Neuroinflammation and neuronal apoptosis are closely associated with a poor prognosis in patients with subarachnoid hemorrhage (SAH). We investigated the role of the C-C motif chemokine receptor 2 (CCR2) in SAH.

Methods: Pre-processed RNA-seq transcriptome datasets GSE167110 and GSE79416 from the Gene Expression Omnibus (GEO) database were screened for genes differentially expressed between mice with SAH and control mice, using bioinformatics analysis. The endovascular perforation model was performed to establish SAH. RS504393 (a CCR2 antagonist) and LY294002 (PI3K inhibitor) were administered to explore the mechanism of neuroinflammation after SAH. SAH grading, neurological scoring, brain water content, and blood-brain barrier (BBB) permeability determination, enzyme-linked immunosorbent assay (ELISA), western blotting, and immunofluorescence were performed. An in vitro model of SAH was induced in H22 cells by hemin treatment. The protective mechanism of CCR2 inhibition was studied by adding RS504393 and LY294002. ELISA detected clinical cerebrospinal fluid (CST) samples.

Results: The expression of CCR2 was upregulated in both datasets and identified as a hub gene. CCR2 expression was significantly upregulated in the cytoplasm of neurons after SAH, both in vitro and in vivo. RS significantly reduced the brain water content and blood-brain barrier permeability, alleviated neuroinflammation, and reduced neuronal apoptosis after SAH. Additionally, the protective effects of CCR2 inhibition were abolished by LY treatment. Finally, the levels of CCR2, inflammatory, and apoptotic factors were elevated in the CSF of patients with SAH. CCR2 levels were associated with patient outcomes at the 6-month follow-up.

CCR2 expression was upregulated in both in vitro and in vivo SAH models. Additionally, inhibition of CCR2, at least partly through the PI3K/AKT pathway, alleviated neuroinflammation and neuronal apoptosis in vivo and in vitro. CCR2 levels in the CSF have a moderate diagnostic value for 6-month outcome prediction in patients with SAH [1)].

1)
Tian Q, Guo Y, Feng S, Liu C, He P, Wang J, Han W, Yang C, Zhang Z, Li M. Inhibition of CCR2 attenuates neuroinflammation and neuronal apoptosis after subarachnoid hemorrhage through the PI3K/Akt pathway. J Neuroinflammation. 2022 Dec 25;19(1):312. doi: 10.1186/s12974-022-02676-8. PMID: 36566220.