The Effect of Body Position on Intraocular and Intracranial Pressure in Rabbits

Marijan Klarica, Tomislav Kuzman, Ivana Jurjević, Milan Radoš, Ante Tvrdeić, and Darko Orešković

Abstract *Background:* The correlation between cerebrospinal fluid (CSF) and intraocular pressure (IOP) is still unclear. We compared CSF and IOP measured by the same invasive technique using a new experimental model in rabbits during changes of body position. *Methods:* Pressure changes were recorded in the lateral ventricle (LV), the cortical subarachnoid space (CSS), and the anterior ocular chamber of anesthetized rabbits ($n=12$). Animals and measuring instruments were both fixed on a board at an adequate hydrostatic level. *Results:* In a horizontal position, control IOP (15.1 ± 1.6 cmH_2O) and CSF pressure in the LV (12.4 ± 0.6 cmH_2O) and CSS (12.2 ± 0.9 cmH_2O) were similar during the 60-min period. When changing the body position from horizontal to vertical (upright), CSF pressures decreased drastically (LV $=-5.5\pm2.6$ cmH_2O and CSS $=-7.7\pm2.3$ cmH_2O), while the IOP decreased moderately (IOP $=13.3\pm0.5$ cmH_2O). *Conclusion:* Change in body position from horizontal to vertical causes drastic changes in CSF pressure and moderate changes in IOP. Thus, IOP is not reflected by the CSF pressure. In an upright position, the values of CSF pressure were equal to the hydrostatic distance between measuring points and the foramen magnum, which suggests that CSF pressure inside the cranium depends on its anatomical and biophysical features, and not on CSF secretion and absorption.

Keywords Body position • Intraocular pressure • Cerebrospinal fluid pressure • Cerebrospinal fluid hydrodynamics

M. Klarica, MD, PhD (✉) • I. Jurjević • M. Radoš • A. Tvrdeić
Department of Pharmacology and the Croatian Institute for Brain Research, University of Zagreb School of Medicine, Šalata 11, Zagreb HR-10 000, Croatia
e-mail: mklarica@mef.hr

T. Kuzman
Department of Ophthalmology, University of Zagreb School of Medicine, University Hospital Center Zagreb, Zagreb, Croatia

D. Orešković
Department of Molecular Biology, Rudjer Boskovic Institute, Zagreb, Croatia

Introduction

Studies published in the literature that analyze the correlation between intracranial pressure (ICP) and intraocular pressure (IOP) report contradictory findings. Some authors suggested that abnormal IOP is an excellent indicator of the abnormal ICP in patients with known intracranial pathological conditions, based on their reports of significant correlations between IOP and ICP [11, 16]. On the contrary, other reports highlight that changes in IOP are a poor predictor of changes in ICP, and that an increase in ICP does not affect IOP [4, 17]. One of the possible explanations for the contradictory data is the methodology used to measure the CSF and IOP: in patients, CSF pressure is recorded using an invasive method, whereas the IOP is measured using a noninvasive method. Second, the measuring instruments were not set to the same reference point. Indeed, large differences were found between the control IOP values that were measured using different methods in animals of the same species. For example, the control IOP values in rabbit models range from 5.8 ± 0.6 mmHg [7], measured using noninvasive methods, to 18.1 ± 3.3 mmHg, measured using cannulation [14]. To overcome this obstacle, we have developed a new experimental animal model in which CSF pressure and IOP are measured using an identical invasive method, with the pressure transducers set to the same reference point and positioned at an adequate hydrostatic level. In this study, CSF pressure was recorded at two different positions (the lateral ventricle and the cortical subarachnoid space). We analyzed the correlations of the changes in CSF pressures and the changes in IOP during the 60-min period in the horizontal position and after the body was raised into a vertical position.

Materials and Methods

The study was performed on 12 male and female adult rabbits (2.6–4.2 kg body weight). The animals were kept in

B.-T. Ang (ed.), *Intracranial Pressure and Brain Monitoring XV*, Acta Neurochirurgica Supplement, Vol. 122,
DOI 10.1007/978-3-319-22533-3_55,

cages with natural light–dark cycles and had access to water and food. The animals were in quarantine for 30 days, and the experiments were performed in accordance with the Croatian Animal Welfare Act. The study was approved by the institutional ethics committee (approval no. 04-76/2008-911).

