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LONG-TERM CARDIAC FUNCTIONAL DISORDERS, TGFB2 OVEREXPRESSION AND GENOME INSTABILITY AFTER NEONATAL GASTROENTERITIS OF VARIOUS ETIOLOGY

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Longitudinal epidemiological studies and extensive experimental data suggest that growth retardation, malnutrition and inflammation during neonatal development increase the risks of cardiovascular diseases in later life. This phenomenon was termed as developmental programming (DP). Pathophysiological triggers and underlying mechanisms of DP are still poorly understood. We investigated the long-term effects of neonatal moderate gastroenteritis of various etiologies on cardiac structure and function. The disease was challenged by lactose intolerance or by Cryptosporidium parvum infection in 6 days old neonatal rat puppies. The data of electrocardiography indicated that compared to health control, the experimental animals had Q-T interval shortening suggesting the increased risk of arrhythmia development. This difference showed higher significance for cryptosporidiosis than for lactose intolerance. To investigate whether the diseases affected heart developmental pathways, we evaluated the expression of cardiomyocyte-specific pluripotency cytokine TGF-beta 2 regulating cell growth, remodeling, epithelial-to-mesenchymal transition, and DNA damage response. Real-time PCR data revealed the link between the disease and several-fold increase of TGFb2 expression in control-cryptosporidiosis (about 9 folds) and control-lactose intolerance (about 7 folds) comparisons. Taking into account the data suggesting that TGFb2 expression increases at DNA instability, we also evaluated the number of cardiomyocytes with chromosome rearrangements. Our data identified numerous chromosome bridges and micronuclei in both groups of experimental animals. They were negligibly low in control. Overall, our data present first evidence that neonatal gastroenteritis may exert long-term negative effect on cardiac function, developmental program and cardiomyocyte genome stability.

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