Article 3

LncRNAs *NEAT1, HOTAIR,* and *GAS5 expression in hypertensive* and non-hypertensive associated cerebrovascular stroke patients, and its link to clinical characteristics and severity score of the disease.

Abstract

Background: Cerebrovascular stroke (CVS) is a potentially fatal disease. The most common risk factor for CVS is hypertension. **Aim**: While most studies in the field have focused on the functional roles of long noncoding RNAs (lncRNAs) NEAT1, GAS5, and HOTAIR in CVS, less attention has been paid to their clinical relevance to stroke incidence and prognosis. Also, a link has not yet been made between these lncRNAs and hypertension, our study aim was to investigate whether the expression of these lncRNAs differed between CVS with and without hypertension, as well as to compare each group to controls. **Method**: In total, 181 CVS patients were enrolled, including 91 chronic hypertensive patients with stroke, 90 stroke patients without hypertension, and 51 control subjects. blood samples were collected on the day of recruitment from patients with CVS and controls. Real-time qRT-PCR was used to detect the expression of target lncRNAs in serum. **Results**: When compared to controls, there was a statistically higher level of lncNEAT1 in each case group (median (IQR)= 3.68 (1.35-7.35) and 3.05 (0.95-6.45) for the hypertensive and non-hypertensive groups, respectively, with a significantly higher level in the hypertensive group (P=0.04). When compared to controls, lncHOTAIR was significantly downregulated in all case groups (medians in hypertensive and non-hypertensive patients were 0.13, and 0.34, respectively), with a significantly lower level in the hypertensive group (P=0.05). LncGAS5 levels in patients were significantly lower (median (IQR)= 0.16 (0.02-0.55) and 0.25 (0.03-0.99) for the hypertensive and non-hypertensive groups, respectively) compared to controls, with a significantly lower level in the hypertensive group (P=0.02). There was a significant positive correlation between NEAT1 and GAS5, but a significant negative correlation between each with HOTAIR in both patients' groups. We also detected a significant negative correlation between each NEAT1 or GAS5 and NIHSS score while a significant positive correlation between HOTAIR and NIHSS. ROC curve analysis for *GAS5* was able to differentiate patients with CVS hypertensive from patients with CVS non-hypertensive. **Conclusion**: Patients in each case group had statistically higher levels of NEAT1 and lower levels of HOTAIR and GAS5 compared to control levels, with higher significant NEAT1 but lower significant HOTAIR and GAS5 in the hypertensive group. Therefore, lncRNAs NEAT1, HOTAIR, and GAS5 could be used as diagnostic and prognostic biomarkers of CVS that correlate with NIHSS score and could produce a novel target for CVS therapy.

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