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Ultra Low Dose Delta 9-Tetrahydrocannabinol Protects Mouse Liver from Ischemia Reperfusion Injury.

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Abstract

BACKGROUND/AIMS: Ischemia/reperfusion (I/R) injury is the main cause of both primary graft dysfunction and primary non-function of liver allografts. Cannabinoids has been reported to attenuate myocardial, cerebral and hepatic I/R oxidative injury. Delta-9-tetrahydrocannabinol (THC), a cannabinoid agonist, is the active components of marijuana. In this study we examined the role of ultralow dose THC (0.002mg/kg) in the protection of livers from I/R injury. This extremely low dose of THC was previously found by us to protect the mice brain and heart from a variety of insults.

METHODS: C57Bl Mice were studied in in vivo model of hepatic segmental (70%) ischemia for 60min followed by reperfusion for 6 hours.

RESULTS: THC administration 2h prior to the induction of hepatic I/R was associated with significant attenuated elevations of: serum liver transaminases ALT and AST, the hepatic oxidative stress (activation of the intracellular signaling CREB pathway), the acute proinflammatory response (TNF- α , IL-1 α , IL-10 and c-FOS hepatic mRNA levels, and ERK signaling pathway activation). This was followed by cell death (the cleavage of the pro-apoptotic caspase 3, DNA fragmentation and TUNEL) after 6 hours of reperfusion. Significantly less hepatic injury was detected in the THC treated I/R mice and fewer apoptotic hepatocytes cells were identified by morphological criteria compared with untreated mice.

CONCLUSION: A single ultralow dose THC can reduce the apoptotic, oxidative and inflammatory injury induced by hepatic I/R injury. THC may serve as a potential target for therapeutic intervention in hepatic I/R injury during liver transplantation, liver resection and trauma. © 2015 S. Karger AG, Basel.

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