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Hepatic Regenerative Capacity after Acetaminophen-Induced Liver Injury in Mouse Model

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Abstract : Acetaminophen (APAP) is a widely used analgesic that is safe at therapeutic doses. The mouse model of APAP has been extensively used for studies on pathogenesis and intervention of drug induced liver injury based on the CytP450 mediated formation of N-acetyl-p-benzo-quinoneimine and, more recently, as model for mechanism based biomarkers. Delay of the fasted CD1 mice to rebound to the basal level of hepatic GSH compare to fed mice is reported in this study. Histologically, 15 hours fasted mice prior to APAP treatment leading to overall more intense cell loss with no evidence of apoptosis as compared to non-fasted mice, where the apoptotic cells were clearly seen on cleaved caspase-3 immunostaining. After 15 hours post APAP administration, hepatocytes underwent stage of recovery with evidence of mitotic figures in fed mice and return to completely no histological difference to control at 24 hours. On the contrary, the evidence of ongoing cells damage and inflammatory cells infiltration are still present on fasted mice until the end of the study. To further measure the regenerative capacity of the hepatocytes, the inflammatory mediators of cytokines that involved in the progression or regression of the toxicity like TNF-α and IL-6 in liver and spleen using RT-qPCR were also included. Yet, quantification of proliferating cell nuclear antigen (PCNA) has demonstrated the time for hepatic regenerative in fasted is longer than that to fed mice. Together, these data would probably confirm that fasting prior to APAP treatment does not only modulate liver injury, but could have further effects to delay subsequent regeneration of the hepatocytes.

Keywords : acetaminophen, liver, proliferating cell nuclear antigen, regeneration, apoptosis
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