INTERMITTENT HYPOXIA AGGRAVATES EARLY PATHOGENESIS OF NON-ALCOHOLIC FATTY LIVER DISEASE IN RATS

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BACKGROUND/AIMS: Chronic intermittent hypoxia (CIH) is associated with recurrent episodes of oxygen desaturation and reoxygenation in obstructive sleep apnea (OSA) patients. The prevalence of OSA is high in patients with non-alcoholic fatty liver disease (NAFLD). The mechanistic effect of CIH on the early pathogenesis of NAFLD remains elusive. Here we tested the hypothesis that IH aggravates oxidative stress and inflammation induced by high fat diet at an initial stage of pathogenesis of NAFLD in the rat liver.

MATERIALS AND METHODS: Female Adult Sprague-Dawley rats were fed with a diet comprising of high fat (30% fish oil) or normal diet for 4 weeks with air (normoxic control) or CIH treatment (8 hours/day) which mimics obstructive sleep apnea condition during the last 2 weeks. Liver injury was detected by serum ALT and AST assay. Liver histology was evaluated by H&E staining. Lipid peroxidation was examined by malondialdehyde (MDA) assay and the expressions of pro-inflammatory cytokines (IL-1β, TNF-α, IL-6) were determined by real-time PCR and ELISA.

RESULTS: Results showed that high fat diet (HFD) or CIH treatment increased liver injury with significant elevated levels of ALT and AST and deteriorated histological features of lipid accumulation in the liver. The effect of HFD was more prominent in the group co-treated with hypoxia. In addition, levels of MDA and the expressions of IL-1β, TNF-α and IL-6 were significantly increased in the HFD- or hypoxia-treated group and were substantially elevated in the co-treated group.

CONCLUSION: Intermittent hypoxia exacerbates oxidative stress and inflammation induced by high fat diet in the rat liver, suggesting a significant effect of CIH on aggravating the early pathogenesis of NAFLD.