope was advised to keep away from factors which made them faint, to drink at least 2 liters of water, till their urine became transparent, to squat on the floor or lay down with their feet above the level of their heart when they feel fainting, to avoid saltless diets, and consume normal amounts of salt.

SPSS 15 was used for the evaluation of data. In our study, we complied with the principles of Helsinki Declaration, Guideline for Good Clinical Practice, and Good Laboratory Practice, and informed consent of the patients was obtained.

## RESULTS

A total of 439 children consulted our outpatient clinics between the years 2014, and 2016. The first admission complaints of the children were palpitation (n=195; 4.4%), syncope (n=88; 2%), presyncope (n=21; 0.5%), and dizziness (n=23; 0.5%).

**Table 1. Characteristics of the cases with positive tilt- table test results**

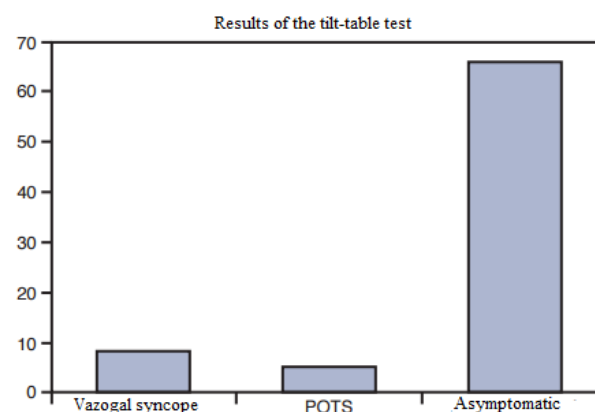
Cases	Age	Gender	Indication	Duration of symptoms (min)	Symptoms	Findings		Result *
						PHR (/min)	ABP (mmHg)	
1	12	Female	Syncope	3	Syncope	57	85/53	Tip 1VVS
2	16	Female	Syncope	3	Dizziness	112	86/39	Tip 3VVS
3	16	Female	Presyncope	21	Syncope	55	103/72	Tip 1VVS
4	17	Male	Dizziness	9	Presyncope	126	109/65	POTS
5	13	Female	Syncope	3	Syncope	135	96/55	POTS
6	14	Female	Syncope	15	Dizziness	59	89/55	Tip 1VVS
7	13	Male	Syncope	9	Syncope	32	91/58	Tip 2BVVS
8	13	Female	Syncope	3	Presyncope	50	96/70	Tip 1VVS
9	10	Female	Syncope	6	Presyncope	132	107/71	POTS
10	15	Male	Dizziness	9	Presyncope	126	96/68	POTS
11	15	Female	Syncope	6	Presyncope	138	118/82	POTS
12	11	Male	Syncope	6	Presyncope	122	109/72	POTS
13	17	Female	Syncope	3	Presyncope	132	130/90	POTS
14	14	Female	Dizziness	15	Presyncope	88	88/59	Tip 1VVS
15	13	Male	Syncope	36	Syncope	34	74/56	Tip 2AVVS
16	14	Female	Syncope	18	Presyncope	36	88/57	Tip 2AVVS
17	16	Female	Presyncope	3	Presyncope	61	57/32	Tip 1VVS
18	15	Female	Syncope	21	Presyncope	54	78/45	Tip 1VVS
19	17	Male	Syncope	15	Presyncope	40	97/50	Tip 2AVVS

\*POTS postural orthostatic tachycardia syndrome . Type 1VVS: Mixed type vazovagal syncope; Type 2AVVS: Cardioinhibitory type without asystole; Tip 2B: cardioinhibitory type with asystole; Type 3VVS: Vazodepressor type vazovagal syncope

Eighty-six study participants underwent tilt-table test (Figure 1).

Fifteen cases presented with complaints of syncope were excluded from the study because of inability to obtain their medical data. Study population (n=73) consisted of 29 male, and 44 female children with an overall mean age of  $12.8 \pm 4.1$  years. The etiologies of syncope were as follows: vasovagal syncope (n=24; 27.2%), neurologic causes (n=7; 6.8%), underlying heart disease including aortic stenosis, Wolff Parkinson White syndrome, Fabry's disease, dilated cardiomyopathy, sinus arrest, and ventricular tachycardia (n=6; 6%), POTS (n=4; 4.5%), orthostatic hypotension (n=3; 3.4%), psychiatric disorders (n=3; 3.4%), and breath holding spells (n=3; 3.4%). In 23 (26.1%) cases underlying cause of syncope could not be detected (Figure 2). During monitorization of 18 (78.2%) out of these 23 cases complaints of fainting did not recur, while in 5 (21.7%) cases complaints of fainting persisted.