The rabbits were anesthetized with urethane (2 g/kg). The anesthetic was applied in the ratios of two thirds and one third into the auricular vein and peritoneum of the rabbit respectively. The animal was fixed in a stereotaxic head holder in the sphinx position. A stainless steel cannula (i.d. of 0.9 mm) was introduced into the left lateral ventricle at 5 mm lateral from the sagittal line, 5 mm posterior from the frontal suture, and 5–7 mm below the dural surface. A second cannula was placed into the cortical subarachnoid space on the right. Cannulas in the LV and CSS were used for the measurement of intracranial CSF pressure.

The leakage of CSF was prevented by applying the cyanoacrylate glue to the dura around the cannula. Bone openings in the cranium were hermetically closed by the application of a dental acrylate. The third cannula (27-gauge) was inserted through the perilimbal side of the cornea into the anterior chamber of the eye for the purposes of measuring IOP. The leakage of aqueous humor was prevented by applying the cyanoacrylate around the cannula.

After setting the measuring cannulas, the rabbit was removed from the stereotaxic device and fixed in a prone position on a board (Fig. 1). CSF and IOP pressures were recorded by pressure transducers (Gould P23 ID; Gould Instruments, Cleveland, OH, USA), which were connected to a system that transformed analog to digital data (Quand Bridge and PowerLab/800; AD Instruments, Castle Hill, NSW, Australia). The system was connected to a computer (IBM, White Plains, NY, USA; Fig. 1).

Pressure transducers were calibrated by the use of a water column; the interaural line was taken as zero pressure (in a prone position the interaural line is at the same hydrostatic level as the line that passes through the middle of the eyeball). Instruments for pressure measurement were fixed on the board in such a way that the membrane of each transducer was at the same hydrostatic level as the corresponding measuring cannula; thus, there was no need to additionally adjust the transducers during the body position changes (Fig. 1). CSF and IOP pressure changes were recorded during the 60-min period in the prone horizontal position, and then the body position of the animal was changed to upright (head-up).

Data are shown as a mean value ± standard error of the mean (SEM). A statistical analysis of all the results was performed using the paired Student's t test. $p < 0.05$ was considered statistically significant.

Results

In the horizontal position, the control pressure in the eye (IOP = 15.1 ± 1.6 cm H_2O) and the pressures in different parts of the CSF system (LV = 12.4 ± 0.6; CSS = 12.2 ± 0.9 cm H_2O) did not differ significantly ($p > 0.05$) during the 60-min measurement period (Fig. 2). After the change of the rabbit body position from horizontal to vertical with the head up, the pressure inside the cranium decreased drastically to a subatmospheric value (LV = −5.5 ± 2.6 cm H_2O; $p < 0.05$; CSS = −7.7 ± 2.3 cm H_2O; $p < 0.05$), while the IOP showed a moderate decrease (IOP = 13.3 ± 0.5 cm H_2O; $p < 0.05$; Fig. 3).

Discussion

During the 60-min period, in the prone (horizontal) position, all the measured pressures had similar values. Thus, it may appear that the IOP might adequately reflect the changes in pressure inside the CSF system. However, it was shown that IOP values are influenced by body positions in different animal species [1, 8]; namely, it was observed that IOP decreases during body verticalization, similar to our results in this study (Fig. 3) and in our previous study on cats [9]. If we observe the results obtained in patients, we can see that the IOP values are higher in the supine position, while they are lower during sitting or standing up. It could be argued that higher IOP in a supine position is due to a higher venous blood pressure and slower venous blood outflow from the head and eyes [12].

