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Does non-pharmacological treatment affect outcomes in dysautonomic syndromes?

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Abstract

Dysautonomic syndromes are very common clinical conditions with different presentations and a wide spectrum of mechanisms. Many non-pharmacological and pharmacological interventions have been recommended to treat dysautonomic patients along these years, but the majority of them were not supported by multicenter controlled trials. General measures, like water drinking and salt intake, avoiding triggers and recognizing prodromal symptoms, as well as performing orthostatic training and physical conditioning are commonly able to improve symptoms and avoid syncope and falls. In this article, we will explore why and how such measures are applied to treat patients with dysautonomic syndromes, based on the physiopathology of these disorders. (Cardiol J 2014; 21, 6: 611–615)

Key words: dysautonomic syndromes, syncope

Introduction

Dysautonomic syndromes leading to orthostatic intolerance and syncope are common clinical issues [1]. In a recent international meta-analysis, involving 43,315 patients with syncope in emergency departments, dysautonomic conditions (situational, orthostatic or vasovagal causes) were present in 30% of patients [2].

Dysautonomic syndromes can be acquired or idiopathic. Some are genetically determined. In general, these disorders have a benign prognosis, but up to one third of patients present physical injury related to falls. Thus, dysautonomic syndromes have a great impact on quality of life [3]. Lack of a robust diagnosis of the mechanisms involved and presence of frequent recurrences can create psychosocial effects including anxiety, panic, and depression. For these reasons, all efforts have to be made to clarify the etiology of syncope, define the prognosis and, consequently, establish the best treatment.

Different clinical presentations and a wide spectrum of mechanisms are involved in the pathophysiology of these syndromes [4], most of which are still not entirely understood. While different non-pharmacological interventions have been proposed, their results are controversial and multicenter controlled trials supporting them do not exist.

Individualizing understanding of autonomic dysfunction in relationship to an organic condition and distinguishing it from a functional disorder is fundamental before planning treatment. Concerning reflex syncope, achieving an ideal treatment is even more difficult, because its paroxysmal nature makes the assessment of the treatment efficacy particularly challenging.

Pathophysiological mechanisms as a goal for therapeutic approaches

Vasovagal syncope seems to be a physiological response with different degrees of individual susceptibility: the reflex pathways involved in vasovagal reflex are the same as those related to the mechanisms of protection against exaggerated bleeding and extreme stress and may occur in

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normal individuals after variable periods of space flights or exposure to ground models of microgravity [5].

Autonomic control of the cardiovascular system depends on the integrity of the brain, spinal cord and nerves; it depends also on the integrity of the heart conduction system, on vasoconstrictor reserve, blood volume, and influences of pharmacotherapy and age. The first step of the treatment is to reassure patients about the benign nature of the condition and to teach patients how to avoid triggers and recognize premonitory symptoms in order to prevent falls and physical injuries [6].

It has been observed that in dysautonomic syndromes, most patients have greater venous volumes and impaired vasoconstriction in response to orthostatic stress and exercise [7, 8]. This condition leads to an inefficient venous return and abnormal central blood distribution. The level of vasoconstriction deficiency is associated with different degrees of orthostatic intolerance, being worse in those patients who faint early during tilt table test [9, 10].

Salt and water

Salt supplementation has an important role for patients with dysautonomic syndromes and it is associated with improvement in orthostatic tolerance [11]. It is recommended in the absence of coexisting hypertension and mainly in patients with 24-h urinary excretion of sodium inferior to 170 mmol/dL. Salt supplementation provokes improvement of the sympathetic control of the vasculature, leading to a better vasoconstriction response to orthostatic stress and a better cerebral auto-regulation, with no change in the resting blood pressure (BP). The recommendation is to add enough salt to the meal as taste allows. If this sodium is insufficient, oral tablets can be added.

The augmented ingestion of water is recommended not only to increase blood volume. Indeed, this is not the most important consequence of the water ingestion on dysautonomic patients. When water is drunk, a pressor response is observed, reaching the maximum effect around 20 min after the ingestion [12, 13]. This consequence was demonstrated in older normal subjects and in patients with autonomic failure. The mechanisms of the pressor response remain unclear, but it has been observed that water incites an increase in the peripheral vascular resistance and consequently, less fall of the stroke volume. There is indirect evidence that water provides a pressor effect even in normal subjects. It was observed that water ingestion increased orthostatic tolerance to head-up tilt test combined with lower body negative pressure [12]. Its effect alone in vasovagal syncope remains unclear but, in the postural orthostatic tachycardia syndrome, water ingestion attenuates the postural rise in heart rate (HR) and in patients with autonomic failure, and also reduces the degree of orthostatic and postprandial hypotension [13].

