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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Clinical analysis and follow-up results of children with vasovagal syncope

Vazovagal senkoplu çocuklarda klinik değerlendirme ve takip sonuçları

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ABSTRACT

Objective: Syncope is a common clinical problem that occurs at all ages and is particularly prevalent in childhood and adolescence. In this study we aimed to investigate the continuity of the symptoms and effectiveness of the therapy in patients who received medical therapy. In addition, we investigated the association of tilt positivity or negativity with the continual syncope complaints by repeating head-up tilt test (HUTT).

Methods: Forty-nine patients with vasovagal syncope followed-up for 6 or more months were contacted with telephone call. Follow-up period, syncope and presyncopal attack frequency and status of drug usage of the patients were recorded. The HUTT was repeated in all patients. Data were evaluated by statistical methods.

Results: There were 27 female (55%) and 22 male (45%) patients with a mean age of 14.9±7.9. The mean follow-up period was 15.6±8.9 months. No significant sexual differences were determined for the negativity and the positivity of the test (p>0.05). Tilt test positivity rate was significantly lower than the first tilt test (p<0.05). Among the patients with continual complaints whose first HUTT results were negative, the positivity rate of the repeated test was 40%. The negativity rates of second tilt test was significantly lower in syncope-free patients than in patients with continual syncope attacks (p<0.05). The impact of syncope complaints on the positivity of the HUTT were significantly higher than presyncope complaints (p<0.05).

Conclusion: We suggested that HUTT must be repeated in pediatric patients with continual syncopal attacks even though the first test result was negative.

Key words: vasovagal syncope, child, head-up tilt test, prognosis

ÖZET

Amaç: Senkop özellikle çocukluk ve adolesan yaş grubunda daha sık olmakla birlikte her yaş grubunda görülebilen klinik bir problemdir. Bu çalışmada, vazovagal senkoplu hastalarda semptomların devamı ve medikal tedavi verilen hastalarda tedavinin etkinliği araştırıldı. Ayrıca tilt testi sonuçlarının pozitif ve negatif olması ile devam eden senkop şikâyetleri arasındaki ilişki incelendi.

Yöntemler: Vazovagal senkop tanısıyla 6 ay veya daha uzun süredir takip edilen 49 hasta telefon ile irtibat kurularak hastanemize çağrıldı. Hastaların takip süreleri, senkop ve presenkop sıklığı, ilaç kullanım öyküleri kaydedildi ve tüm hastalara tekrar tilt testi uygulandı. Elde edilen bulgular istatistiksel olarak değerlendirildi.

Bulgular: Hastaların 27'si kız (%55), 22'si erkek (%45), ortalama yaş 14,9±7,9 yıl, ortalama takip süresi 15,6±8,9 aydır. Kız ve erkekler arasında tilt testi sonucunun pozitif veya negatif olması açısından anlamlı bir fark yoktu (p>0,05). İkinci tilt testinde pozitiflik oranı ilk teste göre anlamlı olarak düşük bulunmuştur (p<0,05). İlk tilt testi negatif olup şikâyeti devam eden hastalarda tekrarlanan tilt testinin pozitif olma oranı %40 idi. İlk tilt testi negatif olup senkop şikayeti bulunmayan hastalarda, ikinci tilt testinin negatif bulunma ihtimali, senkop şikayeti devam eden hastalardan anlamlı olarak daha yüksek saptandı (p<0,05). Senkop geçirenlerde tilt testi pozitifliği, presenkoplulardan anlamlı olarak fazlaydı (p<0,05).

Sonuç: İlk tilt testi sonucu negatif olsa da şikâyeti devam eden pediatrik hastalarda ayırıcı tanı açısından tilt testinin tekrarını önermekteyiz.

Anahtar kelimeler: vazovagal senkop, çocuk, tilt testi, prognoz

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INTRODUCTION

Syncope has been defined as a sudden transient loss of consciousness usually leading to a fall with associated loss of postural tone. Recoveries is usually spontaneous, prompt and complete [1]. It accounts for 3% of admittances to emergency services and 6% of hospitalized patients [2]. Vasovagal syncope constitutes the most frequent cause. Of the patients investigated because of syncope, 40% are of vasovagal origins [3]. An incidence peak occurs around the age of 15 years, with females having more than twice the incidence of males [4].