Similar to our previous study on cats [9], we observed drastic changes in CSF pressure in some parts of the CSF system, in comparison to moderate IOP changes in our rabbit model in an upright position. In this study, the pressure in the LV and CSS measured by cannulas situated about 5 cm from the foramen magnum, and at the similar hydrostatic level, were subatmospheric or negative (Fig. 3). These changes were not transient, but the pressure retained similar values for as long as the animal remained in the same position. Similar to another previous study [6], we tried to explain this phenomenon by the law of fluid mechanics [10], as follows: in our earlier study, the pressure changes, which happened inside the CSF system model and in cats during the body and model verticalization, were compared. The aforementioned new CSF system model consists of a distensible "spinal" part and nondistensible "cranial" part, which are filled with artificial CSF [6]. The model was constructed to imitate the anatomical dimensions and biophysical characteristics (distensible/nondistensible) of the CSF system in cats. This comparison demonstrated that the pressure changes in the

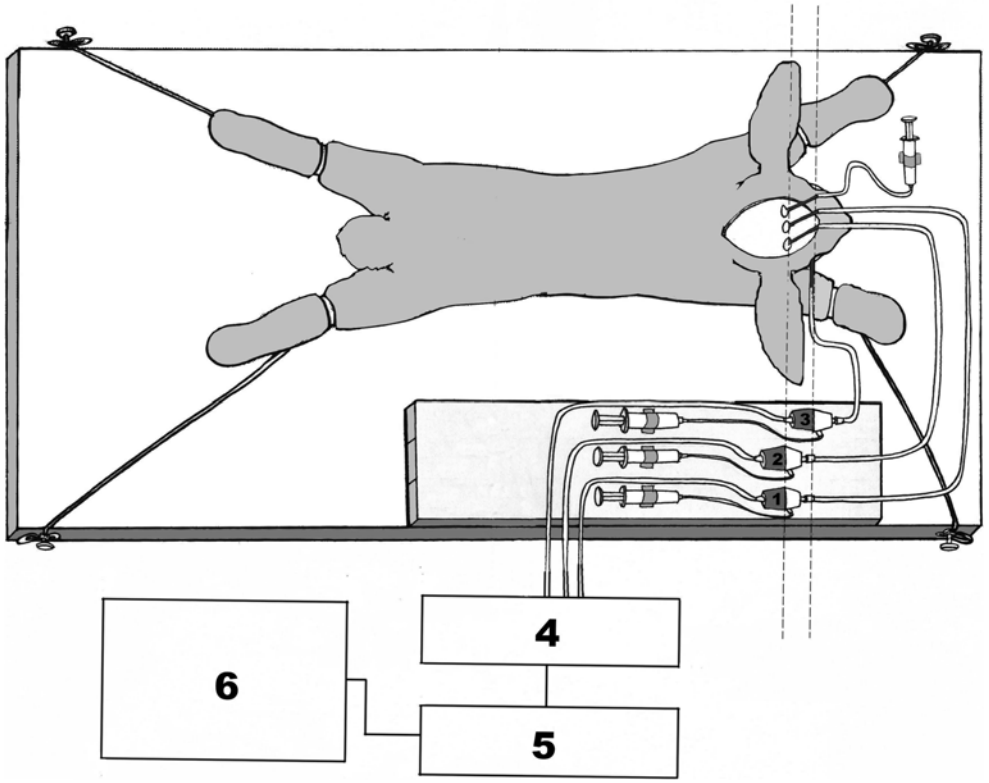

Fig. 1 Scheme of experimental model. *1* pressure transducer connected to the cannula in the anterior ocular chamber, *2* pressure transducer connected to the cannula in the lateral ventricle, *3* pressure transducer connected to the cannula in the cortical subarachnoid space, *4* Quand Bridge, *5* PowerLab/800, *6* personal computer