Three cases presented with presyncope were excluded from the study because of inability to attain their medical data. Study population with presyncope (n=16) consisted of 12 male, and 4 female children with an overall mean age of  $11.8 \pm 4.5$  years. Causes of presyncope included orthostatic hypotension (n=4; 22%), psychiatric etiologies (n=3; 16.5%), vasovagal syncope (n=3; 16.6%), and supraventricular tachycardia (n=1; 5.5%).

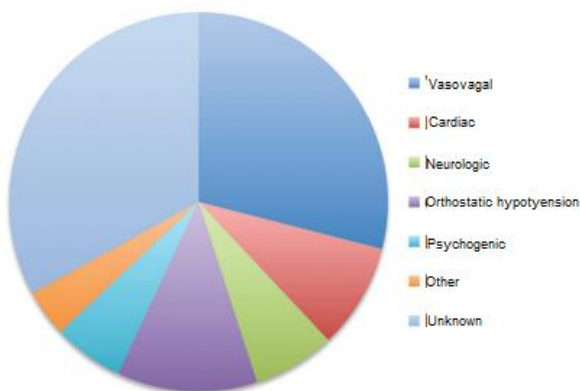


**Figure 1.** Results of the tilt-table test. POTS: Postüral orthostatic tachycardia syndrome

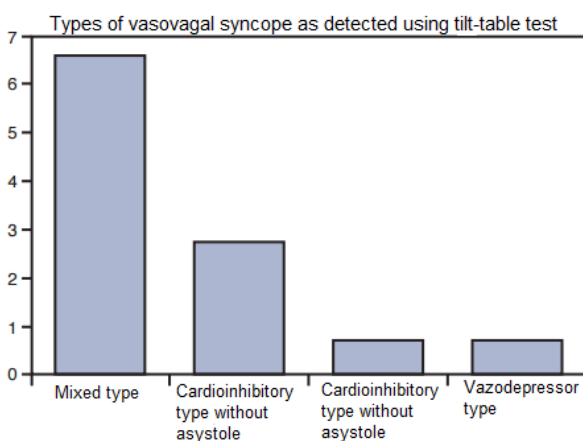
In seven cases (38%) the underlying cause of presyncope could not be detected (Figure 2).

Two cases referred to our outpatient clinic were excluded from the study because of unavailable data. Study population (n=21) consisted of 14 female, and 7 male patients with an overall mean age of  $14.1 \pm 2.8$  years. The causes of dizziness include orthostatic hypotension (n=6; 28.5%), vasovagal syncope (n=3; 14.2%), POTS (n=3; 14.2%), hypertension (n=1; 4.7%), restrictive cardiomyopathy (n=1; 4.7%), side effect of sotalol (n=1; 4.7%), serious weight loss within a short time (n=1; 4.7%). In 5 (23.8%) cases underlying cause of dizziness could not be detected (Figure 2).

The diagnosis of vasovagal syncope was made for 30 cases (female, n=21; 70%, and male, n=9; 30%) with a mean age of  $12.7 \pm 4.3$  years. Admission complaints of 24 cases were syncope (n=24), dizziness (n=3), and presyncope (n=3).



**Figure 2.** Diagnoses of the patients who presented with syncope, presyncope, and dizziness.



**Figure 3.** Types of vasovagal syncope as detected using tilt-table test.

Thirty patients were diagnosed as vasovagal syncope based on detailed anamnesis (n=18; 60%), and tilt-table test results (n=12; 40%). Mixed type (n=7), cardioinhibitory type without asystole (n=3; Type 2A), cardioinhibitory type with asystole (n=1; Type 2B), and vasodepressor type (Type 3) vasovagal syncope were detected in respective number of patients (Figure 3). Medical treatment was not initiated in any patient diagnosed as vasovagal syncope. These patients were followed up for a mean period of  $14 \pm 4.2$  months. Complaints of 26 cases regressed during follow-up period, however complaints of only 4 patients persisted.

