The physiology and pathophysiology of cerebrospinal fluid: new evidence

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This issue of the Croatian Medical Journal is dedicated to advancements in the diagnostics and treatment of neurological diseases. The issue features some of the articles that were originally envisaged as lectures to be delivered at a joint meeting of Croatian and Japanese Neurosurgical Societies on the topic of cerebrospinal fluid (CSF) physiology and pathophysiology. The meeting entitled Physiology and Pathophysiology of Cerebrospinal Fluid – New Evidence was scheduled to be held in Vodice, Croatia, 2020, but was postponed due to the COVID-19 pandemic. Two parts of the meeting were planned: Cerebrospinal Fluid Volume Regulation and Movement – Revision of Classical Concept and Pathophysiology of Hydrocephalus – New Insights.

The first part was to be dedicated to the role of the choroid plexus in physiology and pathophysiology. The classical concept defines the choroid plexus as the main CSF source (1,2), while a more recent theory, although not negating the importance of the choroid plexus in CSF formation, attributes to this organ a much lesser role than previously believed. The new theory postulates that what is important for CSF formation is the influx and exchange of fluid at the capillary level in the central nervous system (1,3-7). Furthermore, the first part of the meeting aimed to discuss the research on the fate of molecules applied in different parts of the CSF system with or without a blockade of the transport systems in various animal models, from genetically modified mice fetuses (8,9) to large experimental animals (rabbits, cats, dog, pigs) (4-6,10). Mice fetus experiments showed that the movement and fate of molecules in the CSF system were determined by their molecular weight (low-weight molecules move faster), that CSF moved faster in the ventricles than in the subarachnoid space, and that CSF did not circulate (8,9). These observations accord with the new concept of CSF physiology, first published about ten years ago. The new concept draws on research involving big experimental animals showing that CSF was not formed exclusively in the brain ventricles, that it did not unidirectionally move from the ventricles to the subarachnoid space, and that it was not dominantly reabsorbed in the arachnoid granulations of the dural sinuses (4-6). Since substances and metabolites applied in different parts of the CSF system were observed to distribute in all directions, many questions remain regarding drug application in the CNS (2). In addition, advanced radiological techniques provide detailed images of the CNS, with excellent contrast between CSF and the surrounding structures (bones and parenchyma). Therefore, these techniques enable us to precisely segment all CSF spaces and quantify their volumes both in the intracranial and spinal part. Aside from the time spatial inversion pulse (Time-SLIP) method, volumetric MR imaging (for example T2 space and phase-contrast sequences, etc) depicts and even quantifies CSF movement inside the CSF system, especially in regions where this movement is pronounced (the foramen of Monro, mesencephalic aqueduct or cranio-cervical...
Several lectures were prepared on the pathophysiology of normal pressure hydrocephalus (18-22). Idiopathic normal pressure hydrocephalus (iNPH) is a clinical condition with great variations and without a standard symptom pattern that would clearly separate it from other neurodegenerative diseases. Since CSF drainage treatment yields inconsistent results, the introduction of various CSF biomarkers could improve the clinical approach to this condition (22). The symposium was planned to raise the unresolved questions related to the diagnostics and treatment of hydrocephalus, such as: 1) Does every disruption of physiological pulsatile motions of CSF within the CSF system result in ventricular enlargement? 2) Is mechanical blockade of the CSF pathway by arachnoid granulations in and of itself enough for hydrocephalus development and why does a clear block of the CSF pathway or a severe stenosis not always lead to a development of acute obstructive hypertensive hydrocephalus? 3) How often does the CSF movement in the spinal space cause hydrocephalus development? 4) What is the mechanism of hydrocephalus development in H-Tx rats, DNAH14 knockout mice, and similar experimental models? 5) What is the pathophysiological significance of increased CSF motion through the aqueduct in the development of iNPH? 6) What is the predictive role of CSF biomarkers for the development and treatment of different types of hydrocephalus, especially iNPH? 7) How to differentiate INPH from the hydrocephalus developing as a result of different neurodegenerative diseases and dementia? 8) How can modern radiological techniques aid in hydrocephalus research?

The recent understanding of the correlation between CSF physiology and the development of some forms of hydrocephalus should be thoroughly presented, analyzed, evaluated, and discussed. This could bring about new insights into hydrocephalus etiopathology and new treatment approaches that are in accordance with the experimental and clinical data.

References


