Portal vein cross-sectional area and flow and orthostatic tolerance: a 90-day bed rest study.

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Arbeille, Philippe P., Stephane S. Besnard, Pascaline P. Kerbeci, and Dania M. Mohty. Portal vein cross-sectional area and flow and orthostatic tolerance: a 90-day bed rest study. J Appl Physiol 99: 1853–1857, 2005; doi:10.1152/japplphysiol.00331.2005.—The objective of this study was to evaluate the changes in the portal vein cross-sectional area (PV CSA) and flow during a stand test associated with orthostatic intolerance. Eighteen subjects underwent a 90-day head-down tilt (HDT) bed rest at 6°: 9 controls (Con) and 9 with flywheel exercise countermeasures (CM). At post-HDT, nine subjects (5 CM, 4 Con) were tolerant, and nine were intolerant. The PV CSA was measured by echography. We found that at HDT day 85, the PV CSA at rest had increased less in the CM subjects than in the Con (+12 vs. +27% from pre-HDT supine; P < 0.05), whereas it increased similarly in tolerant and intolerant subjects (23 and 16%, respectively). Two days after the HDT, there was a decrease in the PV CSA supine compared with the pre-HDT PV CSA supine that was similar for all groups (Con: −11%, CM: −21%; tolerant: −10%, intolerant: −16%; P < 0.05). The PV CSA decreased significantly less from supine to standing in the Con than in the CM group (−2 vs. −10% compared with the pre-HDT stand test; P < 0.05). The PV CSA also decreased significantly from supine to standing compared with the pre-HDT stand test in the tolerant group but not in the intolerant group (−20 vs. +2%; P < 0.05). From these findings, we conclude the following. 1) Because the portal vein is the only output from the splanchnic vascular area, we suggest that the lower reduction in the PV CSA and flow associated with orthostatic intolerance was related to a lower splanchnic arterial vasoconstriction. 2) The flywheel exercise CM helped to reduce the distention of the splanchnic network at rest and to maintain partially the splanchnic vasoconstriction, but it did not reduce the orthostatic intolerance.

HEAD-DOWN TILT (HDT) bed rests of short duration (24 h/day for several days) have been found to induce cardiovascular deconditioning and orthostatic intolerance as measured by heart rate and blood pressure responses to orthostatic tests (8, 11, 12, 21, 23, 27, 29, 33, 35).

Hemodynamic measurements during orthostatic tests (lower body negative pressure, tilt and stand tests) have shown that in tolerant subjects (finishers) the stroke volume drops, the cerebral flow decreases slightly, and the lower limb flow drops because of a significantly increased vascular resistance in the lower limbs (2, 31). As a consequence, the cerebral-to-femoral flow ratio, which quantifies the distribution of blood flow in favor of the brain, increases significantly. In tolerant and intolerant subjects, the stroke volume is reduced by a similar factor, but the femoral flow is reduced to a lesser extent and the vascular resistance of the lower limbs vascular resistance increases significantly less in intolerant subjects than in tolerant subjects. The reduction of the lower limb flow in tolerant subjects may be considered to be part of the hemodynamic adaptation to the drop in stroke volume (1, 2, 31). Conversely, in nontolerant subjects, the lower limb flow does not decrease, which reduces the effectiveness of the hemodynamic adaptation. The second major hemodynamic change found in intolerant subjects is the greater distension of the lower limb vein in the stand test, which does not favor the venous return (2, 6, 9, 10, 18).

Such responses in the lower limbs have been observed and measured in a significant number of HDT subjects and cosmonauts, but limited data are available on the possible contribution of the splanchnic arterial and venous networks to the flow redistribution in response to the fluid shift induced by an orthostatic test. The portal vein flow, which is ∼1 l/min, is the exclusive output from the splanchnic system, which means that the portal flow combines all the flows delivered to this network by the celiac trunk, mesenteric vessels, etc. The objectives of this study were 1) to quantify the changes induced in the portal flow volume at rest by HDT and 2) to quantify the portal vein cross-sectional area (PV CSA) changes associated with the fluid shift induced by a stand test in normal subjects before and after a 90-day long-term HDT bed rest with and without countermeasures.

