Effects of Metabolic Dysfunction-associated Fatty Liver Disease on the Pharmacokinetics of Naproxen in Rats

Li Chen¹, Lu Chen¹, Lin Qin², Daopeng Tan², Yan Zhu¹, Wu-Cai Tan³, Zhao-Jun Bai⁴, Yuqi He², and Yu-He Wang¹

¹Affiliated Hospital of Zunyi Medical University
²Zunyi Medical University
³Sinopharm Group Zunyi Co., Ltd
⁴Guangxi Shenli Pharmaceutical Co., Ltd

June 26, 2023

Abstract

Background and Purpose: Metabolic dysfunction-associated fatty liver disease (MAFLD) refers to fatty liver disease related to systemic metabolic dysregulation. The altered pharmacokinetics of drugs in MAFLD have been reported in several studies. Naproxen, a non-steroidal anti-inflammatory drug, is often used as an analgesic and anti-inflammatory agent. However, the pharmacokinetics of naproxen in MAFLD remains unknown. Experimental approach: High-fat diet (HFD)-fed rats were used to establish the MAFLD disease model. Serum triglyceride (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) were used as evaluation indicators. And hematoxylin-eosin staining was employed to observe the histomorphological changes in the liver to ensure a viable MAFLD model. After naproxen administration in MAFLD rats, the plasma concentrations of naproxen were measured by high-performance liquid chromatography. Key Results: Compared with normal diet (ND)-fed rats, the body weight, TC, and LDL-C were significantly increased in HFD-fed rats. And the hepatocytes in HFD-fed rats were significantly swollen, with most hepatocytes showing large vesicular steatosis, severe ballooning indicating successful modeling. The pharmacokinetic study of naproxen revealed that after naproxen administration, the mean plasma concentrations of naproxen were significantly lower in the HFD group compared to the ND group. Compared with ND-fed rats, the main pharmacokinetic parameters t1/2z, AUC0-t, AUC0-τ, and MRT0-τ were significantly decreased, while CLz/F was significantly increased in HFD-fed rats. Conclusions & Implications: The pharmacokinetics of naproxen in the MAFLD rat model demonstrated reduced absorption, accelerated metabolism, and reduced retention time, which may provide some evidence for individualized treatment of patients with MAFLD.

Hosted file


Hosted file
