Abstract. – Background: The cardiovascular system works to maintain homeostasis through a series of adaptive responses to physiological requirements. Different self-regulatory mechanisms prevent the effects induced by hydrostatic pressure changes on oncotic pressure caused by postural changes.

Gravity exerts a strong influence on the postural changes with implications on the cardiovascular system. In orbit, gravity (+Gz) is responsible of mass redistribution of circulating blood flow.

The aim of this study was the evaluation of the adaptive responses of cardiovascular system to postural changes with and without the use of the Lower Body Negative Pressure (LBNP).

We considered that pressure changes that occur in human body in orbit can be simulated experimentally with use of Tilt-Test (Clino/ortho; Clino/head-down; head-down/ortho).

This investigation could be useful for studying the influence on astronauts of long flights.

Subjects and Methods: We studied in 12 months, 30 young healthy volunteers (20 males, 10 female) during postural change tests. In the first evaluation they were submitted to tilt-test for 40 minutes, remaining in head-up +60° (this state corresponds to a kind of gravitational stress +Gz) and in head-down to -30° (-Gz) for 20 minutes. During the second assessment (after 5 ± 1 days) all volunteers wear a device that simulate a state of LBNP at -20 mmHg. Afterwards, they were processed to 20 minutes in Head Down -8° and after 2 hours of rest to 20 minutes at -15°. Volunteers were monitored measuring blood pressure, heart rate and by Transthoracic Echocardiogram (TTE)

Results: Collected data were elaborated by a statistical analysis. We observed during orthostatic position for 40 min (+60°) without LBNP, lower diameters and volumes of left and right ventricular (p < 0.05) and an increase in heart rate in comparison with the baseline conditions in clinostatism. Despite the reduction of preload volume, the mean value of cardiac output does not vary significantly.

In Trendelemburg (-15°) data show a non-significant variation (p > 0.05) of left and right ventricular diameters and volumes, while cardiac output and systolic blood pressure varies significantly (p < 0.05) compared to clinostatic and orthostatic position.

With LBNP in head down to -8° and -15°, systolic and diastolic arterial pressure, ventricular volumes and cardiac output were unchanged if compared to values obtained in clinostatism with and without LBNP. If compared to -30° in Trendelemburg without LBNP, data reached statistical significance (p < 0.05)

Conclusions: The cardiovascular system and the autonomic nervous system, respond to postural changes and to volemia alterations, maintaining the physiological cardiac output, in order to preserve the metabolic requirements of body.

Key Words:
Elasticity/distensibility of the ascending aorta; Windkessel function; Microgravity conditions; Simulation.

Introduction

The cardiovascular system works to maintain homeostasis with a series of adaptive responses to physiological requirement. Many self-regulation mechanisms (buroreceptor, chemoreceptor, hormonal system, nervous system) prevent the effects induced by the change of hydrostatic pressure on the oncotic pressure caused by postural changes. These regulation guarantees an
adequate cardiac output to vital organs. Postural changes if not compensated, can determine both inadequate cerebral perfusion and formation of peripheral edema in the legs.

The relationship between these mechanisms and cardiovascular system is not yet fully defined. In fact other structures (i.e. vasoactive substances endothelium dependent) participate to general homeostasis, especially when the body is subjected to sudden changes of gravity such as during space flights. The strategic location of the endothelium allows it to “sense” changes in hemodynamic forces and blood-borne signals and “responds” by releasing a number of autocrine and paracrine substances. A balanced release of these vasoactive factors, as endothelin, angiotensin II, vasopressin with vasocostriction action and other as Nitric Oxide, bradykinin, acetylcholine, prostaglandins with vasodilation action, facilitates vascular homeostatis. Endothelial cell dysfunction disrupts this balance, thereby predisposing the vessel wall to vasocostriction, leukocyte adherence, platelet activation, oxidation, thrombosis, impaired coagulation, vascular inflammation and atherosclerosis.

Gravity exerts a strong influence on postural changes with implications on the cardiovascular system. During space flights, gravity causes a redistribution of blood circulating mass. This phenomena causes a stagnation of blood in the area under the diaphragm (by venous return reduction) increasing both precapillary hydrostatic pressure and fluids in the interstitial space. The cardiovascular system assures an adequate venous return to neutralize the effects of gravity and to maintain an adequate flow in the area over the diaphragm. The important role of vascular system to assist the cardiac output during postural and gravitational changes has already been investigated by the Authors, trough an evaluation of aortic function and properties with echocardiography and non invasive measurement of pulse pressure curve.

