Postural influence on intracranial and cerebral perfusion pressure in ambulatory neurosurgical patients

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Postural influence on intracranial and cerebral perfusion pressure in ambulatory neurosurgical patients. Am J Physiol Regul Integr Comp Physiol 310: R100–R104, 2016. First published October 14, 2015; doi:10.1152/ajpregu.00302.2015.—We evaluated postural effects on intracranial pressure (ICP) and cerebral perfusion pressure [CPP: mean arterial pressure (MAP) – ICP] in neurosurgical patients undergoing 24-h ICP monitoring as part of their diagnostic workup. We identified nine patients (5 women, age 44 ± 20 yr; means ± SD), who were “as normal as possible,” i.e., without indication for neurosurgical intervention (e.g., focal lesions, global edema, abnormalities in ICP-profile, or cerebrospinal fluid dynamics). ICP (tip-transducer probe; Raumedic) in the brain parenchyma (n = 7) or in the lateral ventricles (n = 2) and cardiovascular variables (Nexfin) were determined from 20° head-down tilt to standing up. Compared with the supine position, ICP increased during 10° and 20° of head-down tilt (from 9.4 ± 3.8 to 14.3 ± 4.7 and 19 ± 4.7 mmHg; P < 0.001). Conversely, 10° and 20° head-up tilt reduced ICP to 4.8 ± 3.6 and 1.3 ± 3.6 mmHg and ICP reached −2.4 ± 4.2 mmHg in the standing position (P < 0.05). Concordant changes in MAP maintained CPP at 77 ± 7 mmHg regardless of body position (P = 0.95). During head-down tilt, the increase in ICP corresponded to a hydrostatic pressure gradient with reference just below the heart, likely reflecting the venous hydrostatic indifference point. When upright, the decrease in ICP was attenuated, corresponding to formation of a separate hydrostatic gradient with reference to the base of the skull, likely reflecting the site of venous collapse. ICP therefore seems to be governed by pressure in the draining veins and collapse of neck veins may protect the brain from being exposed to a large negative pressure when upright. Despite positional changes in ICP, MAP keeps CPP tightly regulated.

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ICP is important for estimating cerebral perfusion pressure [CPP = mean arterial pressure (MAP) – ICP] (26). Sufficient CPP is required to maintain adequate cerebral blood flow (11, 34), and in the case of intracranial disease or head trauma, treatment is often directed towards maintaining CPP. However, no consensus has been reached regarding target values (28, 33, 36) and normal range, while also the possible effects of posture on CPP have yet to be determined (8).

For ethical reasons, it is not possible to measure ICP invasively in healthy humans. It remains debated whether lumbar CSF pressure reflects ICP accurately especially during changes in posture (15, 40). As noninvasive estimates of ICP are not currently reliable enough to replace invasive measurements (21), we determined the postural effects on ICP in selected ambulatory neurosurgical patients with a tip-transducer catheter inserted in the brain parenchyma or within the ventricular system (3). ICP and central cardiovascular variables were measured from a 20° head-down tilt position to upright standing to test the hypotheses that short-term positional changes in ICP depend on pressure in the draining veins while concordant changes in systemic blood pressure maintain CPP regardless of body position.

METHODS

The protocol was approved by the Ethical Committee of Copenhagen (H-3-2012-110), and all patients provided oral and written informed consent in compliance with the declaration of Helsinki.

From the 98 patients who underwent ambulatory 24-h diagnostic parenchymal or ventricular ICP monitoring from November 2013 to November 2014, we identified nine patients who fulfilled the inclusion criteria (Table 1): five females; age: 44 (21–70) yr (mean and range); height: 169 (152–185) cm; weight: 69 (52–89) kg; and body mass index: 23.7 (21–26). The included patients were, at the end of the diagnostic workup, considered not to be surgical candidates, i.e., they were free of focal lesions or global edema on CT and/or MRI scan; had a 24-h ICP profile within the generally accepted normal range (1), and for the subgroup of patients provided with a ventricular catheter an infusion-test demonstrated normal CSF dynamics (22).
The indications for ICP monitoring included arrested congenital hydrocephalus (n = 4); unexplained headache/fatigue and assessment for possible idiopathic intracranial hypertension (n = 3); and headache/fatigue following trauma (1 with a head/neck trauma 9 yr earlier; 1 with a subdural hematoma 6 yr earlier).