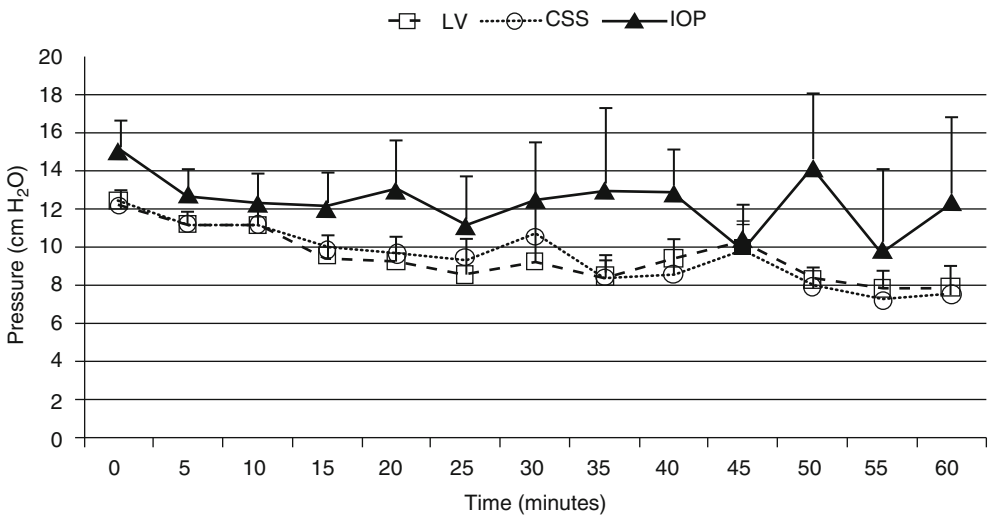

Fig. 2 Intraocular pressure (*IOP*; *triangles*), intracranial pressure in the lateral ventricle (*LV*; *squares*) and in the cortical subarachnoid space (*CSS*; *circles*; cm H_2O) of 12 rabbits in the horizontal position over the 60-min period. Results are shown as mean value ± standard error of the mean (SEM)

new CSF model faithfully imitate the changes in the CSF pressure in cats.

Our previous study on cats [9] showed the same patterns of the ICP and IOP changes during the body position alterations, as noticed in this study on rabbits. Since the "cranial" part of the model is nondistensible, it is evident that it cannot change its total fluid volume. However, in spite of this, pressure change could happen, which is in accordance with the law of fluid mechanics [10]. Namely, the law indicates that fluid pressure inside a nondistensible tube, opened at the bottom, should be negative and of a value that corresponds to the height of the hydrostatic column [10].

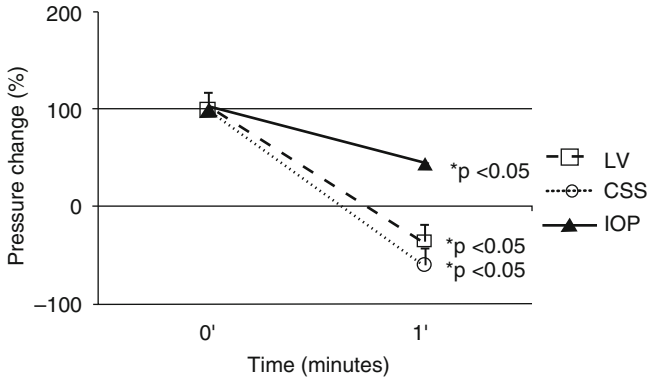

Fig. 3 Effects of the change in body position from horizontal to upright on CSF pressure (cmH_2O) in the lateral ventricle *(LV*; *squares*), cortical subarachnoid space (*CSS*; *circles*), and on intraocular pressure (*IOP*; *triangles*) in 6 rabbits. Results are shown as percentages from starting values as the mean value ± SEM

Our results from this and those from previous studies [6, 9] indicate that the decrease in intracranial pressure in an upright position is not due to the displacement of cranial CSF or blood volume to hydrostatically lower body parts, as is usually assumed [2, 13]. This means that the incompressibility of the cranial osseous vault enables constant blood brain perfusion despite sudden changes in the head position during the activities of normal life. In addition, it suggests that in an upright position normal ICP might be subatmospheric, and that the cerebral perfusion pressure might be higher than was previously assumed.

Conclusion

All of our results described here obviously cannot be explained with the generally accepted hypothesis of secretion, unidirectional circulation, and absorption of CSF. Namely, in an upright position, the CSF cannot flow from the ventricles, where the pressure is negative, to the cisterna magna, where the pressure is higher. These results are in accordance with the new hypothesis of CSF physiology [3, 5, 15], which suggests that the volumes of CSF and interstitial fluid are regulated by hydrostatic and osmotic forces present among the capillaries, central nervous system tissue, and CSF. Moderate changes in IOP and drastic changes in CSF pressure in certain parts of the CSF system suggest that IOP and CSF pressure might not show a significant correlation, and that we should be more cautious in considerations regarding the changes in CSF pressure based on IOP.

