Modulation of Gene Expression in the Liver of Mice 48-H Post-Treatment with Ccl₄

Karam Mahdy¹, Abdel-Razik Farrag² and Sonya El-Sharkawy²

Medical Biochemistry¹ and Pathology² Departments
Medical Research Division, NRC, Egypt

Abstract

Background and Aim: Carbon tetrachloride (CCL₄) has been widely used to study mechanisms of hepatic injury and repair following toxic induced injury. This study was undertaken to evaluate the changes in gene expression in hepatocyte of injured liver of mice 48-h post-treatment with CCL₄.

Methods: Twelve adult male wild type mice were used in this experiment. The mice were fasted overnight and classified into two groups, (six mice each) the first group received in the following morning 4 ml/kg Olive oil, while the second group was received 8 ml/kg CCL₄ (50% in olive oil) by gavages. After 48-h, the mice were anesthetized and killed to obtain blood and excise the liver. Gene’s expression analysis in the liver tissue was carried out using cDNA microarray technique. Serum liver function tests, histopathological, histochemical and immunohistochemical examinations were also done.

Results: Serum transaminases (AST and ALT) activities exhibited significant increase with the induced hepatic pathological changes included typical inflammation and necrosis observed in CCL₄-treated mice. The cDNA microarrays analysis revealed that 63 genes have clearly changed their levels of expression. Of these, 37 genes were up-regulated and 26 genes were down-regulated. Of the up-regulated genes were ribosomal, transcription, stress, proteolysis and peptidolysis encoded proteins. The most interesting up-regulated gene is metallothionine-1 gene which was observed by microarray and immunohistochemistry techniques. On the other hand, the down-regulated genes encoded proteins for xenobiotic metabolism, detoxification, lipid metabolism and hormones proteins.

Conclusion: These results demonstrated that changes in gene expression profile correlate with the biochemical and pathological alterations in the liver in response to CCL₄ intoxication and most of them can be related to CCL₄ mechanism of toxicity. However, the majority of the up-regulated genes are occurred in ribosomal protein. Furthermore, Mt-1 can be used as a biological marker for CCL₄ toxicity.