METHODS

Subjects. Eighteen healthy young male subjects participated in a 90-day 6° HDT bed rest trial at the Medes Institut at Rangueil Hospital medical facility (Toulouse, France). At the start of the bed rest, the subjects were aged 33.1 ± 0.9 yr, with average height and weight of 1.75 ± 0.01 m and 71.1 ± 1.1 kg, respectively. All subjects passed the orthostatic tolerance test (10 min × 80° head-up tilt test) during the selection process. They received a complete description of the experimental procedure before giving their written consent to the protocol approved by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale, Midi-Pyrénées (France). The protocol was in accordance with the Declaration of Helsinki. None of the subjects were taking cardiovascular medication at the time of the study and all subjects were nonsmokers. The subjects were randomly divided into two groups: nine controls and nine countermeasure (CM) subjects. The CM subjects performed a combined eccentric-concentric resistance exercise (flywheel exercise) every 3 days. At a later stage, after the bed rest the orthostatic intolerance was evaluated, the subjects were again divided into tolerant and intolerant subjects (9 in each group).

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**RESULTS**

All subjects completed the HDT period of 90 days. The day after the HDT, a tilt test identified nine subjects (5 Con and 4 CM) as tolerant and nine as intolerant. On the 85th day of HDT, the PV CSA had increased less in the CM subjects than in the Con (+12 vs. +27% greater than...
The portal vein flow volume increased similarly in all groups (from 27 to 33%; \(P < 0.05\); Fig. 2, Table 1).

Two days after HDT, the PV CSA, in a supine position, had significantly decreased by a similar amount in all groups (Con: \(-11\%\), CM: \(-21\%\); tolerant \(-10\%\), intolerant \(-16\%\) compared with pre-HDT, \(P < 0.05\)).

The decrease in PV CSA from supine to standing position 2 days after HDT was significantly less in the Con than in the CM group (\(-2\%\) vs. \(-10\%\) compared with pre-HDT stand test; \(P < 0.05\)). PV CSA decreased from supine to standing significantly in the tolerant group but not in the intolerant group (\(-20\%\) vs. \(+2\%\) compared with pre-HDT stand test \(P < 0.05\); Fig. 3, Table 2).

**DISCUSSION**

**HDT induced splanchnic blood volume stagnation (at HDT day 85; Fig. 2, Table 1).** This study shows that the portal vein flow volume (in ml/min; Table 1) increases significantly after several weeks of HDT in a similar proportion in all subjects (Con, CM, tolerant, intolerant). Because the portal vein is the only output of the splanchnic network, this result shows that there is an increased splanchnic arterial blood flow associated with the reduction of the vascular resistance in the splanchnic network. The capacity of the splanchnic arterial network to generate a vasoactive response has already been demonstrated during exercise. A progressive splanchnic vasoconstriction during exercise was first reported using invasive studies of indocyanine green uptake, and Doppler ultrasound has confirmed progressive reductions in the blood cell velocity, cross-sectional area, and quantitative portal vein flow (24). After 85 days of HDT, the subject is hypovolemic \([10\%\) plasma volume reduction (7)], which also suggests that there is splanchnic vasodilatation.

Moreover, the significant increase in the PV CSA (about +12 to +33\%) suggests that there is an increase in blood

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**Table 1. Portal vein blood flow volume**

<table>
<thead>
<tr>
<th>PV Flow</th>
<th>Supine pre-HDT</th>
<th>HDT day 85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerant</td>
<td>1,199 (170)</td>
<td>1,595 (316)</td>
</tr>
<tr>
<td>Nontolerant</td>
<td>1,384 (286)</td>
<td>1,751 (339)</td>
</tr>
<tr>
<td>Control</td>
<td>1,365 (261)</td>
<td>1,753 (387)</td>
</tr>
<tr>
<td>CM</td>
<td>1,135 (51)</td>
<td>1,515 (184)</td>
</tr>
</tbody>
</table>

Values are means (SD) in cm²/min. Measurements were performed pre-head-down tilt (HDT) in the supine position and at HDT day 85 in tolerant, nontolerant, counter measure (CM) and control groups. PV, portal vein.

**Table 2. Portal vein cross-sectional area in supine and standing position, at pre- and post-stand test**

<table>
<thead>
<tr>
<th>PV CSA</th>
<th>Supine Pre</th>
<th>Stand Pre</th>
<th>Supine Post</th>
<th>Stand Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerant</td>
<td>1.25 (0.3)</td>
<td>1.02 (0.2)</td>
<td>1.11 (0.2)</td>
<td>0.69 (0.11)</td>
</tr>
<tr>
<td>Nontolerant</td>
<td>1.34 (0.21)</td>
<td>0.93 (0.13)</td>
<td>1.17 (0.11)</td>
<td>0.85 (0.13)</td>
</tr>
<tr>
<td>Control</td>
<td>1.39 (0.2)</td>
<td>1.02 (0.18)</td>
<td>1.21 (0.18)</td>
<td>0.88 (0.2)</td>
</tr>
<tr>
<td>CM</td>
<td>1.22 (0.23)</td>
<td>0.91 (0.2)</td>
<td>1.08 (0.16)</td>
<td>0.69 (0.14)</td>
</tr>
</tbody>
</table>

