Cerebral blood flow during supine rest and the first minute of head-up tilt in patients with orthostatic intolerance

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KEYWORDS
postural tachycardia syndrome; syncope; dizziness; cerebral blood flow velocity

Abstract  Aim  To assess the cerebral blood flow velocity during the first minute of head-up tilt in patients with postural tachycardia syndrome (POTS) or neurally-mediated reflex syncope compared with patients with dizziness.

Methods  We evaluated 120 patients selected from 470 patients who underwent head-up tilt testing: 40 with POTS, 40 with typical neurally-mediated reflex syncope and 40 who complained of dizziness with no history of loss of consciousness and a negative head-up tilt test (with and without isosorbide). Transcranial Doppler sonography of the middle cerebral artery, heart rate and brachial blood pressure were recorded during a 70° head-up tilt test.

Results  During both baseline in supine position and the first minute of upright tilt, patients with postural tachycardia syndrome showed higher heart rate and cerebral blood flow velocity than patients with dizziness and patients with neurally-mediated reflex syncope (P < 0.05, ANOVA), but no significant difference was observed on the Gosling’s pulsatility index.

Conclusion  Patients with POTS have an autonomic dysfunction that is not triggered by upright posture but is accentuated by it.

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Introduction

In healthy individuals, most of the orthostatic pooling of venous blood in the legs and abdomen occurs within the first 10 s after standing [1]. This pooling in the dependent parts results in a rapid decrease in central blood volume, cardiac filling pressure and stroke volume. The initial adjustments are mediated exclusively by the neural pathways of the autonomic nervous system. In patients with autonomic dysfunction, impaired compensation for the venous pooling leads to orthostatic intolerance.

Orthostatic intolerance is the development of symptoms during standing, which are relieved when the subject adopts a recumbent posture. The two most frequent causes of orthostatic intolerance are neurally-mediated reflex syncope (NMR-syncope) and postural orthostatic tachycardia syndrome (POTS). Neurally-mediated reflex syncope is characterized by premonitory signs and symptoms followed by loss of consciousness while in the upright position, which returns within seconds in the supine position. If the patient sits or lies down, syncope may be aborted. POTS is characterized by an increased heart rate accompanied by symptoms of cerebral hypoperfusion and sympathetic activation, which become manifest in the upright posture.

Two studies have demonstrated that during head-up tilt, patients with NMR-syncope show cerebral arteriolar constriction and reduced cerebral blood flow velocity before cardiovascular changes occur [2,3]. However, in patients with POTS, head-up tilt typically induces persistent sinus tachycardia associated with a mild reduction in systemic blood pressure [4] and a substantial decrease in cerebral blood flow velocity can occur despite a well sustained blood pressure [2,5]. In a previous study, aimed to compare cerebral blood flow velocity responses to head-up tilt in patients suffering from typical NMR-syncope and patients showing POTS, we observed that patients with POTS have larger oscillations and an earlier decrease in cerebral blood flow velocity than patients with NMR-syncope [6]. These results suggested that patients with POTS, on standing up, could have an inefficient regulation of cerebral blood vessels and the tachycardia may occur to compensate the diminished cerebral blood flow and even contribute to prevent hypotension. To evaluate further these findings, we studied the first minute of cerebral blood flow velocity response to head-up tilt test in patients with POTS compared with patients with typical NMR-syncope and patients with dizziness, without syncope and negative tilt test.

Methods

Subjects

From 470 consecutive patients who underwent head-up tilt test, we selected 120 adults:

- Forty patients with POTS (mean age 36 ± 10 years) [7], 30 women and 10 men. They reported orthostatic symptoms (e.g. light-headedness, nausea, weakness) that resolved with recumbency, 43% of them reported loss of consciousness. During the first 10 min of head-up tilt, patients developed orthostatic symptoms accompanied by an increase in heart rate of more than 30 bpm [7].
- Forty patients with typical NMR-syncope (mean age 34 ± 11 years) [8], 22 women and 18 men. They reported orthostatic symptoms followed by loss of consciousness with spontaneous recovery within seconds. Head-up tilt testing (with or without isosorbide) provoked syncope or pre-syncope accompanied by systemic hypotension (systolic blood pressure ≤ 80 mmHg or >30% reduction from baseline) and/or bradycardia (heart rate < 50 bpm or >20% reduction in heart rate from baseline) [9]. During head-up tilt, none of these patients had an increase in heart rate of more than 30 beats per minute (bpm) or a heart rate ≥ 120 bpm.
- Forty patients with dizziness (mean age 39 ± 11 years), 30 women and 10 men. Patients denied having a history of loss of consciousness. Head-up tilt testing with and without isosorbide was negative.

Patients with structural heart disease, sick sinus syndrome, intraventricular conduction disturbance, orthostatic hypotension, chronic and paroxysmal atrial fibrillation, and permanent pacemakers were not included in the study. To exclude other causes of syncope, all patients underwent clinical evaluation (including neurological) by detailed history and physical examination, carotid sinus massage and orthostatic heart rate and blood pressure measurements, supine and standing upright for 10 min, 12-lead electrocardiograms; transthoracic echocardiograms, and other non-cardiac investigations when deemed necessary.