There exists very limited evidence on the long-term outcome of the children with vasovagal syncope, whether they are treated or not. In our study, we investigated the continuity of the symptoms and effectiveness of the medical therapy after performing head-up tilt test (HUTT). In addition, we investigated the association of tilt positivity or negativity with the continual syncope complaints with repeated HUTT.

METHODS

Forty-nine patients with vasovagal syncope who were followed-up for 6 or more months at the Pediatric Cardiology Unit of Meram School of Medicine of Necmettin Erbakan University were contacted with telephone call. Patients were included if they had two or more episodes of syncope before HUTT. Patients were excluded from the study if they had other causes of syncope (including orthostatic syncope, neurologic cause, cardiac syncope, and medication-related syncope). Informed parental consent was obtained from all cases and the protocol was approved by the ethics committee of Meram School of Medicine. Initial data of patients were obtained from the file records. The HUTT was repeated in all patients. The diagnosis of vasovagal syncope was based on a positive tilt test result and exclusion of all other possible causes of syncope. To exclude other causes, a careful history and physical examination, full neurological assessment, standard laboratory tests, supine and orthostatic blood pressure measurements, ECG and conventional echocardiography were performed to all patients. Other diagnostic investigations, such as exercise stress testing, 24-hour holter recording and electrophysiological study, were performed only when clinically indicated. Advices given to all patients were; increased fluid and salty intake, lying on the ground when the symptoms were starting. In addition to advices, medical therapy (propranolol, disopyramide, flurohydrocortisone) was administered to patients who formed severe bradicardia and asystolia during the syncope attack with no prodromal findings.

Head-up tilt testing was always performed in the morning, after 8 hours fasting, in a quiet, slightly darkened room. The patients were positioned at an angle of 70° from the horizontal plane after allowing them to rest in supine position for 10 minutes. HUTT was considered to be negative if no symptoms were observed after 45 minutes. Positive HUTT was defined as the development of syncope or presyncope. If symptoms had developed, test was stopped immediately and patient was returned to horizontal position. Patients were connected to a standard cardiac monitor for continuous recording of heart rate and rhythm throughout the test. A manual sphygmomanometer of appropriate size was used for blood pressure measurements in 5 minutes intervals and in 1 minute intervals when the symptoms were started. Electronically controlled tilt table with hydraulic was used for HUTT. No intravenous fluid infusions or pharmacological provocation was used during the HUTT. Syncope was defined as a transient loss of consciousness and postural tone, and presyncope was defined as a sensation of lightheadedness, dizziness, weakness and nausea [5]. Mixed response was defined as syncope or presyncopal attacks with hypotension and vasodepression, bradicardia and cardioinhibitory response, hypotension and bradicardia. Hypotension response was defined as at least 30 mmHg or 30% decrease from the highest measured systolic blood pressure, and bradicardia as a decrease of at least 20% in the heart rate [6,7].

Statistical analysis

The statistical analysis was carried out using the SPSS 15.0 statistical software package for Windows. We used Pearson, Fisher's Exact, McNemar and Yates's corrected χ^2 tests. $P<0.05$ was considered as statistically significant.

RESULTS

There were 27 female (55%) and 22 male (45%) patients. Mean age at first admission was 11.9±5

years, and 14.9±7.9 at the second tilt test. Median follow up period was 15.6±8.9 months (Table 1).

Forty-three patients had a history of at least two syncopal attacks and 6 patients had only 1 syncope and at least 4 presyncopal attacks. Forty patients (82%) were standing up and 5 (10%) were sitting just before the syncopal attack, 4 cases developed syncope after injury, 37 (76%) patients were hungry and 12 (24%) were full during the attack. Thirty-seven patients (76%) had syncope or presyncopal attacks at morning hours. Headache (84%), lightheadedness (73%), and nausea (26%) were the frequent prodromal signs. Unpleasant feeling, sweating were rare (8%) prodromal signs. Three patients (6%) had trauma, 8 patients (16%) had convulsion and 2 patients (4%) had trauma and convulsion history during the syncopal attack.