Instrumentation. All ICP measurements were performed using a tip-transducer catheter (Neurovent-P; Raumedic) inserted under local anesthesia and sterile conditions through a right frontal burr hole. In seven patients the tip of the probe was inserted 2 cm into the brain parenchyma and in two patients the tip of the probe was placed in the frontal horn of the right lateral ventricle at a depth of 5–6 cm. With the use of pulse wave analysis, cardiovascular variables (blood pressure, heart rate, stroke volume, cardiac output, and total peripheral resistance) were determined by the volume-clamp method from a cuff around the third finger of the nondominant hand (COTrek; Nexion, BMeye, The Netherlands) and referenced to the fourth intercostal space using a height sensor. Analog data were transferred to a computer via an analog-to-digital (AD) converter (Powerlab; ADInstruments, New South Wales, Australia) at 1.000 Hz.

Protocol. Cardiovascular variables and ICP are presented as the average of the last minute following a 5-min rest period in each of six positions in a randomized order: standing, supine, and during 10° and 20° head-up and head-down tilt.

Statistics. A one-way ANOVA (SAS Enterprise guide 4.3, SAS Institute, Cary, NC) for repeated measures and post hoc multiple range test (Tukey-Kramer) was used to detect statistically significant differences (P < 0.05) compared with the supine position with data presented as mean (SD).

RESULTS

Compared with the supine position head-up or down tilt to 10° and 20° did not change central cardiovascular variables significantly. Standing up increased MAP from 87 ± 8 to 103 ± 19 mmHg (P < 0.05) and reduced stroke volume from 107 ± 22 to 92 ± 44 ml (P = 0.002), while heart rate increased from 62 ± 9 to 75 ± 11 beats/min thus maintaining cardiac output (P = 0.89) and increasing total peripheral resistance from 1,242 ± 244 to 1,623 ± 490 dyn·s/cm5 (P < 0.0001; Table 2).

In the supine position parenchymal ICP (n = 7) was 8.9 ± 3.7 mmHg and increased with both 10° and 20° head-down tilt to 14.6 ± 4.7 mmHg (P = 0.008) and 20.0 ± 4.7 mmHg (P < 0.0001) respectively. Conversely, head-up tilt to 10° and 20° decreased parenchymal ICP to 5.1 ± 3.7 mmHg (P = 0.0003) and 0.2 ± 4.0 mmHg (P < 0.001), respectively, and ICP reached −5.4 ± 5.0 mmHg in standing position (P < 0.0001).

Ventricular ICP (n = 2) in the frontal horn of the right lateral ventricle was 11 and 12 mmHg when supine and increased with 10° (to 16 and 22 mmHg) and 20° head-down tilt to 19 and 23 mmHg. Conversely, head-up tilt to 10° and 20° decreased ventricular ICP to 7 and 8 mmHg and 2 and 5 mmHg, respectively. In the upright position ventricular ICP was −2 and 2 mmHg (Table 2).

Correlations and the hydrostatic pressure gradient. In the absence of obstructive lesions, CSF circulates freely within the skull, and it can be assumed that ICP is uniformly distributed within the skull (36). Pressures obtained from the parenchyma or the ventricle (i.e., 3 cm more caudal in the brain) can therefore be assumed congruent and combined when corrected for the hydrostatic pressure gradient. The level of the ventricles was chosen to reflect mid-brain level (ICPMidbrain). Parenchymal pressures were therefore corrected by adding the hydrostatic pressure difference during head-up tilt and subtracting the gradient during head-down tilt. MAP was likewise corrected from the fourth intercostal space to reflect mid-brain level (Table 2) and CPP calculated as CPP = MAPMidbrain − ICPMidbrain.

