Syncope Recurrence in Children: Relation to Tilt-test Results

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ABSTRACT. *Objectives.* **To examine the intermediate-term outcome of children with syncope and its relationship to tilt test.**

Design. **This was a retrospective study of 45 children. In 20, the tilt test was negative. Follow-up with respect to the recurrence of syncope was obtained via chart review, a mailed questionnaire, or telephone interview.**

Results. **Follow-up data were available on 15 children whose tilt test was negative and on all 25 tilt-test positive children. Recurrent syncope was significantly greater in the positive-tilt children (13 of 25) than the negative-tilt children (2 of 15). There was no difference between the syncope-free group and the recurrent syncope group or between the tilt-positive and tilt-negative groups with respect to age at initial syncope, duration of symptoms, age at tilt test, and duration of follow-up. Children with a positive tilt test and those with recurrent syncope had more syncopal episodes before their evaluation than either the group with a negative tilt test or the group with no recurrent syncope, respectively.**

Conclusions. **Syncope may recur after either a negative or a positive tilt test. The recurrence rate, however, is higher for the tilt-positive children.** *Pediatrics* **1998;102: 924–926;** ***syncope, tilt test, recurrence, children, male, female.***

Syncope is a common complaint in the pediatric age group, and its incidence seems to peak in midadolescence.[1] In children with a normal heart, neurocardiogenic syncope is the most prevalent form. It seems to affect female more often than male children.[1] Tilt testing is used widely in establishing the diagnosis of neurocardiogenic syncope.[2,3] Tilt testing attempts to reproduce the orthostatic stress that led to syncope, and thus is used as an indicator for the treatment of children and adults with syncope. In adults, without pharmacologic therapy, the recurrence of syncope has been found to be similar in those with a positive versus those with a negative tilt test.[4,5] In most institutions, however, pharmacologic therapy and subsequent care are offered to children and adults with a positive test whereas patients with a negative tilt test are discharged from further follow-up.[6] The recurrence rate of syncope in children is unknown. Thus, the goals of this study were to examine the intermediate-term outcome of such children and to compare the recurrence of syncope in children with a positive versus a negative tilt test.

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METHODS

From May 1992 through November 1995, 45 children with a history of one or more syncopal episodes underwent tilt-test evaluation; 25 had a positive test. All children had a normal electrocardiogram and echocardiogram. All tilt tests were performed in the morning hours after a light breakfast. A peripheral intravenous catheter was inserted to provide ready access in case of an emergency. In our protocol, the patients lay supine for 1 hour in an ambient temperature of 22°C to 24°C under soft lights with minimal verbal stimulation. Then, the patients were asked to stand for 20 minutes. The heart rate was monitored continuously using a commercially available recorder (Marquette, Electronics Inc, Milwaukee, WI), and blood pressure was measured at 1-minute intervals by an automated sphygmomanometer (Dinamap, Critikon, Inc, Tampa, FL). Isoproterenol infusion was not used. A positive tilt-test response was defined as the development of syncope or severe presyncopal symptoms associated with significant changes in blood pressure and/or heart rate. A decrease in the systolic blood pressure >20 mm Hg associated with no change or an increase in the heart rate of >25 beats/minute was considered a vasodepressor response. A cardioinhibitory response was defined as the sudden onset of bradycardia (heart rate ≤40 beats/min), a decrease in heart rate >25 beats/minute, or asystole ≥3 seconds. A cardioinhibitory/vasodepressor response was the combination of bradycardia and hypotension.[7]

After a negative tilt test, the patients were informed that they did not require any pharmacologic therapy. Each was encouraged to increase his/her fluid intake and was referred back to his/her primary care physician. Patients with a positive tilt test were started on oral fludrocortisone acetate (0.3 mg/day for 1 week and 0.1 mg/day thereafter). The initial high dose of fludrocortisone acetate was used to reach a steady state rapidly. They also received 1 g of sodium chloride/day. Their serum electrolytes were checked weekly for 4 weeks then every month.[8]

Data were collected from chart review on those patients with ongoing care. Updated follow-up information on tilt-negative children and those with a positive tilt response but no recent follow-up was obtained by a questionnaire approved by the University of Tennessee Institutional Review Board. The questionnaire was mailed to the last known address of each patient at a mean of 2 years after the tilt test. If no response was received after 3 weeks, a second questionnaire was mailed. Patients who did not respond to the second questionnaire were contacted by telephone and an interview was conducted with the patient or a parent. Every effort was taken to include all patients in the follow-up. The questions concentrated on the recurrence of syncope and the frequency of syncopal episodes. Presyncopal symptoms were noted; recurrence was determined only if frank syncope occurred. A history of medication usage that might have had an effect on syncope was also obtained.

