Genetics and Molecular Research

Effect of uric acid on mitochondrial function and oxidative stress in hepatocytes

Y. Yang[1], Y. Zhou[2], S. Cheng[1], J.L. Sun[1], H. Yao[3] and L. Ma[1]

[1]School of Public Health, Xinjiang Medical University, Xinjiang, Urumqi, China
[2]School of Basic Medicine, Xinjiang Medical University, Xinjiang, Urumqi, China
[3]The First Affiliated Hospital of Xinjiang Medical University, Xinjiang, Urumqi, China

Corresponding author: L. Ma
E-mail: maling3633@126.com

Genet. Mol. Res. 15 (2): gmr.15028644
Received March 23, 2016
Accepted April 11, 2016
Published June 24, 2016
DOI http://dx.doi.org/10.4238/gmr.15028644

ABSTRACT. Here, we investigated the effect of uric acid (UA) on hepatocyte mitochondria. Hepatocytes cultured *in vitro* were treated with varying concentrations of UA. The change in apoptotic activity was detected by flow cytometry. The DNA damage index 8-hydroxy-deoxy-guanosine (8-OHdG) and mitochondrial function indices succinate dehydrogenase (SDH), cytochrome C oxidase (CCO), and adenosine triphosphate (ATP) were detected by enzyme assays. Reactive oxygen species (ROS) accumulation was confirmed by a dichloro-dihydro-fluorescein diacetate assay. We observed an increase in apoptotic activity, ROS accumulation, and 8-OHdG activity in hepatocytes treated with UA for extended periods, indicating DNA damage; specifically, we observed a significant increase in these activities 48, 72, and 96 h after UA addition, compared to those observed at 24 h ($P < 0.05$). Cells treated with 30 mg/dL UA for 96 h showed a peak in apoptotic activity. We also observed a significant decrease in ATP, SDH, and CCO activities with the increase in uric acid concentration over time.

Cells treated with 30 mg/dL UA for 96 h showed the highest ATP levels, while SDH and CCO activities at 48, 72, and 96 h post-UA treatment were significantly lower than those at 24 h ($P < 0.01$). Moreover, cells treated with 30 mg/dL UA showed a 0.02 ± 0.02 and 0.15 ± 0.01 μmol/mg/min decrease in SDH and CCO levels after 72 h. Therefore, we concluded that high concentrations of UA may induce oxidative stress in hepatocyte mitochondria, increasing ROS production and ultimately resulting in mitochondrial damage.

Key words: Uric acid; Mitochondrial damage; Oxidative stress; Cell apoptosis; DNA damage

