Folia Cardiologica 2015
tom 10, nr 4, strony 283–287
DOI: 10.5603/FC.2015.0050

ISSN 2353–7752

Application of orthostatic test and lower body negative pressure in investigation of circulatory reflexes in humans

Zastosowanie testu pionizacyjnego i podciśnienia wokół dolnej połowy ciała w badaniach odruchowej regulacji krążenia u ludzi

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Abstract

The aim of this paper is to present methods applied in analysis of tolerance to gravitational acceleration (±Gz) changes and diagnostics of the dysfunction of the autonomic nervous system (ANS) concerning cardiovascular system adaptation to the vertical body position.

The head-up tilt test (HUT), head-down tilt test (HDT), and lower body negative/positive (LBNP/LBPP) pressure are widely used for evaluation of integrated ANS reflexes.

Due to its simplicity, ease of application and full control over the level of excitation, HUT has become a frequently used clinical test in orthostatic hypotony.

LBNP is widely used in aviation medicine to study cardiovascular regulation. In clinics, the method is applied as a reliable procedure to study results of the shift of physiological fluids in the head–legs direction. Due to the supine patient position during the test, muscle contraction (pump) and vestibular influences can be avoided and a pure cardiovascular reflex is observed.

Abrupt and/or fast repeatable changes in the direction of gravitational acceleration (±Gz) can result in loss of consciousness (G-LOC). Recent results suggest that tolerance to +Gz is reduced when preceded by HDT (–Gz) (push-pull effect).

Key words: orthostatic test, LBNP, circulatory reflexes, push-pull effect

(Folia Cardiologica 2015; 10, 4: 283–287)

Introduction

The first information about the use of gravity field changes in medicine date back to 1818. Acceleration in the legs-head direction (–Gz) induced by a primitive centrifuge was then applied in neurosis treatment [1]. Yet, spectacular progress in methods based on variable gravitational field was achieved in the 1960s when G-force centrifuges, tilt tables, and negative or positive pressure chambers that facilitated quantitative control of the G-force stimuli applied were devised to meet the needs of aviation and aerospace medicine. In current clinical practice, tilt and lower body negative pressure tests are used for assessment of the threshold of tolerance to G-force (±Gz) or diagnosis of the autonomic nervous system (ANS) in terms of dysfunctions of cardiovascular system adaptation to the vertical body position.

The aim of this paper is to present methods applied in the analysis of tolerance to gravitational acceleration (±Gz) changes and the diagnostics of the dysfunction of

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the autonomic nervous system concerning cardiovascular system adaptation to the vertical body position.

The head-up tilt test, head-down tilt test, and lower body negative/positive pressure are widely used for evaluation of integrated ANS reflexes.

Methods of application of variable and/or simulated gravity field

Three methods are employed for changes and/or simulation of the direction and values of the gravity field vector affecting the examined individual:

- **change of the body position:** a passive head-up tilt test (HUT or HUTT) and/or a passive head-down tilt test (HDT or HDTT), prolonged head-down bed rest (HDBR, BR, Trendelenburg position), and an active head-up tilt test (change of the body position from horizontal, sitting, or squatting into the vertical position);
- **application of a pressure stimulus** (LBPP, lower body positive pressure) **and/or a negative pressure stimulus around the selected anatomical body region** (LBNP, lower body negative pressure), and **neck pressure** (NP) **or neck suction** (NS) **in the carotid sinus region**;
- **use of an acceleration centrifuge.**

Depending on the type of test, the ±Gz stimuli applied can be constant and/or uniformly increasing, stepwise, pulse and/or with variable duration, alternating (push-pull), and close to loss of consciousness — A-LOC and/or G-induced loss of consciousness — G-LOC type.

A series of tests based on many types of stimuli are used for assessment of the threshold of G-force tolerance. The most common combinations include HUT with LBNP, HDT with HUT, HUT with stimulation of the carotid sinus region, or a G-force centrifuge with LBPP. The aim of these investigations is to accelerate of the appearance of almost loss of consciousness symptoms (increased load) or, conversely, to mitigate the effects of the stimulus and control the responses of the regulatory mechanisms triggered by the stimulus.

The integrity of the ANS reflexes is assessed using provocation tests and interventions that are not strictly associated with changes in the gravity field vector. These include Valsalva Maneuver (VM), static hand grip (HG) test, deep breathing test (DB), response to sympathomimetics and/or sympathetic and/or parasympathetic blockade, sympathetic ganglion blockade, mental load, or increased respiratory resistance (flow or elastic).