Statistical Analysis

Paired and unpaired Student's t test was used for analysis where appropriate. Kaplan-Meier curves were used to illustrate the estimates of syncope-free rates. A $P < .05$ was considered significant. Data are reported as mean plus or minus standard deviation.

RESULTS

The demographics of the populations of tilt-positive and tilt-negative children were not different except that the tilt-positive group reported a significantly higher number of syncopal episodes before the tilt test (Table 1). The follow-up duration was similar for the two groups. There was no difference in gender distribution between the tilt-positive and tilt-negative groups. Prescription medications in use at the time of the tilt test were bronchodilators in 6 patients, psychotropic drugs in 2 patients, medications for migraine in 2 patients, and 1 patient each on cimetidine, thyroxine, and sodium chloride supplement. There was no difference in the use of bronchodilators or psychotropic drugs between the tilt-positive and tilt-negative children. The other medications were used only in the tilt-positive group.

Patients with recurrent syncope (both with positive and negative tilt test) were not different from those without recurrent syncope with respect to age at initial syncope, duration of symptoms, age at tilt test, and duration of follow-up (Table 2). Those with recurrent syncope had had significantly more episodes before the initial tilt test. They also tended to have a longer duration of symptoms before their evaluation, but when corrected for the duration of symptoms, there was no difference between the groups.

Negative Tilt

Of the 20 (10 female) tilt-negative children, follow-up was available on 15 (8 female). One patient died of severe asthma. Three patients were still on bronchodilator therapy for chronic asthma; another patient was taking imipramine for behavioral modification. None of the remaining patients was on any medication. Of the 15 tilt-negative patients with follow-up, 2 (13%) reported recurrent syncopal episodes; both were female. None of the children with recurrent syncope was on any medication during follow-up or at the time of tilt test; they reported one to four recurrent syncopal episodes. Of a total of five episodes in these patients, two episodes of syncope occurred while standing, two while running or shortly after exercise, and one while arising from supine to standing. We had to rely on the children's or parents' reports regarding the true nature of the recurrent syncopal episodes. However, because we specified loss of consciousness as the criteria for considering an episode to be an actual syncopal episode, we believe that only true syncope was reported.

TABLE 1. Demographics of the Population (Mean ± SD)

	Tilt Positive (n = 25)	Tilt Negative (n = 20)	P Value
Age at initial syncope, y	12.0 ± 3.5	12.2 ± 3.4	.8
Duration of symptoms, y	1.2 ± 2.0	0.6 ± 0.8	.30
Number of syncopal episodes	7 ± 6	3 ± 3	.013
Number of syncopal episodes/month	4 ± 7	5 ± 10	.7
Age at tilt-test, y	13.2 ± 2.9	13 ± 3.4	.85
Follow-up, y	2.8 ± 1.4	1.9 ± 1.3	.062
Gender, female	15 (60%)	10 (50%)	.31

TABLE 2. Comparison of Patients With and Without Recurrent Syncope (Mean ± SD)

	Recurrent Syncope (n = 15)	No Recurrent Syncope (n = 24)	P Value
Age at initial syncope, y	11.8 ± 3.4	11.9 ± 3.4	.93
Duration of symptoms, y	1.7 ± 2.4	0.7 ± 0.8	.065
Number of syncopal episodes	7.7 ± 5.8	4.4 ± 4	.037
Number of syncopal episodes/month	3 ± 5	5 ± 10	.43
Age at tilt-test, y	13.5 ± 2.6	12.7 ± 3.3	.41
Follow-up, y	2.6 ± 1.0	2.3 ± 1.6	.49
Gender, female	8 (53%)	15 (62.5%)	.57

Only 1 of the 2 patients with recurrent syncope consented to undergo a repeat tilt test. During the test, she complained of dizziness after the first 5 minutes of standing, and although she had a marked reduction in her diastolic pressure from 70 to 35 mm Hg, she did not experience loss of consciousness. Nonetheless, she was treated with fludrocortisone and salt without recurrence of her symptoms.

