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Protective effect of combination therapy with ischemic preconditioning and rapamycin in fibrotic rat livers

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Introduction: Ischemic preconditioning has been shown to reduce hepatic injury in patients. Our objective was to investigate the effect of combination of ischemic preconditioning with rapamycin on experimentally induced chronic liver injury (liver fibrosis) in rats.

Methods: Chronic liver injury (liver fibrosis) was induced in Wistar rats by oral administration of carbon tetrachloride (CCl₄) for 7wks, an animal model with persistent severe hepatic fibrosis. Rat were randomized to five major groups that were treated as follows: (1) the normal control group; (2) the sham operated group; (3) the I/R group; (4) ischemic preconditioning group; (5) ischemic preconditioning + rapamycin group.

Results: Combination therapy with remote ischemic conditioning and rapamycin resulted in significant protection against I/R with less attenuation of hepatic damage and lower LFT levels. The number of infiltrating macrophages in the liver and cytokines in peripheral blood were diminished in this group. The preconditioning I/R showed a decrease in liver cell apoptosis with positive results of EPK, P38, JUN, BCL2, BAX level.

Conclusion: Ischemic preconditioning and rapamycin therapy has a significant therapeutic potential in ischemic hepatic injury.