Table 1. Clinical characteristics of subjects

	n or mean ± SD
Sex (M/F)	22/27
Age (years)	14,9±7,9
Follow-up duration (months)	15,6±8,9
Age at onset of syncope (years)	11,9± 5
Two or more syncopal episode (n)	43
Prodromes (n)	41
Injury from syncope (n)	4
Seizures (n)	8

SD: Standard deviation

Twenty-nine patients (59%) developed a positive response during the initial HUTT. A negative test was observed in 20 patients (41%). In the second test 15 patients (31%) showed positive and 34 patients (69%) negative response. Positive tilt test rates were significantly decreased in the second test when compared with first test (P=0.008). Of 29 patients who showed positive response in the initial HUTT, 13 (45%) had still positive response and 16 (55%) had negative response in the second test. Of 20 patients who showed negative response in the initial HUTT, 18 (90%) had still negative response and 2 (10%) had positive response in the second test (Figure 1). There was statistically significant difference between the patients who still had negative response in the second test and the patients who had positive response in the first test and negative response in the second (P=0.048). Additionally there was statistically significant difference between patients who showed positive response in both tests and who had negative response in the first and positive in the second test (P=0.01).

There was no significant differences for the vasovagal responses between the first and second HUTT (P=0.738). Syncope complaint continued in 7 of the 29 patients (24%) who had positive response and 5 of the 20 patients (25%) who had negative response. No significant difference was determined for syncope continuity between the patients with positive or negative response to HUTT (P=0.978).

The second HUTT was negative in all 15 patients who had no syncopal attack after the first test. Three of the 5 patients (60%) who still had syncopal attacks after the first test had negative response and the remainder 2 patients (40%) had positive response. Patients who had no syncopal complaint after the negative HUTT showed higher tendency for negative response in the second test than the patients who still had syncopal complaints (P=0.05).

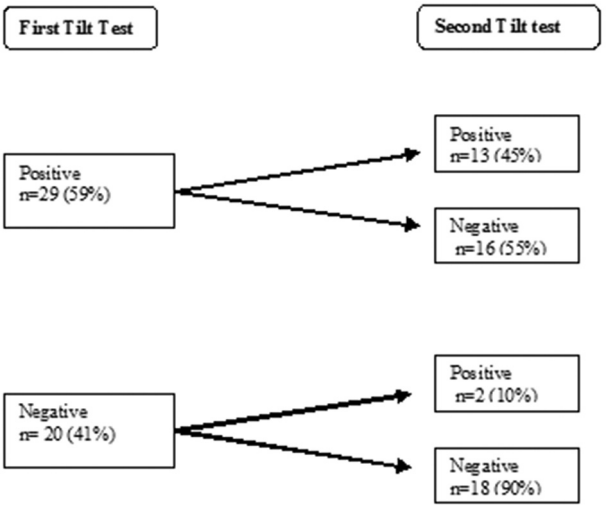

Figure 1. Results of first and second head-up tilt test in patients

While medical advices were informed to 20 (69%) of 29 who had negative response to first HUTT, medical treatment was given to the remainder 9 patients (31%). Four of the 9 patients (44%) who had medical therapy showed positive and 5 patients (56%) negative response in the second HUTT. Nine of the untreated patients (45%) had positive response to second HUTT, where 11 patients (55%) had negative. There existed no statistically significant difference for a positive response to second HUTT between the patients who were treated and

untreated (P>0.05). While 2 of the 9 patients (22%) who received medical therapy had continual syncopal attacks, 5 of the 20 patients (25%) without medication showed continual syncopal attacks. There was no significant difference for syncope continuity or recovery between the patients who received medical therapy or not (P>0.05).

DISCUSSION

Vasovagal syncope is the most frequent cause of syncope in any setting and age group representing 21% of all syncopes in the general population [1]. HUTT is widely used in the diagnosis of vasovagal syncope which has no definite protocol. Its outcomes are effected from several factors including, tilt angle, duration, replacement of venous catheterization. Because the steeper angles decreases the specifity of the test we used the European Society of Cardiology proposal of 70° tilt angle [6]. In regard to several reports suggesting that venous catheterization effects the test results, we studied without any invasive procedure [8]. The specificity and the sensitivity of passive HUTT was reported as 93-100% and 43-49% respectively in the pediatric studies which included control groups [9,10]. Several reports found out that drugs such as isoproterenol had decreased the specifity of the test [11-13]. In the report of American College of Cardiology, it is informed that passive HUTT is more useful in the diagnosis of vasovagal syncope [13]. For this reason we used passive HUTT in our study and found a positive rate of 59%.

