Standing up to the challenge of standing: a siphon does not support cerebral blood flow in humans

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Standing up to the challenge of standing: a siphon does not support cerebral blood flow in humans. Am J Physiol Regul Integr Comp Physiol 287: R911–R914, 2004. First published June 10, 2004; 10.1152/ajpregu.00196.2004.—Model studies have been advanced to suggest both that a siphon does and does not support cerebral blood flow in an upright position. If a siphon is established with the head raised, it would mean that internal jugular pressure reflects right atrium pressure minus the hydrostatic difference from the brain. This study measured spinal fluid pressure in the upright position, the pressure and the ultrasound-determined size of the internal jugular vein in the supine and sitting positions, and the internal jugular venous pressure during seated exercise. When the head was elevated ∼25 cm above the level of the heart, internal jugular venous pressure decreased from 9.5 (SD 2.8) to 0.2 (SD 1.0) mmHg [n = 15; values are means (SD); P < 0.01]. Similarly, central venous pressure decreased from 6.2 (SD 1.8) to 0.6 (SD 2.6) mmHg (P < 0.05). No apparent lumen was detected in any of the 31 left or right internal veins imaged at 40° head-up tilt, and submaximal (n = 7) and maximal exercise (n = 4) did not significantly affect internal jugular venous pressure. While seven subjects were sitting up, spinal fluid pressure at the lumbar level was 26 (SD 4) mmHg corresponding to 0.1 (SD 4.1) mmHg at the base of the brain. These results demonstrate that both for venous outflow from the brain and for spinal fluid, the prevailing pressure approaches zero at the base of the brain when humans are upright, which negates that a siphon supports cerebral blood flow.

Cerebral blood flow is autoregulated and as such remains relatively stable when mean arterial pressure (MAP) at the level of the brain remains within the range of ∼60 to ∼140 mmHg (10). Despite this, both middle cerebral artery flow velocity and tissue oxygenation decrease somewhat when standing up (17) with only two-thirds of the decrease explained by the concomitant reduction in the arterial carbon dioxide tension. This may be due to a concomitant reduction in the arterial carbon dioxide tension (18). However, it remains unknown how cerebral blood flow is maintained in the upright position. One suggestion is that a siphon supports cerebral blood flow when the head is elevated above the level of the heart (1). A siphon is established in a fluid-filled U-shape tube of any size, cross-sectional area, or orientation, and because the pressure gradients are equal and opposite in a direction along the two arms of the tube, no net work is needed to move the fluid “uphill” against gravity. The only work that is needed to move the fluid is that required to overcome viscous friction (14). For maintaining cerebral blood flow in the upright position, Hicks and Badeer (6) argue that in a closed system like the circulation, gravity acts on all of the system, indicating that a siphon does support cerebral blood flow. In the upright position, the major outflow pathway from the brain is shifted from the internal jugular veins to posterior veins (16), suggesting an increase in resistance. However, even if the internal jugular veins collapse, other veins may maintain a siphon, and pressure in the brain would reflect central venous pressure (CVP) minus the vertical distance from the right atrium to the brain. On the other hand, if all veins draining the brain collapse in the upright position, a siphon does not support cerebral blood flow and the heart has to produce a pressure great enough to overcome gravity, i.e., to raise a column of blood from the level of the heart to the brain.

Interest in the perfusion pressure to the brain has focused on the blood pressure of the giraffe, in which MAP at the base of the skull equals that of other animals (5, 7). With a siphon supporting cerebral blood flow, its MAP of ∼260 mmHg, which is more than twofold that of humans, is considered to be necessary to overcome the viscous resistance of blood (6). With respect to cerebral outflow of the giraffe, it has been concluded that a siphon is not established (5). However, that conclusion was based on pressure in the external jugular vein even though it does not drain the brain. Due to its anatomic position outside the cervical fascia, the atmosphere affects the transmural pressure, while the fascia could prevent collapse of the veins that drain the brain and allow its outflow to be supported by a siphon.

To evaluate whether a siphon supports cerebral blood flow in the erect position, we investigated the postural influence on the internal jugular pressure at the base of the skull as well as on the external venous pressure. Internal jugular venous pressure was also obtained during submaximal and maximal exercise to evaluate the potential influence of an increasing pressure drop over the brain, due to an increase in MAP and potentially enhanced venous return by heavy breathing. We considered that venous pressure is influenced by the position of the head since the external jugular vein is most prominent when the head is turned to the opposite side. Therefore, external jugular venous pressure was determined while the head was positioned facing forward, to the left, and to the right. The diameter of the internal jugular veins was assessed by ultrasound from supine rest to sitting up. In humans, veins within the central nervous system cannot be cannulated, but we considered their pressure...
to be in equilibrium with that of spinal fluid, which can be assessed by lumbar puncture.

