Resolvin D1 prompts inflammation resolution in ACLF rats by increasing the proportion of Treg

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Abstract

Objective: Acute-on-chronic liver failure (ACLF) causes organ system failures and the high mortality, and there is currently a lack of effective means of prevention. The purpose of the study was to explore the therapeutic effects of Resolvin D1 (RvD1) on ACLF rats and its underlying mechanism. Methods: ACLF rat model was constructed by intraperitoneally injecting CCl4 and porcine serum for 6 weeks and then induced acute liver injury by treating with both LPS and D-Galn. The ACLF rats were pretreated with different doses of RvD1 (0.3 or 1 ug/kg) before the acute liver injury. Biochemical analysis, H&E and sirius red staining, flow cytometry assay and real-time PCR were used to assess rat liver histopathological injury, determine the Treg cell frequencies in spleen and the mRNA levels of transcription factors and immunologic cytokines in liver. Results: The necro-inflammatory scores and the serum levels of transaminase significantly increased in ACLF model rats compared to those in normal control rats, with the peak at 8 h. Low-dose of RvD1 could limit necrosis and inflammation and decrease the ALT level of ACLF rats. The degree of damage in ACLF rats was related to the increased mRNA levels of IL-17 and IL-6 in the ACLF rats' liver and Treg cells reduction in the spleen. Low-dose of RvD1 could protect against liver injury in ACLF rats, as indicated by increasing Treg cell frequency in rats' spleen and the mRNA levels of Foxp3/RORγ and decreasing the expression of both IL-6 and IL-17. Conclusion: Low-dose of RvD1 plays a protective role in ACLF rats by increasing the proportion of Treg cells. It is the first time to reveal the function of RvD1 in the treatment of ACLF. This work may help us clarify the pathogenesis of ACLF and find effective therapeutic drugs for ACLF.

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