Diagnosis of postural orthostatic tachycardia was made in 4 female, and 3 male patients with an overall mean age of  $14.4 \pm 2.2$  years. Admission complaint of 4 cases was fainting, while 3 patients applied to our outpatient clinic with complaint of dizziness. Homocystinuria (n=1), and hypertrophic cardiomyopathy (n=1) were detected in cases diagnosed as POTS. Exercise stress test was performed to investigate the etiology of hypertrophic cardiomyopathy, and for ten days the patients carried an event recorder. In both tests a significant pathology was not detected. In one case POTS was associated with Raynaud's phenomenon. This case had been followed up for four years at different centers, and still remained undiagnosed. In order to rule out other diseases, and elucidate the etiology of POTS, levels of vanillylmandelic acid, angiotensin converting enzyme, 25-OH D vitamin, anti-nuclear antibody (ANA) anti-double strain DNA (anti-ds DNA), anti-topoisomerase- I (anti-SCL70), anti-U1 ribonucleoprotein (anti-U1 RNP) antibodies in 24-hour urine sample, and blood tryptase were measured. During tilt-table test blood pressure was measured as 130/85 mmHg. Blood norepinephrine levels of the patient who demonstrated a slight increase between blood pressures measured at horizontal, and vertical positions were investigated (at horizontal position 500 pg/mL, and 300 pg/mL at vertical position) without any significant difference. For the treatment of this case beta-blocker (metoprolol), serotonin reuptake inhibitor, angiotensin receptor blocker (losartan), alpha-agonist (midodrine), and ivabradine were used. Midodrine treatment was initiated for the patient with isolated POTS whose life is severely affected.

Two female patients who presented to our outpatient clinic with complaint of palpitation were diagnosed as inappropriate sinus tachycardia syndrome.

The average heart rate of the first case aged 16 years as revealed by 24-hour Holter monitorization was 92 bpm. Baseline heart rate of 118 bpm increased up to 173 bpm shortly after the test started. The patient underwent tilt-table test for differential diagnosis of POTS, and normal test results were obtained. Beta-blocker (metoprolol: 25 mg/d) treatment was initiated. However complaints of the patient did not regress. Daily dose of metoprolol was increased up to 50 mg which somewhat decreased patient's complaints. Twenty-four hour Holter monitorization of our second case aged 15 years revealed an average heart rate of 93 bpm. Baseline heart rate of 112 bpm increased up to 160 bpm shortly after the test started. Tilt-table test results were within normal limits. Treatment with a beta-blocker, and ivabradin was initiated. However the patient's complaints were not relieved, so we switched to midodrine treatment.

## DISCUSSION

Syncope, and its etiology are still debatable issues. Apart from classical pathophysiologic definitions, multiple number of studies have been published to elucidate the etiology of vasovagal syncope.<sup>[9,10]</sup> One must exert utmost care to understand detailed clinical history of the patient. Tilt-table test may aid in diagnosis. However for every patient with suspect vasovagal syncope tilt-table test is not required. Indeed in our study, 18 of 30 patients were diagnosed based on detailed anamnesis, while 12 of them required tilt-table test for the establishment of diagnosis. Tilt-table test aids in the diagnosis of vasovagal syncope, besides two other important reasons have been also emphasized. First of them is to rule out dysrhythmias which induce fainting episodes, and to investigate cardiovascular autonomic nervous system disorders as autonomic neuropathy, neurogenic orthostatic hypotension, and POTS.<sup>[6]</sup> In the treatment of vasovagal syncope, mostly compliance with recommendations, and increasing in salt-water intake usually suffice. In our study application of the above-mentioned measures regressed complaints in 86% of the cases. However in patients whose complaints persisted despite these measures, beta-blockers, hydrocortisone, fludrocortisone, midodrine, and serotonin reuptake inhibitors can be used. In none of our cases medical treatment was initiated. Similar to our study results, Song et al.<sup>[11]</sup> reported a recurrence rate of 25 %, while in 75% of the cases syncope did not recur without any need for treatment .