METHODS

All subjects were free of any known cardiovascular disease and were not using any over-the-counter medication. The subjects gave their informed written consent, and the studies were approved by the ethics committee of Copenhagen and Frederiksberg (KF-01–3399/7; KF-01–230/00) and conducted in a laboratory at ~20°C.

Rest. Nine subjects with a mean age, height, and weight of 23 (SD 2) yr, 181 (SD 5) cm, and 76.6 (SD 10.9) kg, respectively [mean (SD)], participated in the study and reported to the laboratory at 8:30 AM after a light breakfast. A catheter was placed in either the right or left external jugular vein (1.3 mm, 18 gauge), and its pressure was measured with a transducer (Edwards Life Sciences, Irving, CA) placed corresponding to the tip of the catheter and attached to a patient monitoring kit (IBC-Danica, Copenhagen, Denmark). The subjects were lying on a bed, and the head end was raised from supine to 40° upright, resulting in an increase in the vertical distance from the heart to the catheter in seven steps. For each step, 5 min were allowed before the pressure was recorded. In each position the pressure was taken with the head facing forward, with the head turned toward the side of the catheter, and with it turned away from the catheter. In seven of the subjects, resting pressure in the spinal fluid column at L2–L3 was assessed by lumbar puncture (27 gauge pencil-point cannula, Braun, Melsungen, Germany) while sitting up, and the transducer was placed at the level of the needle. Spinal fluid pressure at the base of the brain was calculated from the lumbar spinal pressure and the distance from the needle assuming a density of spinal fluid of 1.070 g/ml (2).

Internal jugular venous pressure was obtained in four subjects [age, weight, and height: 24 (SD 2) yr, 185 (SD 7) cm, 83.8 (SD 6.2) kg] also while the head-end of the bed was raised in seven steps to 40°. A catheter (2.2 mm, 14 gauge) was placed in the right internal jugular vein and advanced in the retrograde direction to the bulb and referred to the base of the skull. A jugular venous blood sample was obtained and saturation determined on an ABL 725 machine (Radiometer, Holm, Sweden) at 360 (SD 10) W [heart rate 187 (SD 2) beats/min].

Exercise.

Eleven healthy trained males with an age, height, and body weight of 25 (SD 5) yr, 180 (SD 8) cm, and 70.0 (SD 6.9) kg, respectively, were recruited to participate in the study. The subjects reported to the laboratory at 8:30 AM after a light breakfast. On arrival, a catheter was placed into the brachial artery (1.1 mm, 20 gauge) of the nondominant arm, and MAP was measured with a Bentley transducer (Uden, The Netherlands) positioned at the level of the right atrium and connected to a pressure monitoring system (Hewlett Packard M1275A), while the same catheter as used in the resting study was placed in the right internal jugular vein and pressure was referred to the base of the skull. An additional catheter (2.1 mm, 14 gauge) was placed into an antecubital vein and advanced to the right atrium for measurement of CVP via a similar transducer placed at the level of the heart.

After subjects rested in the supine position for 30 min, supine measurements of MAP, internal jugular venous pressure, and CVP were recorded. The subjects then sat up on the bed, and after a 5-min resting period values were obtained. Seven of these subjects remained seated in a semirecumbent position on a modified Krogh ergometer (4) and then began to cycle at a workload of 10 W, which was adjusted to a target heart rate of 130 beats/min [132 (SD 4) beats/min]. Exercise lasted for 15 min, and the pressures were taken between the 7th and 12th min. In the other four subjects, maximal exercise for 7.5 (SD 0.4) min was carried out on a cycle ergometer (Monark, Stockholm, Sweden) at 360 (SD 10) W [heart rate 187 (SD 2) beats/min].

Cerebral perfusion pressure was taken as the MAP at the level of the brain minus the internal jugular venous pressure. Assuming that a siphon is established for the circulation in the head, the internal jugular venous pressure at the level of the brain was estimated from CVP and the vertical distance from the head to the heart and applying a blood density of 1.063 g/ml (2). Values are presented as means (SD), and a repeated-measures one-way ANOVA was used to evaluate differences among variables with the Tukey post hoc test employed when main effects appeared significant at a P value of <0.01.

