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Cigarette smoke exacerbates Acetaminophen-induced liver injury by modulating oxidative stress and inflammation via JNK signal pathway in mice

Jing Zhao[1], Kyuhong Lee[2], Moo-Yeol Lee[3] and Bumseok Kim[1]
[1]Chonbuk National University, South Korea
[2]Korea Institute of Toxicology, South Korea
[3]Dongguk University, South Korea

Acetaminophen (APAP) overdose induces inflammation and oxidative stress that can lead to severe liver injury. Cigarette smoking is considered to be a crucial modifiable risk factor for disease and death worldwide. Our previous data revealed that cigarette 3R4F aggravated APAP-induced liver injury in a dose-dependent manner. This study aimed to investigate the effects of commercial cigarette A on the progression of APAP-induced acute liver injury. Seven-week-old C57BL/6 mice were exposed to cigarette A (300, 600 μg/L) or standard cigarette 3R4F (600 μg/L) or fresh air for 2 hours once daily and 5 days per week. After 4 weeks, mice were intra-peritoneally injected with PBS or APAP (500 mg/kg). Eight hours later the mice were euthanized and blood and tissues were collected for analysis. The results showed that cigarette smoke exposure significantly increased APAP-induced liver injury by increasing serum ALT and AST levels, exacerbated hepatic pathological damages with inflammatory cell infiltration and hepatocellular apoptosis and accompanied by up-regulated inflammatory mediators including tumor necrosis factor (TNF-α) and interleukin (IL)-1β. Cigarette smoke could increase the expressions of cytochrome P450 (CYP) 2E1 and 1A2 which could metabolize a large number of compounds in liver and lead to the down-regulation of antioxidant such as glutathione peroxidase (GSH-Px) and heme oxygenase-1 (HO-1) in APAP treated mice. Furthermore, cigarette smoke exposure obviously increased the activation of c-Jun N-terminal kinases (JNK) signal induced by APAP. Mice exposed to commercial cigarette A had no significant difference between those exposed to standard cigarette 3R4F after APAP injection. Overall, these findings suggested that cigarette smoke exposure could exacerbate APAP-induced hepatotoxicity and possible mechanism might be associated with the activation of JNK signal pathway.

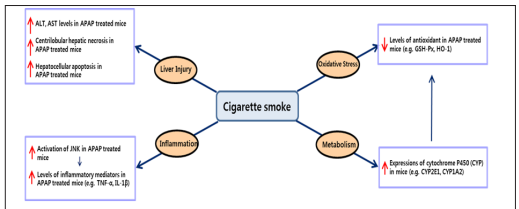

Figure 1: Effects of cigarette smoke on APAP-induced liver injury. (↑: increase or enhancement; ↓ decrease or deterioration)

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Biography

Jing Zhao is currently a Doctoral student of Veterinary Pathology in Chonbuk National University of South Korea and has received her Master's degree of Veterinary Medicine in China in July 2015. Her experiments focus on the liver diseases and damages in mice, including Acetaminophen-induced liver injury and Concanavalin A-induced liver injury.

zhaojing19901230@126.com