Vasovagal syncope is by far the most frequent cause of syncope in children and adolescents. The HUTT is a widely used method for investigation of syncope, presyncope, dizziness, palpitations related to orthostatism and dysautonomia symptoms. However, the main indication has been to investigate the vasovagal syncope [6]. The test also allows diagnosing other forms of orthostatic intolerance, such as the dysautonomic response, characterized by slow and progressive drop in blood pressure to below 80 mmHg, without any drop in heart rate, associated with symptoms of hypotension such as sudoresis, dizziness and blurred vision. Another frequent dysautonomia is the postural orthostatic tachycardia syndrome, in which the main complaints of patients are palpitations, dizziness and presyncope related to orthostatism. HUTT is essential to confirm the diagnosis, which is considered positive when there is a heart rate increment greater than or equal to 30 beats per minute (bpm) after orthostatic exposure or maintenance of heart rate above 120 bpm during the tilt [14].

It was reported that the reproducibility rate of a positive response to HUTT on the same or several days after the first test was 50-60% and this was relatively lower than the rates of reproducing a negative response which was 95% [15,16]. Alehan et al. investigated the reproducibility of HUTT of 58 pediatric patients and found out that positive tilt test was 74.4%, the negative tilt test was 84.2% [17]. In our study, when the first and second HUTT were compared, the positivity rate of the second test was significantly lower than the first test. The 15.6±8.9 months duration between the tests is thought to be the reason of this lower rate. Although the duration between the tests was 15.6±8.9 months in our study, we reproduced positive and negative response 45% and 90% respectively.

Pavri et al. reported that 9 of 154 (6%) patients who had negative response in the first HUTT showed positive response to second test which was performed on the next day [18]. In our study 2 of 20 cases who had initially negative response, showed positive response in the second test which was performed 15.6±8.9 months after the first test. The second HUTT was negative in all 15 patients who had no syncopal attack after the first test. The continuity of syncopal complaint affected the positivity of second HUTT significantly, and the positivity rate was 40% (2 cases) in patients with continual syncopal attacks. It is known that the sensitivity (43-49%) of passive HUTT is lower and the specifity is higher (93-100%) [9,10]. Probably some patients with vasovagal syncopal attack had negative response in the first HUTT because of this lower sensitivity (false negative). The 2 cases who produced positive response in the second test probably had vasovagal syncope with negative response in the first test. Three patients with continual syncopal attacks who still had negative response in the second test may produce positive response in the third test.

The association of syncope recurrence and HUTT results are investigated in several studies [19,20]. Koukam et al. reported that the recurrence rate of syncope in children and adolescents was 32% and there was no significant difference between the

patients who had positive or negative response to HUTT [19]. Syncope continuity rates in our patients who had positive or negative response in the first test was 24% and 25% respectively. No significant difference was determined for syncope continuity between the patients with positive or negative response to first HUTT.

No significant difference was found between drug therapy and placebo group for syncope recurrence, in previous long term placebo controlled studies [19,21]. Kouakam et al. reported that 43 of 67 head-up tilt-positive children and adolescents were treated empirically with oral fluids, beta-blockers, disopyramide, midodrine, psychotherapy [19]. The remaining 24 tilt-positive patients and all tilt-negative patients received no treatment. During follow-up there was no difference in syncope recurrence between tilt-negative or tilt-positive patients either treated or untreated. In our study, drug therapy had been stopped when the second HUTT was performed to patients who received drug therapy initially. There existed no statistically significant difference for a positive response to second HUTT between the patients receiving and not receiving medical therapy after first positive HUTT. Likely, there was no significant difference for syncope continuity between the patients who were treated and untreated.

In conclusion, patients with vasovagal syncope showed decreased syncopal attacks and tilt positivity in time. It can be speculated that HUTT must be repeated in pediatric patients with continual syncopal attacks who showed negative response to first test.

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