RESULTS

Rest. The external jugular venous pressure depended on the position of the head with a decrease from 3.4 (SD 3.3) mmHg during supine rest to ~4.7 (SD 3.3) mmHg, when sitting up (see Fig. 2, external jugular vein forward). In all tilt positions the external jugular venous pressure was highest when the head was away from the catheter and lowest with the head turned toward the catheter. When the head was turned away from the catheter, its lumen became prominent and pressure fell to 4.8 (SD 4.5) mmHg, whereas pressure was close to zero [0.8 (SD 4.5) mmHg] when the head was turned toward the catheter. In all three head positions, there was little variation when the head was elevated by more than ~10 cm above the heart, indicating that the veins never established more than an ~10-cm column of blood toward the right atrium.
Effects of body position and exercise

Table 1. Effects of body position and exercise on measured IJVP estimated IJVP assuming a siphon is in place, and CSP

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Sitting</th>
<th>Submaximal</th>
<th>Maximal</th>
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</thead>
<tbody>
<tr>
<td>Measured IJVP, mmHg</td>
<td>9.5 (1.2)</td>
<td>0.2 (1.0)</td>
<td>-3.3 (1.0)</td>
<td>0.2 (1.0)</td>
</tr>
<tr>
<td>Estimated IJVP, mmHg</td>
<td>9.5 (1.2)</td>
<td>-20.1 (2.1)</td>
<td>-19.0 (3.0)</td>
<td>-18.4 (2.0)</td>
</tr>
<tr>
<td>CSP at IJV bulb, mmHg</td>
<td>0.23 (1.0)</td>
<td>0.20 (0.00)</td>
<td>0.45 (0.00)</td>
<td>0.20 (0.00)</td>
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Values are means with SD in parentheses. Pressures were obtained during supine rest (n = 15), when sitting up on a bed (rest sitting; n = 15), during submaximal exercise at a heart rate of ~130 beats/min (n = 7) on a modified Krogh cycler ergometer, and during maximal exercise at a heart rate of ~185 beats/min (n = 4) on a cycle ergometer. Measured IJVP, internal jugular venous (IJV) pressure measured with the catheter tip placed in the IJV bulb with the transducer placed at the level of the catheter tip; estimated IJVP, internal jugular venous pressure estimated from central venous pressure minus the hydrostatic distance (using the specific gravity of blood in males; Ref. 2) to the jugular venous bulb. CSP at IJV bulb, cerebral spinal pressure measured with the catheter tip placed at L2–L3 and corrected for the hydrostatic distance (using the specific gravity for spinal fluid; Ref. 2) to the base of the skull.

Table 2. Right and left IJV diameter measured by ultrasound from supine to sitting up

<table>
<thead>
<tr>
<th></th>
<th>Right IJV Diameter, cm</th>
<th>Left IJV Diameter, cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine</td>
<td>0.69 (0.28)</td>
<td>0.55 (0.25)</td>
</tr>
<tr>
<td>10°</td>
<td>0.42 (0.18)</td>
<td>0.31 (0.09)</td>
</tr>
<tr>
<td>15°</td>
<td>0.36 (0.19)</td>
<td>0.43 (0.04)</td>
</tr>
<tr>
<td>20°</td>
<td>0.23 (0.12)</td>
<td>0.20 (0.00)</td>
</tr>
<tr>
<td>25°</td>
<td>0.50 (0.13)</td>
<td>0.45 (0.00)</td>
</tr>
<tr>
<td>30°</td>
<td>0.73 (0.31)</td>
<td>collapsed</td>
</tr>
<tr>
<td>35°</td>
<td>collapsed</td>
<td>collapsed</td>
</tr>
<tr>
<td>40°</td>
<td>collapsed</td>
<td>collapsed</td>
</tr>
</tbody>
</table>

Values are means with SD in parentheses. Values are obtained during supine rest and with the head-end of the bed tilted up. Right (n = 19) and left IJV (n = 12) diameter was measured with the transducer placed close to the clavicle.

Fig. 2. IJV and external jugular venous (EJV) pressure at body positions from the supine to a seated position. Values were attained ~5 min after lifting the upper section of the bed. IJV is evaluated with the head forward, and EJV with the head forward, toward, and away from the catheter. Values are means (and SD) for 15 (IJV) and 9 healthy subjects (EJV). Both IJV and EJV pressures remain relatively stable when the head is raised and the veins collapse. The higher pressure in the IJV than in the EJV demonstrates that the cerebral fascia maintains a positive tissue pressure.

Of more relevance for cerebral blood flow, internal jugular venous pressure at the base of the skull was 9.5 (SD 1.2) mmHg during supine rest, and MAP was between 90 and 95 mmHg (Figs. 1 and 2; Table 1). When the head was elevated ~25 cm above the level of the heart by raising the bed to 40°, internal jugular venous pressure fell to 0.2 (SD 1.0) mmHg, while MAP was between 90 and 100 mmHg and CVP fell from 7.0 (SD 0.5) to 3.0 (SD 1.0) mmHg. While the subjects were sitting up, spinal fluid pressure was 26 (SD 4) mmHg, corresponding to a pressure of 0.1 (SD 4.1) mmHg at the base of the brain. Cerebral blood flow was maintained in the upright position as jugular venous pressure [62.0 (SD 2.4)_TD%] and frontal lobe oxygen saturation [68.4 (SD 1.1)_TD\%] did not change significantly.

