INFLUENCE OF PRENATAL VITAMIN C DEPRIVATION ON THE PATHOGENESIS OF NEURONAL MIGRATION DISORDERS

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Introduction: Structural integrity of the basement membrane is necessary for proper migration of the neurons. Collagen is one of the key structural units of the basement membrane, and its synthesis is dependent on vitamin C. Based on the fact that neither humans nor guinea pigs are able to synthesize vitamin C we created a unique animal model in which prenatal vitamin deprivation in guinea pig fetuses led to a collagen synthesis disturbances, weakness, and finally a breach of pial basement membrane.

Materials and methods: The experiment included control (21) and vitamin C deprived-experimental group (21) of guinea pig fetuses. In experimental group pregnant guinea pig were deprived for vitamin C from 10th to 50th day of gestation. In each group we euthanized their pups at 50th fetal day (E50). In histological analysis of cerebrum and cerebellum we used the following immunohistochemical antibody for neurons: anti-NeuN, anti-calbindin, anti-synaptophysin, and glial cells: anti-S100, anti-GFAP, anti-Olig2, anti-TPPP, anti-MBP.

Findings and arguments: In gross analysis of cerebrum we found well-demarcated subarachnoid hematomas localized over parietal cortex and numerous small superficial petechial bleeding. Histologicaly cerebral cortex in the region of subarahnoid hematomas was completely damaged with disturbance of neuronal migration. Analysis of the cerebellum in vitamin deprived group showed the absence of folia with flattening of the brain surface. Histological analysis of pial basal membrane was showed multiple ruptures and fragmentations with consequential alteration of Bergmann glial cells and fusion of opposing folia. In the affected areas, the cerebellar cortex had a loss of normal linear arrangement of Purkinje cells with a clear protrusion of the external granular layer and molecular layer into the subarachnoid space.

Conclusions: Prenatal vitamin C deficiency in guinea pigs represents a novel animal model to study the effects of collagen synthesis on development of breaches in the pial basement membrane, disordered migration of neurons, dysplasia of cerebellar cortex, prenatal vascular bleeding and the new look on the pathogenesis of neurodevelopmental disorders.

Keywords: vitamin C, deficiency, neuronal migration, cerebrum, cerebellum