The Turkish Journal of Pediatrics 1997; 39: 573-577

VASOVAGAL SYNCOPE: ASYSTOLE PROVOKED BY HEAD-UP TILT TESTING UNDER SERTRALINE THERAPY*

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SUMMARY: Lenk MK, Alehan D, Özme Ş, Çeliker A, Özer S. (Cardiology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Vasovagal syncope: asystole provoked by head-up tilt testing under sertraline therapy. Turk J Pediatr 1997; 39: 573-577.

Syncope is defined as a sudden transient loss of consciousness. Vasovagally mediated hypotension and bradycardia are believed common, yet difficult to diagnose, causes of syncope in healthy children and adolescents. These episodes are often both sudden and sporadic in nature and, if recurrent and severe (malignant vasovagal syncope), can be a source of morbidity and possibly mortality. Head-up tilt testing has emerged as a useful investigation in patients who are thought to have recurrent vasovagal syncope with systemic hypotension, bradycardia, or both, and it has been suggested as a potential method to test for vasovagal episodes.

Sertraline hydrochloride, a serotonin reuptake inhibitor, has been reported to be effective in preventing the vasovagal syncopal episodes in children and adults. Here, two cases of recurrent, unexplained syncope are presented. Both were under sertraline therapy and underwent provocative head-up tilt testing that resulted in asystole.
Key words: vasovagal syncope, head-up tilt test, childhood.

Recurrent unexplained syncope is a common and often frustrating clinical problem. Syncope annually accounts for up to three percent of all adult emergency room visits and six percent of all hospital admissions[1]. Although the exact incidence of syncope in children is unknown, it is thought to be similar to that in adults. As much as 15 percent of children will experience syncope prior to the end of adolescence[2]. With the introduction of the head-up tilt test in 1986, a significant number of these recurrent unexplained syncopal episodes were attributed to transient periods of vasovagally mediated hypotension and bradycardia[3], which was reported as the leading cause of syncope in children[4].

The purpose of this report is to present two patients with normal hearts who had unexplained syncopal episodes and prolonged duration of asystole with provocative head-up tilt test after having been treated with sertraline hydrochloride.

Case Reports

Case 1

A 16-year-old girl who was previously well had the onset of frequent syncopal episodes consisting of weakness, pallor, dizziness, nausea and losses of

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consciousness for three to four minutes. The episodes were not accompanied by palpitations or other cardiac signs, but myoclonic movements in her hands and urine incontinence were reported. The spells occurred while standing and occasionally appeared to be provoked by stress or pain. There was no history in the family of syncope, epilepsy, deafness or sudden death.

Neurologic and cardiovascular examinations, including electrocardiogram, ambulatory 24-hour Holter monitoring, echocardiogram, treadmill exercise testing, electroencephalogram, and laboratory tests (complete blood count, urinalysis, electrolytes, blood urea nitrogen and glucose), were all normal.

At the first head-up tilt test, the patient's blood pressure was 110/75 mm Hg and her heart rate was 95 beats per minute in the supine position. At the tenth minute of the 60° tilt, she had an extremely abnormal response of a fall in heart rate to 40 beats per minute and in blood pressure to 60/30 mm Hg with reproduction of symptoms and syncope. A mixed type syncope was diagnosed, and she was started on sertraline hydrochloride, 50 mg orally each day. Six weeks later, her response to the head-up tilt test was reevaluated under the same conditions using the same tilt protocol. In the first minute of the 60° tilt, her systolic blood pressure dropped to 60 mm Hg and her heart rate slowed to 50 beats per minute. As she was returned to the supine position she lost consciousness; the electrocardiogram demonstrated a 20-second interval of atrial and ventricular asystole (Fig. 1). With the intiation of external chest compression and intravenous atropine, the asystolic episode was terminated, resulting in a return to sinus rhythm with effective blood pressure and a return of consciousness. Cardioinhibitory syncope was diagnosed and the patient was started on atenolol (a beta-blocking agent), 1 mg/kg/day at once orally. At the writing of this report, she has been without symptoms for eight months.

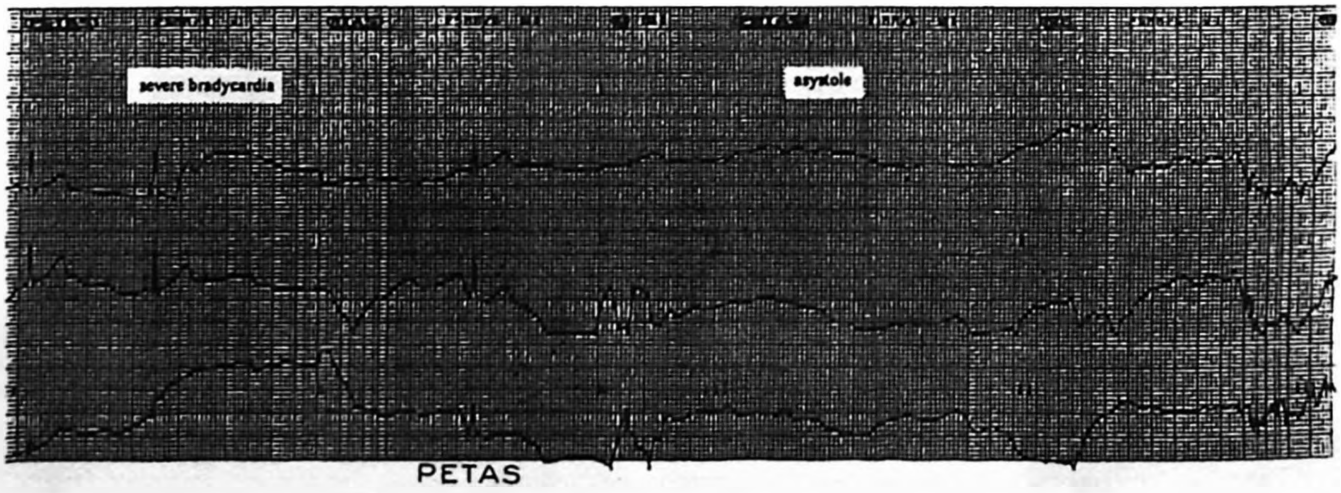

Fig. 1: Severe bradycardia and prolonged asystole during head-up tilt testing, showing a continuous tracing of electrocardiographic leads I, II and III.