During supine rest, the diameters of the right and left internal jugular veins were 0.69 (SD 0.28) and 0.55 (SD 0.25) cm, respectively, and they both collapsed at various degrees of head-up tilt (Table 2; Fig. 3). Thus no apparent lumen was detected in any of the 31 left or right internal veins imaged at 40° head-up tilt.

Exercise. During submaximal exercise, MAP [104 (SD 3) mmHg] and CVP [2.1 (SD 1.0) mmHg] were not significantly changed from sitting rest, while internal jugular venous pressure decreased to ~3.3 (SD 1.0) mmHg (Table 1). Likewise, maximal exercise did not change CVP [-2.5 (SD 0.8) mmHg] or internal jugular venous pressure [0.2 (SD 1.0) mmHg] markedly, while MAP increased to 117 (SD 3) mmHg and internal jugular venous saturation was not changed for as long as the arterial carbon dioxide tension remained stable (39 (SD 1) mmHg). Thus enhanced MAP and heavy breathing provoked little, if any, change in internal jugular venous pressure, and under no circumstances was internal jugular venous pressure representative of CVP and the hydrostatic distance to the right atrium.

DISCUSSION

The data provide several arguments against a siphon supporting cerebral blood flow in upright humans. In agreement with the observation from the giraffe (5), the external jugular vein collapses in the upright position, and the height at which it occurs is the classical bed-side estimate of CVP. Although the internal jugular vein is protected by the connective tissue surrounding the neck, the postural influence on pressure in internal and external jugular veins was similar in that they approached zero in the upright position as opposed to the approximately ~20 mmHg that would be expected if a continuous column of blood was established from the base of the
skull to the right atrium (Fig. 2). The results thereby provide an experimental confirmation of studies in which the gravitational influence on cerebral blood flow has been modeled (8, 14) although an alternative model is provided as well (6).

Visualization by ultrasound demonstrated that the internal jugular vein collapses when upright and, as illustrated from the external jugular vein, the lumen varies with position, so that pressure depends critically on the established column of blood. However, in normal conditions an intact column of venous blood is established only in the supine position, as confirmed during a Valsalva maneuver when an increase in CVP is transmitted instantaneously to the outflow from the brain and reduces middle cerebral artery flow velocity (12). In contrast, in the upright position it takes \( \sim 3 \) s before an increase in CVP affects middle cerebral arterial flow velocity (12). Similarly, when the head is elevated in dogs, increased end-expiratory pressure ventilation is only transmitted to the cerebral venous pressure when it exceeds 19 mmHg (15), and internal jugular venous pressure remained close to zero both during submaximal and maximal exercise. Both for venous outflow from the brain and spinal fluid, the prevailing pressure approaches zero at the base of the brain and a siphon may be established only within the skull where the major veins are encompassed in rigid connective tissue. However, with a relatively small distance from the base to the top of the brain, the circulatory consequence of an internal cerebral siphon would be considered to remain modest. Neck veins behave like other peripheral veins, establishing a pressure close to zero when they collapse as, for example, when a limb is raised above the level of the heart (9).

To estimate cerebral perfusion pressure in the upright position, MAP at the level of the brain should be compared with zero rather than with the CVP or with CVP minus the hydrostatic difference to the heart if the venous outflow pressure is not measured. We found a cerebral perfusion pressure of \( \sim 80 \) mmHg during supine rest decreasing to \( \sim 65 \) mmHg when upright and increasing to \( \sim 90 \) mmHg during maximal exercise.

Although a siphon does not support cerebral blood flow in upright humans, it remains that pressure in filled neck veins is negative when the head is raised with an implicit danger of air insufflation during cannulation. We consider veins to behave like a Starling resistor in which a collapsible vascular segment is submitted to an external pressure (9). Blood flows when the internal pressure exceeds the extravascular pressure and opens the vessel. When upright, neck veins are only intermittently filled with blood and over a relatively short distance because the cervical fascia maintains a positive tissue pressure. Although the level of arterial pressure compensates for the absence of a siphon in support of cerebral blood flow on earth, a siphon is likely to be maintained in space where there is no external pressure on the neck veins although it is likely to be of little consequence in that situation. Of potential importance is the use of the internal jugular veins to assess global cerebral blood flow and metabolism in the upright position. The data support those from monkeys (3) and humans (13), indicating that the jugular veins are not the main outflow from the brain in the upright position and cerebral blood flow and metabolism are likely to be underestimated when based on variables derived from that vein. The implication of not having a siphon to support cerebral blood flow in the upright position is that stability of flow becomes dependent on cerebral autoregulation as the perfusion pressure decreases. It is of clinical relevance that in response to raising the head, the decrease in cerebral perfusion pressure is to a level close to what is considered the lower limit of cerebral autoregulation explaining why sometimes cerebral blood flow and oxygen become affected and the subject feels dizzy.

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GRANTS

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REFERENCES