In our country, Başpınar et al.<sup>[12]</sup> observed recurrence of attacks of syncope in only 18% of 88 untreated cases. In our 4 patients whose attacks of syncope recurred, any medical treatment was not administered because attacks persisted for a very short time, and did not create a life-threatening condition

Postural orthostatic tachycardia syndrome is defined as 30 bpm increase in heart rate or heart rate exceeding 10 bpm within the first 10 minutes when the patient was laid from horizontal to vertical position. In some recently published studies POTS has been defined as an increase of 40 bpm in pediatric cases.<sup>[13]</sup> In order to make a diagnosis of POTS blood pressure should not drop more than 20 mm Hg. Otherwise, diagnosis of orthostatic hypotension is conceived. However small increases, and decreases can be seen in blood pressure.<sup>[14,15]</sup> Indeed, in one of our patients a slight increase in blood pressure was noted. Most of the patients are in the age bracket of 15–25 years, and more than 75% of them consist of female patients.<sup>[16]</sup> In 4 out of our 7 cases diagnosed as POTS were female patients with a median age of 14.4 years. Many mechanisms have been proposed for the etiology of POTS.<sup>[17]</sup> Most frequently proposed mechanisms include autonomic denervation, hypovolemia, hyperadrenergic stimulation, and lack of condition. Palpitation when assuming standing position, fainting, tremor, blackout, feeling of fatigueness, and exercise intolerance are frequently encountered complaints in patients with POTS. Admission complaints were syncope in our 4, and dizziness in 3 patients. A detailed history taking, and perfect physical examination constitute the first, and the most important phase of the assessment of POTS patients. Most of the time, history, physical examination, and tilt-table test suffice for making a diagnosis, and further tests are not required. In an article published by World Heart Rhythm Society in 2015, further evaluation was recommended in case of need. In line with these recommendations we established diagnosis in our patients based on medical history, physical examination, and tilt-table test. In order to elucidate diverse etiological mechanisms in POTS various tests can be used. For the evaluation of autonomic neuropathy, thermoregulatory sweat test may be utilized. For the assessment of hypovolemia Na level in 24-hour urine, and for the appraisal of hyperadrenergic POTS blood epinephrine, and norepinephrine levels of the patients lying in horizontal, and vertical positions may be measured.

One of our patients with concomitant Raynaud's phenomenon who had been followed up for years at many centers because of fainting episodes but remained undiagnosed, demonstrated a slight increase in blood pressure at tilt-table test which necessitated measurement of norepinephrine levels so as to investigate the presence of hyperadrenergic stimulation. However we couldn't detect any finding supporting the diagnosis of hyperadrenergic POTS. Since many diseases are considered in the differential diagnosis of POTS, in case of need, tests for differential diagnosis can be performed. Vanillylmandelic acid, and angiotensin converting enzyme levels in 24-hour urine may guide the physician. Since mast cell dysfunction can be seen in cases with POTS, in selected cases evaluation of blood tryptase levels is recommended.<sup>[18]</sup> Psychologic evaluation has an utmost importance in this disease which is mostly seen in adolescent girls. We also evaluated all diseases considered in the differential diagnosis of the disease in our case who presented with Raynaud's phenomenon. Therefore we evaluated levels of ANA, anti ds-DNA, anti SCL 70, and anti RNP, and urinary vanillylmandelic acid, angiotensin converting enzyme, vitamin 25-OH D, and blood tryptase levels which were within normal limits. Psychological evaluation of this patient was also unremarkable. From detailed medical history of another patient of ours who presented with hypertrophic cardiomyopathy, we learnt that fainting episodes happened following sudden rise from bed, and the patient had then felt blackout, and dizziness but recovered within a short time. During tilt-table test, when syncope occurred peak heart rate increased 35 bpm. At the time when our patient was complaining of fainting, we couldn't detect supraventricular and/or ventricular arrhythmias. Since complaints of fainting were associated with the diagnosis of hypertrophic cardiomyopathy we evaluated our case with exercise stress test, and event recorder carried by the patient for 10 days, but couldn't detect ventricular tachycardia. Under the light of all these data, we concluded that fainting complaints of our patient were related to the diagnosis of POTS syndrome. Our adolescent female patient with Marfanoid appearance who received diagnosis of POTS had been followed up with the indication of homocystinuria. In the literature, association of POTS with cellular matrix protein disorders as Marfan Syndrome, and Ehlers –Danlos Syndrome has been also reported. However we couldn't encounter any case with POTS associated

with homocystinuria. The concomitancy between POTS, and homocystinuria might be a coincidental finding or it might possess similar pathophysiologic basis with previously defined cellular matrix protein disorders. Since different mechanisms play a role in the etiopathogenesis of POTS, it has also very diverse treatment alternatives. Very few of them have been investigated in randomized clinical studies, and a general consensus does not exist about effective treatment method.<sup>[6]</sup>