The adaptive responses of the cardiovascular system and morphological and functional variations of cardiac chambers have been analyzed in response to postural changes with and without use of the Lower Body Negative Pressure (LBNP). It has been assumed that using the LBNP during postural changes, it is possible to simulate pressure variations that occur in a human body during space flights. The studied condition is potentially useful argument for the permanence of the astronauts in long-term flight.

Subjects and Methods

30 young healthy volunteers (20 males, 10 females) were studied during postural change tests in 12 months. The first observation was made at the Laboratory of Tilt Test of Cardiology of the University of Rome “Sapienza” – Poli Pontino. The second, was conducted at the Centro Sperimentale di Volo, at the “Military Airport of Pratica di Mare”. The enrolled volunteers are in a good state of health and they aren’t taking any medication. An automatic tilt-test and echocardiography (Acuson CV 70 Siemens Healthcare, Issaquah, WA, USA) are used in the study.

In the first evaluation the subjects underwent to Tilt-test, for 40 minutes remaining in head-up +60° (this state corresponds to a kind of gravitational stress + Gz) and in head-down to -30° (-Gz) for 20 minutes.

During the second assessment (after 5 ± 1 days) all volunteers wear a device that simulate a state of LBNP (J & S, Rome, Italy) at -20 mmHg. After that, all subjects were processed to 20 minutes in Head Down -8° and after 2 hours of rest to 20 minutes at -15°. All volunteers were monitored measuring blood pressure, heart rate and with Transthoracic Echocardiogram (TTE).

All volunteers were examinated by transthoracic echocardiography (standard projections in accordance with the criteria of the American Society of Echocardiography. During the study the following parameters are collected: telediastolic and telesystolic ventricular diameters and the volumes, ejection fraction (EF) with Teicholz formula, transverse and longitudinal diameters of atrial chambers with volumes, cardiac output (through the estimation of the systolic output and heart rate).

Diastolic function was valued with Doppler technique measuring: ratio E/A, relative peak velocity, acceleration and deceleration time, isovolumetric relaxation time. Peak velocity of systolic and diastolic pulmonary veins, atrial reverse wave, and systolic and diastolic diameters of inferior vena cava. The same measurements were made in orthostatic position (+60°) after 30 minutes and after 10 minutes in a Head Down (Trendelenburg) and in basic conditions.

Echocardiography started 10 minutes after the beginning of the experiment with the LBNP set at -20 mmHg. All measurements were assessed independently by two different operators.
Statistical Analysis
For the statistical processing of data, the mean and the standard deviation were calculated. For the comparison of the average values the Student’s t test were used. All data were tabulated and processed using Microsoft Excel.

Analysis of Data
30 volunteers (20 male and 10 female, mean age 27 ± 2.7 years, M 26 ± 1.6, F 29 ± 1, height: 1.77 ± 0.08 cm, weight: 74.17 ± 10.45 kg, BMI 23.68 ± 2.18).

Parameters were observed during clinostatism conditions (base group), in head-up tilt test +60° (Gr. +60°) and in head-down tilt test -30° (Gr. -30°). The same measurements were repeated after LBNP application at -20 mmHg, in head-down tilt test -8º (Gr. LBNP -8) and -15° (Gr. LBNP -15°). A statistical comparison between the values obtained from the different experiment were made in order to observe a change in parameters that characterize the morpho-functionality of cardiac chambers.

Results
All data were reported in Table I.

The mean values of systolic blood pressure and heart rate, without LBNP, differ significantly (p < 0.01) from clinostatic position to orthostatic position (+60°), while the values of diastolic pressure don’t show significant changes (p = NS).

From clinostatic position to Trendelemburg (-30°), without LBNP, there is a significant difference of Systolic Pressure (SAP) (p < 0.01) but not of Diastolic Pressure (DAP) (p = NS), and heart rate (HR). From Trendelemburg position (-30°) to orthostatic (+60°), without LBNP, there is significant difference (p < 0.01) for the SAP and HR, but not for the DAP.

Without LBNP activated, there is a significant statistically difference (p < 0.01) for the mean values of right and left ventricular diameters and volumes from clinostatic position to orthostatism.

The same statistical significance (p < 0.01) regarding the values of left and right atrial diameters and volumes.

During transition from clinostatic position to orthostatism without LBNP, there is a statistical significance (p < 0.01) for the values of the mitral and tricuspidal E wave velocity, peak of tricuspidal A wave, acceleration and deceleration time of tricuspidal E wave.