ICPMidbrain (n = 9) was 9.4 ± 3.8 mmHg in the supine position and increased with both 10° and 20° of head-down tilt.
ICPMidbrain increased corresponding to a hydrostatic fluid pressure maintained CPP at midbrain-level regardless of position at 77.1 mmHg, and in the standing position, ICPMidbrain reached calculated as \[\text{ICP(0)}\] the height of the corresponding hydrostatic fluid column was \[\text{ICPMidbrain}\] correlated to a hydrostatic pressure column of \[10^\circ\]. At \[20^\circ\] head-up tilt the decrease in ICP was slightly below the heart, which was consistent during head-up tilt to ensure from a column of \[35\text{ cm}\] below the fourth intercostal space (31). A hydrostatic indifference point, or HIP, exists within all fluid-filled compartments and reflects the balance between the hydrostatic pressure and mechanical properties of the compartment walls. For the arterial system, HIParterial has been estimated at the level of the aortic arch (17), while for the CSF system, a HIPCSF has been estimated somewhere between C6 and Th5 (24).

During head-down tilt, ICPMidbrain increased corresponding to a hydrostatic fluid pressure from a column of some \[35\text{ cm}\], i.e., with a reference just below the heart and corresponding to the location of the HIP vein (31). It therefore seems that, given an open venous system, the pressure is transmitted to the brain. Conversely, the decrease in ICP during head-up tilt angles above \[20^\circ\] was attenuated and when upright, ICPMidbrain correlated to a fluid column of only \[12–15\text{ cm}\], likely reflecting the site of internal jugular venous collapse (14, 18; Fig. 2) and corresponding to where CSF pressure is considered to be zero (14). Had the veins remained open, ICP would have been expected to reach more negative values (ICPExpected; Fig. 1). In the supine position, the internal jugular veins constitute the primary route of drainage from the brain, but in upright postures these veins respond to the decreasing transmural pressure and collapse thus acting as Starling resistors (20). Cerebral drainage thereby depends increasingly on alternative pathways such as the vertebral venous system (18, 39, 43), which is believed to remain open and thus could constitute a continuous hydrostatic fluid column and support rather large negative pressures (2, 5). Furthermore, in the standing position, CSF is displaced from the skull to the spinal compartment (25). While both displacement of CSF and pressure of alternative venous systems is likely to play a role for ICP, we consider from the present data that overall positional ICP is governed predominantly by pressure in the venous sinus, which is in turn influenced by pressure in the internal jugular veins. Collapse of neck veins in upright postures, i.e., the internal jugular veins, therefore, seems to counteract development of large negative pressures within the brain (Fig. 1).

Our results are consistent with Davson’s equation stating that given unaltered CSF formation, ICP in all body positions is determined by the sum of CSF outflow resistance and venous pressure in the sagittal sinus, both of which are influenced by...
hydrostatic forces. Qvarlander et al. (32) estimated ICP at mid-brain level from CSF lumbar-pressure measurements at six angles of head-up tilt and found that the gravitational decrease in estimated ICP correlated with the hydrostatic pressure gradient in the venous system if collapse of the neck veins at higher angles of head-up tilt was assumed.

Slight head-down tilt bed-rest is used to simulate the headward fluid shift in microgravity and such studies have indicated an initial increase in ICP. Murthy et al. (27) used a tympanic membrane displacement technique while Macias et al. (23) used intraocular pressure and the cranial ultrasound pulse amplitude and both found increased ICP although no numeric value could be derived (38). Our study using direct measurement of ICP supports these findings of a close relationship between gravitational blood-volume redistribution and ICP as predicted by the hydrostatic gradient to HIP\textsubscript{ven}. A head-ward fluid shift and accompanying increase in ICP is believed to play a role in the headache and nausea experienced by most astronauts during the initial hours or days in weightlessness (37). These symptoms appear to resolve after hours or days, which is consistent with head-down tilt weightlessness-simulation studies, indicating attenuation of the increase in ICP (35). Adaptive mechanisms to weightlessness include a reduction in blood and total fluid volume (19), altered cerebral autoregulation (6), and changes in compliance of vasculature, membranes and bony structures (29, 42). Gabrion et al. (16) found that a head-ward fluid shift induced by either weightlessness (9 and 14 days during NASA STS 40 and 56 missions) or (9 or 14 days) tail suspension of rats caused similar changes in the choroidal plexus, indicating reduced CSF formation, which could attenuate ICP during long term head-down tilt or weightlessness (35). Shortly after return to earth or termination of tail-suspension (within 8 h), the rats displayed return towards normal choroidal differentiation (16). ICP thus seems to adapt to weightlessness.