From our viewpoint, as a first step the patients, and their families should be told that POTS syndrome which is mostly detected in adolescent girls, and stress them immensely has not any previously defined risk of death up to now. At the first step non-pharmacologic treatments should be instituted. Use of norepinephrine reuptake inhibitors which might aggravate symptoms of POTS should be discontinued. Daily salt, and water intake should be increased (water, 2–3 litre, and salt, 10–12g/d), and the patients should be directed to sportive activities as swimming which decrease orthostatic stress.<sup>[19–21]</sup> With these approaches, complaints of many patients regress. However in patients whose complaints persist despite these measures, pharmacological treatment should be tried. Indeed, complaints of our seven patients who were diagnosed as POTS regressed without the need for medical treatment. We initiated midodrine treatment for our remaining two cases. Midodrine was not effective in the POTS patient associated with Raynaud phenomenon, however it increased quality of life, and decreased complaints of the patient with isolated POTS. Ivabradine is another alternative which decreases sinus rhythm without effecting blood pressure. As indicated in a study, complaints of 60% of the patients with POTS regressed with ivabradine treatment.<sup>[22]</sup> Indeed, despite use of different drug treatments complaints of our patient with concomitant Raynaud's phenomenon persisted, however ivabradine treatment decreased these complaints. Various drug treatments as serotonin reuptake inhibitors, angiotensin- receptor blockers, clonidine, and methyldopa are being used in the treatment of the cases with POTS.<sup>[23,24]</sup>

Inappropriate sinus tachycardia is defined as resting heart rate above 100 bpm or average heart rate estimated for 24 hours above 90 bpm in a patient with complaints of palpitation.<sup>[6]</sup> The underlying mechanism has not been clearly understood.<sup>[25,26]</sup> Especially a detailed history, and a perfect physical examination which will rule out other etiologic factors of sinus tachycardia are very important in the establishment of diagnosis. Evaluation of thyroid function tests, and urinary tests as for the presence of



hypovolemia are recommended. Twelve-channel EKG obtained to observe sinus rhythm of the patient is helpful in the differentiation of this syndrome from atrial tachycardias. Twenty-four hour Holter monitorization should be performed to calculate average heart rate. We also diagnosed these two patients who presented with complaints of palpitation based on 24-hr Holter monitorization. Patients with inappropriate sinus tachycardia or POTS face us with similar symptoms.

Inappropriate sinus tachycardia is triggered by physiologic, and emotional stress, while POTS is generally induced by orthostatic stress. Therefore tilt-table test is a reliable method for discriminating between these two disease states. We also performed tilt table test for differential diagnosis among two cases which we thought to be inappropriate sinus tachycardia, and excluded the diagnosis of POTS. Exercise stress test can be useful for the demonstration of exaggerated tachycardiic response.<sup>[27]</sup> We also detected rapid increase in heart rate within a very short time. Inappropriate sinus tachycardia causes decrease in quality of life of the cases. However a drug which might be used in the treatment of this disease with proven effectiveness demonstrated in prospective, placebo-controlled studies has not been formulated yet. Various publications have indicated the use of very different drugs including beta blockers, fludrocortison, phenobarbital, clonidine, and erythropoietin in the treatment of inappropriate sinus tachycardia syndrome.<sup>[25]</sup> However many publications have advocated that ivabradine is the most effective drug in the treatment of inappropriate sinus tachycardia syndrome.<sup>[28]</sup> Whereas some studies have claimed that combined use of ivabradine, and a beta-blocker is an effective treatment modality. In our first case beta-blocker treatment regressed patient's complaints. In our second case, despite prior beta-blocker, and then ivabradine treatment, complaints of the patient did not regress, and then only midodrine treatment was initiated. Midodrine treatment decreased patient's complaints.

In conclusion, apart from vasovagal syncope, and more rarely autonomic cardiovascular dysfunctions as POTS, and inappropriate sinus tachycardia syndrome should be considered in the differential diagnosis of the children, and adolescents without any structural heart disease, and rhythm disorders who presented to the outpatient clinics with complaints of palpitation, syncope, presyncope, and dizziness.

### Ethics Committee

For this retrospective study, approval of the ethics committee of our hospital was obtained

### Conflict of interest : none declared

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