A Putative Role for Homocysteine in the Pathophysiology of Bacterial Meningitis in Children

Cordeiro, A.P.\textsuperscript{1}; Calegare, B.F.A.\textsuperscript{5}; Teixeira, F.A.\textsuperscript{1}; Martins, J.C.C.\textsuperscript{4}; Campos, F.A.\textsuperscript{4}; Candiani, T.M.S.\textsuperscript{4}; Oliveira, G.\textsuperscript{1,2}; Alves, T.M.A.\textsuperscript{3}; D’Almeida, V.\textsuperscript{5}; Coimbra, R.S.\textsuperscript{1,2}

\textsuperscript{1}Genomics and Computational Biology Group, CPqRR-FIOCRUZ, Minas Gerais; \textsuperscript{2}Center for Excellence in Bioinformatics, CPqRR-FIOCRUZ, Minas Gerais; \textsuperscript{3}Laboratory of Chemistry of Natural Products, CPqRR-FIOCRUZ, Minas Gerais; \textsuperscript{4}Hospital Infantil João Paulo II – FHEMIG, Minas Gerais; \textsuperscript{5}Department of Psychobiology, Universidade Federal de São Paulo (UNIFESP/EPM), São Paulo.

Although viral meningitis (VM) is mostly benign, up to 50% of bacterial meningitis (BM) survivors develop neurological sequelae due to brain injury. Homocysteine (HCY)-associated neuronal death involves the same mechanisms that lead to neuron loss in BM, such as the activation of poly(ADP-ribose) polymerase and the stimulation of NMDA receptors. We aimed to investigate the involvement of HCY in the pathophysiology of BM. HCY and cysteine (CYS) levels were assessed by HPLC in cerebrospinal fluid (CSF) samples collected by lumbar puncture from 40 children (median age: 4 years-old; range: <1 to 13) at admission at the Hospital Infantil João Paulo II – FHEMIG, Belo Horizonte, Brazil, with suspected meningitis from Jan/2010 to Nov/2011. The casuistic comprised nine patients with BM, 13 with VM, and 18 controls. CSF levels of HCY and CYS were higher in BM than in VM and control groups (median HCY/CYS: 0.69/29.34 µM for BM, 0/8.19 µM for VM, and 0/8.33 µM for controls; p<0.05 at Kruskal-Wallis/Dunn’s post test). In patients with BM, the median HCY concentration was higher than that previously reported to induce apoptosis in hippocampal neurons in culture (0.5 µM). There was no correlation between the CSF levels of HCY, CYS, age, duration of hospitalization, protein, glucose, white blood cells, or percentage of neutrophils. These findings corroborate with the hypothesis that HCY is produced intrathecally during BM and accumulates in the CNS to reach potentially neurotoxic levels. Our results suggest that HCY may play a pivotal role in the pathophysiology of brain damage associated BM.

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