As neck veins remain open for the duration of a stay in space (4), venous pressure is continuously transmitted to the brain, unlike on earth where veins collapse in the standing position thus creating a separate hydrostatic pressure system separating cerebral pressures from systemic venous pressure. Central venous pressure has been shown to decrease in space compared with supine and head-down positions (9), and an increase in ICP during weightlessness above supine levels is therefore speculative. However, the lack of orthostatic collapse of neck veins in space, and thus lack of positional “unloading” of ICP, may be one of the mechanisms responsible for remodeling of the eye and changes in vision experienced by some astronauts during long-term space mission, changes that are usually seen in association with persistently increased ICP.

Pressure regulation within the brain differs from that of other fluid filled compartments in the body as the brain is enclosed in a rigid skull in which the sinus and large veins are suspended, and can therefore support a negative pressure. On the other hand, the steep pressure/volume relationship implies that even a moderate increase in volume will increase pressure and possibly impede cerebral blood flow (11). A sufficient perfusion gradient across the brain is pivotal for maintaining cerebral blood flow. In the intensive neurosurgical ward, treatment is directed towards maintaining CPP; however, target values and normal range of CPP are unknown and thus CPP-guided therapy remains controversial (8). This study indicates that CPP is tightly regulated within a range of some 75–80 mmHg despite positional variation in ICP.

Limitations. The patients were selected to be “as normal as possible”; i.e., not diagnosed with a neurosurgical disorder at the end of their diagnostic work-up. However, it remains that all had an indication for undergoing ICP monitoring, and it cannot be ruled out that these patients responded differently to gravitational stress than healthy subjects. We consider it to be a strength that the study included patients with different indications for undergoing ICP monitoring, thus reducing the risk of systematic error.

The experiment was carried out at least 12 h after insertion of the ICP transducer; however, it is possible that the intervention in itself somehow influenced the biological system we investigated. ICP was measured at two sites; intraparanchymal and 3–4 cm more caudally in the frontal horn of the right lateral ventricle. The patients were selected based on the absence of major pathology and other exclusion criteria rather than probe placement. Uniformly distributed ICP was assumed as space occupying and obstructing lesions were ruled out and all measurements combined.

We did not confirm collapse of neck veins during head-up tilt; however, this has been done previously both visually (ultrasound) and by pressure measurement of the internal jugular vein (14). Although perfusion pressure (CPP) to the brain is maintained during a change in position, we did not measure cerebral blood flow and future research should focus on this.

Perspectives and Significance

Pressure in the draining veins seems to be the major contributor to short-term postural changes in ICP, while regulation of systemic arterial blood pressure compensates to maintain CPP regardless of body position; During head-down tilt postural changes in ICP seem to be governed by pressure of the draining veins as predicted by the height of the hydrostatic gradient to the HIP\textsubscript{ven}. During head-up tilt, the decrease in ICP was attenuated corresponding to formation of a separate hydrostatic gradient with reference to the base of the skull, which could be explained by progressive collapse of neck veins. Collapse of neck vein thus separates ICP from systemic venous pressures and may in this way protect against development of a large negative pressure within the brain in upright postures. The open venous system in weightlessness allows for continuous transmission of central venous pressure to the brain, and this lack of positional “unloading” of ICP may contribute to the symptoms associated with increased ICP experienced in space.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: L.G.P., N.H.S., and M.J. conception and design of research; L.G.P., J.C.G.P., and M.A. performed experiments; L.G.P. and
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