Values are means (SD) in cm². PV-CSA, portal vein cross-sectional area; Pre, pre-stand test; Post, post-stand test.
volume inside the splanchnic network associated with a significant blood stagnation. This enlargement of the PV CSA, like the enlargement of main cephalic veins (3), may be related to the fluid shift toward the upper half part of the body induced by the head-down position. If it is assumed that all the vessels participating in the splanchnic network increase in the same proportion as the portal vein, it can be suggested that the splanchnic blood volume increases by ~30%. This hypothesis suggests that a significant amount of blood is trapped in the splanchnic network and will be redistributed rapidly in response to a fluid shift toward the legs, induced during orthostatic testing or exercise. Additionally, although the flywheel exercise CMs did not reduce the degree of hypovolemia in the CM group compared with the Con (7), it significantly reduced the increase in the PV CSA and flow volume after 85 days of HDT and thus the stagnation of the splanchnic blood.

Potential role of splanchnic blood volume in the cardiovascular response to orthostatic tests (PV CSA change during stand test: Fig. 3, Table 2). This study demonstrates that, during the stand test after HDT, the PV CSA reduces significantly in tolerant subjects, whereas it does not change or reduces less in nontolerant subjects. In a previous study, our laboratory found that, during the stand test, the PV CSA measured by Doppler ultrasound, increases significantly (40–60%) during stand test in tolerant subjects and cosmonauts (15, 31), whereas it increases significantly less in intolerant subjects. Conversely, in stand tests after HDT or spaceflight, lower limb vascular resistance of some tolerant subjects did not increase, whereas the cerebral-to-femoral flow ratio increased significantly and adequately (4). Thus the cardiac output redistribution is not necessarily linked to lower limb vasoconstriction, and it is suggested that other vascular networks (renal, splanchnic, etc.) may contribute to the flow redistribution to the brain. Rowell et al. (26) have shown that the splanchnic circulation is extremely important for the regulation of the blood pressure in humans.

Nevertheless, here are potential differences in how vascular beds (e.g., splanchnic, lower limb, or skin) respond to orthostatic stress. The splanchnic reservoir is highly compliant and, unlike muscle vascular networks, subject to reflex control of the total intraluminal volume (14, 25). Vascular capacitance may be reduced by constriction of the veins and by constriction of the precapillary resistance vessels to alter flow and passive distention (20). Thus, in response to acute hypovolemia, there is a reflex discharge of splanchnic blood into the rest of the circulation (34), which is mediated by reflexes arising from the unloading of the atrial volume receptors and a reduced arterial baroreceptor activation (13, 16, 17).

Orthostatic stress (lower body negative pressure) induces splanchnic vasoconstriction that is dependent on the activation of both the sympathetic nervous system and the renin angiotensin system (30). If this reflex is attenuated, through reduced baroreflex gain or through attenuated end organ vascular response, the splanchnic flow reduction in relation to vasoconstriction will be less efficient, and therefore the reduction of the splanchnic flow will be lower.

Until now, the two main peripheral hemodynamic factors contributing to the redistribution of the cardiac output toward the brain in tolerant subjects were thought to be the reduction of the femoral flow by ~50% (1, 31) and the absence of lower limb vein distension in upright position after HDT (2, 6, 9, 10, 18). This study has identified another hemodynamic factor: the reduction in the PV CSA in the upright position. It can be seen that the reduction in the PV CSA was greater in CM than in Con subjects, which suggests that exercise CM may help to

![Fig. 4. Relationship between portal vein cross-sectional area (CSA; in cm²) and portal vein flow volume (in l/min) in supine (Q sup; A) and in standing position (Q ST; B).](http://jap.physiology.org/)

Adapted from Arbeille et al. (5).
empty this splanchnic compartment in response to the stand test by reducing splanchnic blood stagnation. Unfortunately, this observation was not associated with a measurably higher orthostatic tolerance in the CM group.

In conclusion, this study confirms that the fluid shift induced by a stand test triggers a significant reduction of the PV CSA. As the portal vein is the only output from the splanchnic vascular network we suggest that the arterial flow (celiac, mesenteric, etc.) supplying this network also reduces in the orthostatic position (vasoconstriction?) in the same way as the lower limb arterial flow. Moreover, this study shows that the changes in the portal vein flow volume can be assessed simply by measuring the diameter of the portal vein.

GRANTS

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REFERENCES