Head-up tilt test (orthostatic test)

The orthostatic test is a non-invasive method for assessment of circulatory reflexes in response to a variable gravity field vector. Due to its simplicity, ease of application, and full control over the level of excitation, HUT has been widely used in the diagnostics of syncope [2]. Clinical manifestations of syncope include nausea, diaphoresis, yawning, monochromatic vision (grey out), vertigo, systolic blood pressure (SBP) < 80 mm Hg [3], and a decrease in SBP by 15 mm Hg/min and/or in bradycardia by 15 beats/min [4, 5]. According to the latest guidelines of the European Society of Cardiology [5], the orthostatic test should include a 5-min rest in the supine position before examination and tilting for at least 2 minutes. A drop in systolic and diastolic pressure by 20 mm Hg and 10 mm Hg, respectively, as well as an increased heart rate by 30 beats per minute or a rate exceeding 120 beats per minute are regarded as the threshold values of blood pressure changes. Reduction of systolic blood pressure by more than 20 mm Hg or below the value of 90 mm Hg is defined as orthostatic hypotony, irrespective of occurrence of specific signs.

The orthostatic test should be applied after stabilization of basic physiological parameters such as heart rate and blood pressure. Reduction of the length of the rest period before tilting significantly lowers the test sensitivity. Methods based on the analysis of heart rate variability (HRV) have indicated that hemodynamic stability is regained after at least 30 minutes of rest [6].

The so-called passive orthostatic test is used most frequently in clinical practice; it does not produce the characteristic heart rate and blood pressure oscillations induced in the first seconds after active standing up to the upright position. The active test is only applicable in short-term examinations with a low syncope risk [7].

A comparison of the two orthostatic tests outlined above is presented in the papers of Sung and Tanaka [8, 9]. The authors imply that, regardless of the type of the test, cerebral blood flow is the most efficient way to predict an episode of loss of consciousness. They suggest that paradoxical cerebral vasoconstriction in response to hypotension may be one of the causes of syncope. The largest blood pressure decrease is observed during active tilting from the squatting position. The problem is addressed in detail by Tschakovsky [10], who ascribes the rapid drop in blood pressure to lower limb-localized vascular phenomena. The author regards lower-limb vascular compression occurring in the squatting position and rapid vasodilation at the standing up maneuver as the primary cause of the observed hemodynamic effects.

Head-down tilt test

The head-down tilt test includes two procedures, i.e. head-down tilting HDT [11] and prolonged (from several hours to several weeks) head-down bed rest (HDBR) position (Trendelenburg position) [12–15].

The HDT test is rarely applied alone, in which case it serves as a technique of baroreceptor stimulation during assessment of arterial baroreflex gain [16]. It is usually combined with HUT and then it simulates the push-pull effect, likewise HDBR combined with HUT, LBNP, and less frequently in a LBNP/LBPP combination [16, 17].

In the HDT or HDBR test, the tilt table angle does not exceed –10° [16, 18], whereas at prolonged head-down bed rest it is usually –6° [12, 14, 15, 19, 20]. LBNP is used in prolonged HDBR tests for investigation of hemodynamic adaptation mechanisms [15, 19, 20].

Although neither the head-down tilting test nor the orthostatic test offers the possibility of exceeding the ± 1G thresholds, in clinical conditions they are an easier and cheaper alternatives to the G-force centrifuge. Although relatively weak stimuli (≤ 1G) are applied, a series of neurohormonal reflexes can be observed, which indicate the efficiency of cardiovascular regulatory mechanisms. Previous investigations have shown that tolerance to G-force decreases when the HDT (–Gz) test is applied prior to the +Gz stimulus. Measurements of arterial pressure at the level of the temporal artery demonstrated an initial decline in its value when the +Gz stimulus was preceded by –Gz (push-pull). Sympathetic activity is assumed to play an important role in the enhanced regulatory response during the push-pull test [21].

Push-pull mechanism (PPM)

Rapid and/or repeated changes in the vector of gravity operating in the longitudinal body axis within a short (seconds) period may lead to loss of consciousness (G-LOC). Two hypotheses have been proposed to explain the cause of the enhanced hypotensive response to the sudden change in the gravity vector. The process may be associated with myogenous vasodilation resulting from a decrease in transmural pressure in the lower limb vasculature caused by the legs-head gravity vector or be a result of rapid inflow of blood into vessels relaxed in the "push" phase. Consequently, both mechanisms lead to decreased cerebral tissue perfusion [11, 22–24].

Lower body negative pressure

The technique of lower body negative pressure is extensively used in aviation medicine for assessment of cardiovascular regulatory mechanisms. In clinical investigations, the method is applied as a test providing reproducible hemodynamic responses to the shift of physiological fluids in the head-legs direction. In the orthostatic test, the examined individual is in actual motion in the gravity field, which additionally triggers vestibular reflexes as well as joint and muscle proprioreceptor and ocular reflexes if the test is performed with eyes open [25]. In turn, LBNP tests are carried out (in a majority of cases) in the supine position. This allows avoidance of muscle contraction (pump) and vestibular influences and exploration of a pure cardiovascular reflex.