The head-up tilt test was performed using a protocol authorized by the Local Ethics Committee. The test was carried out in a quiet room and after overnight fasting. Subjects were tilted to 70° head-up using a motorized tilt-table with a footboard support. Tilt was interrupted before...
its planned duration (30 min) when syncope or pre-syncopal symptoms occurred accompanied by systemic hypotension (systolic BP ≤ 80 mmHg or > 30% reduction from baseline) and bradycardia (heart rate < 50 bpm or > 20% reduction in heart rate from baseline).

During the test, ECG leads I, II and III were continuously monitored; brachial blood pressure and blood flow velocity of the middle cerebral artery (Transcranial Doppler Sonography, Multigon 500 Neurovision, Multigon Industries Inc., New York) were assessed before tilt (in supine position) and during tilt. Doppler signals were recorded according to the standard technique [10] to measure cerebral blood flow velocity using systolic peak velocity, end diastolic velocity and mean velocity, which were used to calculate Gosling’s pulsatility index ([(systolic velocity)−(diastolic velocity)])/mean velocity). The latter is an index of vascular resistance, which reflects changes in cerebral small vessels [10].

Individual responses to tilt were calculated by subtracting the measurements obtained during the last minute of baseline to the measurements obtained during the first minute of tilt. Results are described using mean values and standard deviations. Comparisons within each group were performed using t-test for dependent samples. Comparisons among groups were performed using Analysis of Variance; whenever it was significant planned comparisons were performed using the Least Significant Difference test (CSS, Statsoft, Tulsa); P < 0.05 was considered significant.

### Results

Before tilt, during baseline in the supine position, patients with POTS showed higher heart rate than patients with NMR-syncope and patients with dizziness (P < 0.05) (Table 1, Fig. 1). During this time, the systolic peak velocity and mean velocity were significantly higher in patients with POTS compared with patients with dizziness (P < 0.05, ANOVA) (Table 1); patients with NMR-syncope showed values between these two groups. In patients with POTS, the ratio between the Gosling’s pulsatility index and the heart rate were significantly smaller compared with the ratio observed in patients with NMR-syncope or dizziness (P < 0.05, ANOVA).

During the first minute of tilt, in all groups, a significant increase in the heart rate was observed (P < 0.05, ‘’t’’ test) (Fig. 1). However, as could be expected, the group of patients with POTS showed a significantly greater change than
the other two groups \((P < 0.05, \text{ANOVA})\). Also, a small but significant reduction in systolic blood pressure \((P < 0.05, "t" \text{ test})\) and a trend to increase the diastolic blood pressure were evident in all groups, with no significant differences among them. Although no significant changes were observed in the absolute values of the blood flow velocity measurements, the ratios between each of these measurements and the heart rate were significantly reduced after tilt, within each group \((P < 0.05, "t" \text{ test})\) (Table 1). The largest decrease was observed in patients with POTS \((P < 0.05, \text{ANOVA})\).

Comparison of the absolute values of heart rate, blood pressure and cerebral blood flow during the first minute of tilt showed higher values of heart rate and each of the cerebral blood flow velocity measurements in patients with POTS, compared with the other two groups \((P < 0.05, \text{ANOVA})\) (Table 1). No difference in the absolute values of the Gosling’s pulsatility index was observed.

Discussion

Few studies have compared responses to tilt in patients with POTS or NMR-syncope [6,11]. In the present study, we compared the responses of the two groups with the responses of a group of patients with dizziness but no syncope. This allowed us to identify a relatively higher heart rate and cerebral blood flow velocity in patients with POTS, which were consistent with the group differences observed during the first minute of tilt. This finding is consistent with the evidence showing that, even during supine rest, patients with POTS have increased sympathetic activity [12].

In a previous study we observed that, during upright tilt, patients with postural tachycardia can have periods of cerebral blood flow velocity decrease related to the heart rate increase [6], suggesting that tachycardia may occur to compensate for an inefficient regulation of cerebral blood vessels. In the present study we observed that, compared with patients with NMR-syncope and with dizziness and without syncope, patients with POTS had a larger heart rate increase related to the maintenance of cerebral blood flow velocity and pulsatility index, with a larger decrease in the pulsatility index/heart rate ratio. This observation could be compatible with the hypothesis that the tachycardia is a reflex response to an inefficient cerebrovascular autoregulation after standing. However, this explanation is not fully consistent with the finding of a similar pattern of group differences before and after tilt. In the two body positions, we observed group differences in the heart rate and the systolic and mean cerebral blood flow velocity, while the pulsatility index was similar in the three groups. Comparison of the responses within each group showed that only the heart rate response was significantly larger in patients with POTS. To understand these responses better, we should also consider that, in patients with POTS, dependent pooling occurs related to defective vasoconstriction [13] and the response to upright tilt is related to thoracic hypovolaemia [14]. Therefore, the relatively higher heart rate to increased sympathetic activity, which was evident in supine rest, would be exaggerated during the early response to tilt as a reflex response to hypovolaemia. Although the results of the present study support this hypothesis, simultaneous measurements of sympathetic activity and of peripheral blood flow would be necessary to prove it.

The results of this study show that patients with POTS have autonomic dysfunction that can be clinically evident even in the supine position. The autonomic dysfunction, therefore, is not triggered by upright posture but is accentuated by it.

References

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