Tilt training, head-up sleeping

Orthostatic intolerance is a common clinical syndrome observed after space flights and its ground based simulation models, the 6° head down bed rest and diving [14, 15]. In these cases, orthostatic intolerance cannot be explained as a simple consequence of hypovolemia, because restoration of plasma volume does not completely improve the condition. It is already known that microgravity provokes many modifications in the hemodynamic parameters and cardiovascular autonomic responses to orthostatic stress, like impairment in the baroreflex sensitivity, attenuation of vasoconstriction and increase of venous capacitance, which is exacerbated by a decrease in muscular tonus. These data show that similar cardio-circulatory changes are present in ground based microgravity models and in dysautonomic syndromes. Trying to clarify the role of orthostatic training in the management of these conditions, 1 study evaluated healthy subjects, who were divided into two groups. They were submitted to 21 days of head-down tilt bed rest (HDT) [16]. The study group was also submitted to lower-body negative pressure (LBNP). LBNP is an experimental model of orthostatic stress and it is considered similar to head-up tilt table test in assessing predisposition to hypotension. It can also simulate orthostatic or tilt training. Before HDT, all the subjects of the study group and the control group completed the tilt tests. After 10 and 21 days of HDT, all the subjects of the control group and 1 subject of the LBNP group could not complete the tilt test due to presyncopal or syncopal symptoms. The mean upright time before symptoms in the control group was significantly shorter than the one in the LBNP group. Stroke volume and cardiac output decreased significantly in the control group on days 3 and 10 of HDT, but remained unchanged throughout HDT in the LBNP group. The results suggest that brief daily orthostatic training sessions were effective in diminishing the consequence of HDT on orthostatic tolerance. Extrapolating the findings for dysautonomic patients, postural training could be applied to obtain a similar effect. A practical method of performing orthostatic training is head-up sleeping (HUS) [17]. The effect of 3 to 4 months of 10º HUS on orthostatic tolerance was studied in patients with reflex syncope and early presyncope during tilting test associated with graded LBNP. Time to presyncope significantly increased after HUS. Before HUS, all patients experimented presyncope by the end of first level of lower body suction. After HUS, almost 50% of the patients were able to tolerate the test. HUS did not affect HR, whereas mean BP suffered a significant increase. Overall, there was a significant increase in plasma volume after HUS.

Ector et al. [18] proposed that repeated exposure to orthostatic stress and tilt training might be helpful to treat patients with dysautonomic syndromes, based on their potential positive effects on the autonomic function of the cardiovascular system. Experimental studies demonstrated a possible effect on the vasoconstriction reserve [19]. However, randomized controlled trials are controversial and do not confirm the effectiveness of tilt testing, especially because of poor compliance in continuing the training for longer periods [20–22].

Exercise training

Although exercise training is highly recommended for patients with dysautonomic syncope, there are few published data demonstrating its benefits in improving orthostatic tolerance [6].

It is well known that regular programs of exercises improve stroke volume and increase muscle mass and tonus. The active "muscle pump" in the legs, help venous blood return, preventing venous pooling. The stronger the muscle pump, the better [23, 24]. Physical training also induces modifications in the autonomic nervous system, increasing parasympathetic activity to the heart, lowering HR and improving baroreflex sensitivity [24, 25]. All these effects are highly desirable for patients with dysautonomic syndromes.

The most important obstacle faced by dysautonomic patients to perform a program of exercise is that they are unable to tolerate exercise and, consequently, most of them become deconditioned. Deconditioning is especially common in patients with postural orthostatic tachycardia syndrome (POTS) [26, 27]. The intolerance to exercise is usually secondary to high abnormal standing HR and BP responses to exercise. The difficulty to perform exercises increases the deconditioning and a vicious cycle of exercise intolerance is developed in these patients.

However, it was demonstrated that exercise training increases the baroreflex sensitivity in patients with POTS, decreasing the upright HR [28]. Performing low intensity to moderate exercises in recumbent bike, rowing or swimming at first, avoiding the upright position helps the patient to improve physical conditioning and to tolerate the upgrades along time.

A recent report demonstrated that patients with POTS have "smaller hearts" in terms of mass and diameter, associated with reduced blood volume, when compared to control subjects [29]. A program of exercise training applied to these patients increased left ventricular mass and blood volume and reduced HR in all of them. Quality of life was also improved in all patients after the training. The practice of supervised mild exercise in the supine position at the beginning of the program is critical to provide the patient a proper exercise and warrants their adherence to long-term therapy (Fig. 1).

Isometric counterpressure maneuvers

The physical counterpressure maneuvers have been introduced as a manner to avoid loss of consciousness and are recommended when symptoms of impending syncope occur. During the prodromal phase, BP falls prior to HR, due to vasodilatation in the skeletal muscles. Isometric maneuvers induce BP increase, delaying the loss of consciousness or avoiding it. This effect is mediated mainly by sympathetic nerve discharge and mechanical compression of the venous vascular bed [30].

The PC trial [31] was a multicenter, prospective trial, which randomized patients with recurrent vasovagal syncope and prodromal symptoms to conventional therapy alone and to conventional therapy plus physical maneuvers. The treated group had a significantly better outcome, with a relative risk reduction of 39% (95% CI 11–53%). These results motivated the inclusion of physical maneuvers as first-line treatment in patients presenting with vasovagal syncope and recognizable prodromal symptoms.

Conclusions

In conclusion, non-pharmacological therapies, based on lifestyle modifications, postural training and physical exercises are potentially helpful for dysautonomic syndromes. The main objective of

Figure 1. Physical rehabilitation: the patient starts the aerobic training in seated position, on an ergometric bicycle. Tilt training is recommended from the beginning of the rehabilitation program, as well as the lower extremities resistance training. When orthostatic tolerance improves, patient continues the aerobic training on the treadmill; **A.** Lower-extremity resistance training; **B.** Seated in an ergonomic bicycle; **C.** Tilt training; **D.** Treadmill.

these recommendations is to restore quality of life and self-confidence of the patients. Although there is some evidence that these interventions can affect the outcome, prospective studies enrolling larger number of patients are necessary to prove their efficacy.

Conflict of interest: None declared

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