Upon tilting, 500–1,000 ml of blood is pooled within a short time to body regions below the hypothetical hydrostatically neutral plane, mainly to lower extremities and visceral circulation [26]. This leads to hypovolemia, which may cause orthostatic collapse. Hypovolemia also occurs in hemorrhage and G-force tests; hence, it has become the object of interest in emergency and military medicine. Therefore, LBNP is a non-invasive, controlled technique of hypovolemia simulation.

There is no standard LBNP protocol concerning the variation or magnitude of the applied stimulus. Typically, constant negative pressure values between –20 mm Hg [27] and –100 mm Hg [26] and stepwise increasing [28–30] or sinusoidally variable [31] stimuli are used. Wolthuis et al. [32] showed that only strong negative pressure of 130 mm Hg leads to a steady increase in the vessel diameter when smooth muscles are incapable of breaking up the transmural pressure; therefore, this value defines the upper limit of the negative pressure applied in practice.

Less information is available about the dynamics of the stimuli applied. Most authors confine themselves to defining the value of lower-body negative pressure and duration of exposure. A paper by Lindenberger [26] is the only report showing that the rapidly changing stimulus reached the target level after 5 s, which indicates a 20 mm Hg/s rate of change at application of negative pressure of 100 mm Hg.

Based on the analysis of blood flow in the lower extremities and neck induced by changes in the gravity vector generated in a short- and long-arm G-force centrifuge or the LBNP test, Watenpaugh [33] developed an interesting thesis that, from the point of view of the magnitude of cardiovascular responses and simulation of gravity field during prolonged exposure to weightlessness, lower-body negative pressure is a more efficient and practical stimulus than centrifugation.

Analysis of results obtained in variable gravity tests

Irrespective of the adopted research protocol, for application of the orthostatic and LBNP tests, the use of non-invasive measurement techniques facilitating monitoring time-variable signals of the observed physiological processes is more important. Detailed recognition of the interactions between the variable hemodynamic parameters requires a specific approach, which would allow limiting the time of observations. This natural cycle in the circulation system is determined by heartbeat. An analysis of beat-to-beat cardiovascular response to LBNP was presented by Hisdal [34] and Sheriff [35]. Unlike the mean values of the parameters measured during the application period, the beat-to-beat parameters revealed characteristic transient changes in mean arterial pressure (MAP), heart rate (HR), cardiac output (CO), total peripheral resistance (TPR), skin and arterial blood flow, and asymmetry in the responses in stroke volume (SV) to the onset and release of the LBNP stimulus. Knowledge of the dynamics of concurrent changes in hemodynamic indices helps to determine their phase-frequency relationships, thus contributing to development of adequate models of observed physiological processes [36].

Conclusions

Initially, the methods of application of a variable gravity vector for investigation of circulatory reflexes in humans presented above were applicable in military and aerospace medicine. Technological progress, in both mechatronics and techniques of biological signal measurement, has made the clinical use of the tilting and LBNP tests possible.

Conflict of interest(s)

The authors declare no conflict of interest.

Streszczenie

Celem niniejszego opracowania jest przedstawienie dotychczasowych osiągnięć na polu aplikacji zmiennego pola grawitacyjnego do oceny progu tolerancji na działanie przeciążeń (±Gz) lub diagnostyki autonomicznego układu nerwowego (ANS) pod kątem zaburzeń adaptacji układu krążenia do pozycji pionowej. Integralność odpowiedzi ANS bada się, stosując między innymi takie testy prowokacyjne, jak test pionizacyjny (HUT/HDT) lub pod/nadciśnienie wokół dolnej połowy ciała (LBNP/LBPP).

Dzięki swojej prostocie, łatwości wykonania i pełnej kontroli nad siłą bodźca HUT stał się często stosowaną próbą kliniczną w badaniach hipotonii ortostatycznej.

Ocena LBNP jest intensywnie wykorzystywana w medycynie lotniczej do określania krążeniowych mechanizmów regulacyjnych. W badaniach klinicznych metodykę tę stosuje się jako bodziec powodujący powtarzalne odpowiedzi hemodynamiczne na przesunięcie płynów fizjologicznych w kierunku głowa–nogi. Próba prowadzona w pozycji leżącej pozwala uniknąć wpływów mięśniowych oraz układu przedsionkowego i badać czystą odpowiedź krążeniową.

Gwałtowna i/lub wielokrotna zmiana zwrotu działającego w długiej osi ciała wektora grawitacji w krótkim horyzoncie czasowym może spowodować utratę świadomości (G-LOC). Z dotychczasowych badań wynika, że tolerancja na przeciążenie maleje, jeśli przed bodźcem +Gz zastosuje się próbę odwrotnej pionizacji (HDT, –Gz) — efekt *push-pull*.

Słowa kluczowe: test pionizacyjny, LBNP, odruchowa regulacja krążenia, efekt *push-pull*

(Folia Cardiologica 2015; 10, 4: 283–287)

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