Acknowledgments We thank Mrs Ljiljana Krznar for her skilled technical assistance. This work has been supported by the Ministry of Science, Education and Sport of the Republic of Croatia (Projects: 1. Hydrodynamics of cerebrospinal fluid. No. 098-1080231-2328; and 2. Pathophysiology of cerebrospinal fluid and intracranial pressure. No. 108-1080231-0023).

Conflict of Interest Statement The authors declare that they have no conflict of interest.

References

1. Aihara M, Lindsey JD, Weinreb RN (2003) Episcleral venous pressure of mouse eyes and effect of body position. Curr Eye Res 27:355–362
2. Alperin N, Hushek SG, Lee SH, Sivaramakrishman A, Lichtor T (2005) MRI study of cerebral blood flow and CSF flow dynamics in an upright posture: the effect of posture on intracranial compliance and pressure. Acta Neurochir (Wien) 95:177–181
3. Bulat M, Klarica M (2011) Recent insight into a new hydrodynamics of cerebrospinal fluid. Brain Res Rev 65:99–112
4. Czarnik T, Gawda R, Kolodziej W, Latka D, Sznajd-Weron K, Weron R (2009) Associations between intracranial pressure, intraocular pressure and mean arterial pressure in patients with traumatic and non-traumatic brain injuries. Injury 40:33–39
5. Klarica M, Miše B, Vladić A, Radoš M, Orešković D (2013) "Compensated hyperosmolarity" of cerebrospinal fluid and the development of hydrocephalus. Neuroscience 248:278–289
6. Klarica M, Radoš M, Draganić P, Erceg G, Orešković D, Maraković J, Bulat M (2006) Effect of head position on cerebrospinal fluid pressure in cats: comparison with artificial model. Croat Med J 47:233–238
7. Kobayashi A, Yoshita T, Shirao Y (2003) Accuracy of intraocular pressure by Tono-Pen XL over amniotic membrane patching in rabbits. Am J Ophthalmol 135:536–537
8. Komaromy AM, Garg CD, Ying GS, Liu C (2006) Effect of head position on intraocular pressure in horses. Am J Vet Res 67:1232–1235
9. Kuzman T, Jurjević I, Mandac I, Radoš M, Orešković D, Jednačak H, Klarica M (2012) The effect of body position on intraocular and CSF pressures in the lateral ventricle, and in cortical and lumbar subarachnoid spaces in cats. Acta Neurochir Suppl 114:357–361
10. Landau LD, Lifshitz EM (2005) Fluid mechanics, vol 6, 2nd edn, Course of theoretical physics. Elsevier, Amsterdam, pp 5–7
11. Lashutka M, Chandra A, Murray H, Phillips G, Hiestand B (2005) The relationship of intraocular pressure to intracranial pressure. Ann Emerg Med 45:585–591
12. Longo A, Geiser MH, Riva C (2004) Posture changes and subfoveal choroidal blood flow. Investig Ophthalmol Vis Sci 45:546–551
13. Magnaes B (1978) Movement of cerebrospinal fluid within the craniospinal space when sitting up and lying down. Surg Neurol 10:45–49
14. Okuno T, Oku H, Sugiyama T, Yang Y, Ikeda T (2002) Evidence that nitric oxide is involved in autoregulation in optic nerve head of rabbits. Investig Ophthalmol Vis Sci 43:784–789
15. Orešković D, Klarica M (2010) The formation of cerebrospinal fluid: nearly a hundred years of interpretations and misinterpretations. Brain Res Rev 64:241–262
16. Salman MS (1997) Can intracranial pressure be measured noninvasively? Lancet 350:1367
17. Sheeran P, Bland JM, Hall GM (2000) Intraocular pressure changes and alternations in intracranial pressure (letter). Lancet 355:899