Without LBNP activated, from Trendelemburg to orthostatic position, there is statistical significance (p < 0.01) for the values of right and left ventricular telediastolic diameters, left ventricular volume, right ventricular telesystolic diameter, right and left atrial transverse diameter, volumes and value of the longitudinal right diameter.

With LBNP (-20 mmHg), comparing values (group in head-down to -8°) and values of the group in clinostatic position there is no statistically significance (p = NS) for all values except for E and A mitral velocity, mitral acceleration and deceleration time, value of pulmonary artery diastolic velocity and tricuspid acceleration time (p < 0.05).

In the comparison between Trendelemburg -30°, without LBNP on, and Trendelburg -8° with LBNP on, there is statistical significance for the values of E mitral velocity, velocity of diastolic pulmonary flow, atrial wave velocity.

From Trendelemburg (-30°), without LBNP, and Trendelemburg (-15°) with LBNP, there is statistical significance (p < 0.001) for value of mitral wave acceleration time, pulmonary artery diastolic velocity flow, flow, atrial reverse wave, acceleration time of E tricuspid wave.

In the comparison between orthostatic position and Trendelemburg (-8°) with LBNP on, there is statistical significance (p < 0.0001) for the values of the left ventricular telediastolic diameters, E and A mitral wave velocity, mitral acceleration and deceleration time, isovolumetric relaxation time, reverse atrial wave velocity, the ejection fraction (EF) of right ventricular, the value of cardiac output. From orthostatic position and Trendelemburg (-15°), with LBNP, there is statistical significance for the values of left ventricular telediastolic diameters, volumes, mitral E wave acceleration time, diastolic pulmonary velocity flow, reverse atrial wave velocity, right ventricular EF, tricuspidal E wave velocity, acceleration time of tricuspidal E wave and heart rate.

Discussion
Venous return variations during postural changes causes morpho-functional adaptations on the cardiovascular system and particularly in cardiac chambers. In this study, volunteers, are
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young people in good health. They underwent to various conditions: Clinostatism, prolonged orthostatism through head/tail position +60 degrees and Trendelemburg position in head/down to -30°.

The position -30° for 20 minutes was used to verify the maximum variations of cardiovascular system. After a few days (5 ± 1 days) the same volunteers were processed to the same protocol with Lower Body Negative Pressure (LBNP) at a pressure of -20 mmHg.

LBNP was used only for Trendelemburg -8° and -15°, while during orthostatism the LBNP not used because of hypovolemia 10,11.

From data collected and from the statistical analyses, lower diameters and volumes of left and right ventricles $(p < 0.05)$ and an increasing in HR ($r = 0.92$) have been observed comparing baseline condition with orthostatic (+60° for 40 minutes) without use of LBNP.

Despite the reduction in preload volume, the mean value of cardiac output in both positions does not change $(p = NS)$ even if heart rate increases. HR mean value is significantly different $(p < 0.05)$ in two positions.

This behavior, confirms our knowledges about autonomic nervous system.

Positive effects on peripheral resistance and heart rate represent compensatory adaptation to venous return reduction, supporting pump action of the heart 11-20.

In Trendelemburg position to -15°, data show non-significant variation $(p > 0.05)$ of left and right ventricular transverse diameters and volumes, while cardiac output and systolic blood pressure change significantly $(p < 0.05)$.

With LBNP, the orthostatic posture not performed. In fact an excessive decrease in venous return has been observed after the first few minutes spent in orthostatism. Sudden drop in blood pressure (< 80/40 mmHg of) an excessive increasing in heart rate (> 120 beat/min) were observed. Besides pallor and fogging of face occur. Maybe in that situation the compensation mechanisms, were not able to maintain an adequate cardiac output 6,10,13,19.

In others two postures (clinostatic and Trendelemburg to -8° and successively to -15°), use of LBNP does not cause improper effects. All volunteers, during Trendelemburg, have not reported the annoying symptomatology of cephalic and discomfort provoked from the increase of blood flow through cefalic district.

With LBNP on and in head down (to -8° and then to -15°), systolic and diastolic blood pressure, ventricular volumes and cardiac output remained unchanged $(p = NS)$ compared with values in clinostatism with and without LBNP. In Trendelemburg to -30° without LBNP, statistical values are significative $(p < 0.05)$.

Conclusions

Cardiovascular system with autonomic nervous system, respond to postural changes and to volemia variations, maintaining constant cardiac output, preserving in this way the metabolic requirements of body.

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