Delayed cerebral ischemia (DCI) is related to the major causes of morbidity and mortality in patients following a subarachnoid hemorrhage (SAH); however, little is known about the role of epigenetics in DCI pathogenesis.

Kim et al., investigated specific DNA methylation profile, which may affect the inositol 1-,4-,5trisphosphate receptor (ITPR3) expression responsible for cerebral vasospasm following an SAH.

see Inositol trisphosphate receptor.

They prospectively studied SAH patients between March 2015 and October 2018. Methylation degree of distal intergenic region (IGR) located on ITPR3, and gene expression were measured using methylation-specific PCR and quantitative real-time PCR. To investigate the regulatory mechanims of DNA hypermethylation, we further analyzed the mRNA expressions of DNA methyltransferase (DNMT1) and ten-eleven translocation enzymes (TET1, TET2 and TET3).

A total of 42 patients were included for the analysis. SAH patients with DCI had significantly higher levels of methylation intensity of distal IGR upstream of ITPR3 than those without DCI (0.941 [0.857-0.984] vs. (0.670 [0.543-0.761]; p<0.001). In addition, DCI patients showed decreased mRNA expression of ITPR3 than non-DCI patients (0.039 [0.030-0.045] vs. 0.047 [0.038-0.064]; p=0.0328). DCI patietns showed higher DNMT1 (p<0.001) and lower TET1 expression (p=0.040) than the non-DCI patients, however other differences in the levels of TET2 and TET3 were not statistically significant.

Hypermethylation of the distal IGR located upstream of ITPR3 is related to higher DCI development in SAH patients. Further study about the precise mechanism of the methylation degree and DCI development using in vitro and in vivo models are necessary 1 .

1)

Kim BJ, Kim Y, Hong EP, Jeon JP, Yang JS, Choi HJ, Kang SH, Cho YJ. Correlation between altered DNA methylation of intergenic regions of ITPR3 and development of delayed cerebral ischemia in subarachnoid hemorrhage patients. World Neurosurg. 2019 Jun 24. pii: S1878-8750(19)31665-1. doi: 10.1016/j.wneu.2019.06.113. [Epub ahead of print] PubMed PMID: 31247352.

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