Positive Tilt

Twenty-five children (15 females) had a positive tilt test. Outpatient follow-up was available on all patients, either through the initial period after the tilt test (early follow-up) or through the questionnaire and outpatient visits (late follow-up). Five patients had a repeat tilt test after ≥6 months of therapy; in 3 it was still positive. Syncope recurred in 6 children during the early follow-up of 0.8 ± 0.7 years; all were on the standard therapeutic regimen at the time. In 5 patients, the recurrence was experienced within 2 weeks after the positive tilt test, whereas the sixth child had a recurrence within the first 6 months after the tilt test. Three of these 6 children received a β-blocker in addition to the salt and fludrocortisone, however, syncope recurred in all 3. Late follow-up of 3.2 ± 1.2 years after the tilt test was available on 20 children. Of these 20 children, 9 reported recurrence of syncope (2 patients had both an early and a late recurrence). Thus, 13 of the 25 children reported recurrent syncope at some point after a positive tilt test. The recurrence rate was significantly higher (P = .02) in the children after a positive tilt test than in those after a negative tilt test (2 of 15 with follow-up). Kaplan-Meier curves were calculated to assess the probability of syncope-free rates. The probability of being syncope-free for children with a negative tilt test was 87% at 54 months. For children with a positive tilt test the probability was only 48% at 54 months (Fig 1). Six of the 20 children with late follow-up were receiving therapy to prevent syncope (5 on salt and fludrocortisone, 1 on atenolol). Three of these 6 children had recurrent syncope. One of 2 other children on a prescription psychotropic drug (paroxetine hydrochloride) also had recurrence. The only patient on antimigraine therapy had a recurrence of symptoms.

DISCUSSION

The diagnosis of neurocardiogenic syncope relies on the clinical history and the results of tilt testing.[2]

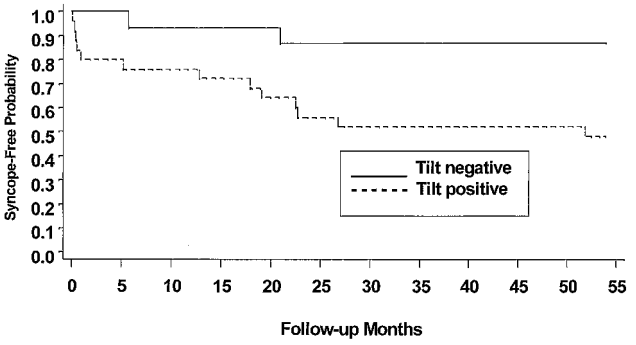

Fig 1. Probability of remaining free of syncope in 25 children with a positive tilt test (broken line) and 15 children with a negative tilt test (solid line). The step functions are the Kaplan-Meier estimates of the survival functions.

Tilt-test results are used to guide therapy and follow-up. Little is known about the long-term outcome of children with syncope and a positive tilt test. In a short-term (6-month) follow-up study of children with a positive tilt test, Scott et al[6] found the cure rate (no recurrence of syncope) to be 48%. As such, their recurrence rate of 52% was similar to the recurrence rate in our patients. To our knowledge, there are no reports on the long-term outcome of children with a negative tilt test.

In our study, children with a negative tilt test had fewer episodes of syncope on follow-up evaluation. Furthermore, our study demonstrates that syncope in children is a chronic disorder. In some children syncope can recur even after a long asymptomatic period. In other children there is a clustering of symptoms around the presentation with recurrences early in the follow-up and no late recurrences. Of 25 children with a positive tilt test, early recurrence was observed in 6 and late recurrence in 9. These data imply that although a majority of children with a positive tilt test (13 of 25) had recurrent syncope on follow-up, a significant number had no recurrence. Differentiating the children who will go on to have further symptoms from those who will not remains problematic. Our study shows that the only significant difference was the number of syncopal episodes reported before the tilt test. Despite the longer duration of symptoms in children with recurrent syncope, the frequency of syncope before the tilt test was not predictive of recurrence. These data may indicate that the chronicity of symptoms predicts a more severe form of neurocardiogenic syncope.

Sheldon et al[4] reported no difference in the recurrence of syncope in adults with either a positive or a negative tilt test and no pharmacologic therapy. Our study differs in that all children with a positive tilt test received some form of therapy for some time after the tilt test, whereas those with a negative tilt test were not on any pharmacologic therapy. Thus, it is difficult to compare the two reports. We agree, however, with Sheldon et al[4] concerning the lack of any significant parameter on pretilt evaluation that can predict recurrence. We are in agreement with other authors[5] who reported recurrence of symptoms in 64.8% of patients after a mean follow-up of 3 years.

There is not a single agent or a combination of agents that have proven completely effective in the prevention of recurrent syncope. Our choice of salt and fludrocortisone as the primary therapy was based on the experience of other pediatric centers.[6,7] β-blockers were used as an adjunct therapy when the initial therapy did not prove to be effective. It has not been shown that either therapy is more effective.[6] We have observed recurrent syncope in our patient population with either volume expansion, β-blockers, or both.

The limitations of this study are: 1) the retrospective nature of the study, 2) the number of children with a negative tilt test who did not have late follow-up. Nonetheless, our data suggest that tilt testing in children can differentiate between a group at high risk for recurrent syncope (tilt-positive patients) and those at low risk for recurrence (tilt-negative patients). Follow-up is indicated for all patients with recurrent syncope. In the absence of randomized placebo-controlled studies on therapy for syncope, the actual risk of recurrence is yet to be defined.

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