Sirolimus for chronic subdural hematoma treatment

Sirolimus, also known as rapamycin, has been the subject of research for its potential role in the treatment of chronic subdural hematoma (CSDH). However, it's important to note that its use for this condition is still in the experimental or investigational stage, and there isn't yet a well-established standard of care involving sirolimus for CSDH treatment.

CSDH is typically managed through surgical intervention, such as hematoma evacuation. While sirolimus has shown promise in some preclinical studies, including the study you mentioned earlier, its effectiveness and safety in human CSDH patients have not been definitively established. Clinical trials and further research are needed to evaluate sirolimus as a viable treatment option for CSDH.

A study of Shen et al. focuses on the functions of rapamycin and its related molecular mechanisms in CSDH management. A rat model of CSDH was induced, which developed significant hematoma on day 5 after operation. The rats were treated with rapamycin or atorvastatin, a drug with known effect on hematoma alleviation, or treated with rapamycin and atorvastatin in combination. The atorvastatin or rapamycin treatment reduced the hematoma development, blood-brain barrier permeability, neurological dysfunction in CSDH rats, and the combination treatment showed more pronounced effects. Human brain microvascular endothelial cells hCMEC/D3 were stimulated by hematoma samples to mimic the CSDH condition in vitro. The drug treatments elevated the cell junction-related factors and reduced the pro-inflammatory cytokines both in rat hematoma tissues and in hCMEC/D3 cells. Rapamycin suppressed the mTOR and STAT3 signaling pathways. Overexpression of mTOR or the STAT3 agonist suppressed the alleviating effects of rapamycin on CSDH. This study demonstrates that rapamycin promotes hematoma resorption and enhances endothelial cell function by suppressing the mTOR/STAT3 signaling [1)].

The research provides important insights into the molecular mechanisms involved and the potential for combination therapy. However, it is essential to acknowledge the limitations of the study, particularly regarding the transition from animal models to human patients. Further research, including clinical trials, is necessary to determine the true efficacy and safety of rapamycin as a treatment for CSDH. This study represents a promising initial step in understanding the role of rapamycin in CSDH management but should be interpreted with caution until more evidence is available.

Eight patients whose outer membranes were obtained successfully during trepanation were included in this study. By Western blot analysis, we examined the expression of mammalian target of rapamycin (mTOR); GβL; UNC-51-like kinase-1 (ULK1); Beclin-1; autophagy-related genes (Atg) 3, 5, 7, 12, 13, and 16L1β,α; the autophagy marker Light Chain3A/B (LC3A/B); and β-actin, which constitute the autophagy signaling pathway. The expression levels of Beclin-1, Atg12, and LC3A/B were also examined by immunohistochemistry. Almost all of these molecules could be detected in all samples. Beclin-1, Atg12, and LC3A/B were found to be localized in the endothelial cells of vessels and

fibroblasts in CSDH. We detected molecules of the autophagy signaling pathway in CSDH outer membranes. Autophagy contributes to the tissue homeostatic process, maintaining cellular integrity by clearing debris. Our data suggest that autophagy might play an important role in the spontaneous resolution of CSDH. Therefore, these molecules may be novel therapeutic targets for the treatment of those with CSDH [2].

The study provides interesting insights into the potential involvement of autophagy-related molecules in the resolution of CSDH. However, its limitations, including the small sample size and lack of a control group, should be acknowledged. This research is a valuable initial step in understanding the molecular mechanisms behind CSDH, but it should be followed by more extensive and rigorous studies to determine the clinical significance of these findings and their potential use in CSDH treatment. It has the potential to open up new avenues of research and may contribute to future therapies for this condition.

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Shen J, Zhang Y, Wu X. Rapamycin promotes hematoma resorption and enhances endothelial cell function by suppressing the mTOR/STAT3 signaling in chronic subdural hematoma. Exp Cell Res. 2023 Oct 23:113829. doi: 10.1016/j.yexcr.2023.113829. Epub ahead of print. PMID: 37879548.
2)
Osuka K, Watanabe Y, Usuda N, Aoyama M, Takeuchi M, Takayasu M. Expression of Autophagy Signaling Molecules in the Outer Membranes of Chronic Subdural Hematomas. J Neurotrauma. 2019 Jan 15;36(2):403-407. doi: 10.1089/neu.2018.5626. Epub 2018 Aug 14. PMID: 30106666.