Case 2

An 11-year-old girl had the onset of syncopal episodes by the age of seven consisting of pallor, weakness, dizziness and loss of consciousness. She had a total of six episodes. All occurred while standing, lasted for four to five minutes and were not related to situational events such as coughing, fever, defecation or severe pain. The episodes were accompanied by myoclonic movements in her hands and mild cyanosis in her lips. No family member had a history of syncope or sudden death; however, one of her uncles had epilepsy. Evaluations for these recurrent syncopal episodes, including neurologic and cardiovascular examinations, were all normal as in Case 1.

Prior to the initial head-up tilt test, the patient's blood pressure was 105/70 mm Hg and her heart rate was 90 beats per minute in the supine position. Mixed type syncope was diagnosed as her blood pressure and heart rate dropped to 50/30 mm Hg and 50 beats per minute, respectively, with reproduction of symptoms and syncope occurring in the fifteenth minute of the 60° tilt. She was given sertraline hydrochloride therapy, 50 mg orally each day, and six weeks later the response to the head-up tilt test was reevaluated. In the fifth minute of the 60° tilt, her blood pressure dropped to 55/20 mm Hg and an electrocardiogram demonstrated a nine-second interval of atrial and ventricular asystole. Cardioinhibitory syncope was diagnosed and the patient was started on disopyramide phosphate therapy, 150 mg three times daily. She also has been without symptoms, at the writing of this report, for seven months.

Discussion

Vasovagal syncope, also known as "the common faint", is a frequent cause of transient loss of consciousness[3, 4]. It is usually assumed to be a benign disorder with a benign prognosis; however, our two cases illustrate that it can cause major disability and possibly death.

Syncope is probably caused by activation of the Bezold-Jarisch reflex[5], provoked by a reduction in cardiac venous return and high concentrations of circulating catecholamines. The afferent limb of the reflex is transmitted to the A5 area of the medulla in the brain stem through vagal A and C fibers and may be activated by stimulation of ventricular mechanoreceptors caused by vigorous contraction of the relatively empty ventricles. Activation of the reflex causes central vagal stimulation and sympathetic withdrawal, resulting in arterial vasodilation, hypotension, and bradycardia. The head-up tilt test is a very useful diagnostic modality for use with patients with unexplained syncope because a significant number of these patients have neurocardiogenic or vasovagal syncope[2, 3, 6, 7]. In addition to the test's diagnostic value, results obtained during tilting can serve as a guide in assessing the efficacy of pharmacotherapies used to prevent

syncopal episodes[8]. The cause of syncopal episodes in our two cases was unclear despite thorough neurologic and cardiovascular examinations. This report supports the utility of a provocative head-up tilt test in diagnosing vasovagal syncope. The upright tilt table protocol we have used has been described previously[2, 8]. Although the methodological aspects vary[9, 10], the head-up tilt test results are generally characterized as vasodepressor, cardioinhibitory, or mixed, depending on the relative degree of hypotension and bradycardia. Mixed type syncope was diagnosed in our cases with the first head-up tilt test. Occasionally, the cardioinhibitory response may be profound, with asystole (an asystolic response is defined as the development of ventricular asystole of ≥5 seconds' duration). This type of response has been implicated in the occasional patient with neurocardiogenic syncope who has abrupt loss of consciousness during tilting[11]. We observed the same type of response in our patients during second tilting, the results of which have been applied in order to assess the efficacy of the pharmacotherapy given to prevent syncopal episodes.

To date, several pharmacotherapies have been used to prevent clinical and tilt-induced vasovagal syncopal episodes, such as transdermal scopolamine[12], theophyline[13], disopyramide[14], and beta-blockers[15]. Recently, the serotonin (5-hydroxytryptamine) reuptake inhibitor, sertraline hydrochloride, has been reported to be effective in treating up to 53 percent of young patients' neurocardiogenic syncope[16]. This was the only study performed in children. The serotonin pathogenesis in neurocardiogenic syncope is unclear. However, serotonin has been shown to be an important component of the responses seen as a result of acute blood loss, a mechanism essentially similar to that of neurocardiogenic syncope[17]. Abboud[18] recently reported that central intracerebrovascular serotonin induces hypotension, inhibition of renal sympathetic nerve activity and excitation of renal sympathetic activity. He further stated that serotonin acts at a central level to inhibit sympathetic activity and that serotonin antagonists are effective in the treatment of neurocardiogenic syncope. In order to evaluate its efficacy in preventing the syncopal episodes in our patients, we started treatment with sertraline hydrochloride (Lustral, Pfizer) and assessed the response by repeating the tilt test. Development of cardioinhibitory response led us to think the therapy with setraline hydrochloride was not effective in preventing tilt-induced syncope in our patients. Our two cases, the first treated with atenolol and the second with disopyramide, have been without symptoms. For eight and seven months, respectively.

Although the optimum treatment has not been defined for patients with cardioinhibitory vasovagal syncope, both drug treatment and permanent pacing have been used with some success[19, 20]. It seems reasonable to start treatment with pharmacotherapy. Permanent pacing, in which the choice is a dual chamber system, should be considered only if these measures fail.

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