SUMMARY

Akşit H. Determination of DNA damage in experimental liver intoxication and role of N acetyl cysteine

We were assigned to HAT and HDAC enzymes, We aimed to investigate whether on the activities of these enzymes (on tanskripsiyon indirectly) the possible effect of oxidative stress, apoptosis and gene transcription is controlled by whether or not a relationship between histone acetylation, N acetyl cysteine on the protective role of DNA damage in experimental liver intoxication.

In this study, totaly 60 rats were used in 6 groups. Liver toxicity of CCl_4 in order to create, intraperitoneally 2 ml / kg, 1 / 1 ratio as a single dose of olive oil solution was injected. N Acetyl Cysteine application (intraperitoneal 50 mg / kg / day) was started 3 days before CCl_4 injection and was continued during the experimental period. Control groups were performed in olive oil and N Acetyl Cysteine. 6. and 72. hours after CCl_4 injection, blood and liver tissue were taken under ether anesthesia. Nuclear extracts were prepared from liver.

Serum AST and ALT levels increased in the group CCl_4 6. hour than the control groups, 72. hour there was an increased but were decreased compared to 6. hour. In the group with CCl_4+NAC 6. and 72. hours there were an increased level compared with control groups but levels were reduced compared to the CCl_4 group. MDA analysis, CCl_4 in the group 6. hour increase than the control groups, 72. hour there was an increased but were decreased compared to 6. hour. In the group with CCl_4+NAC 6. and 72. hour there was an increased level compared with control groups, but levels were decreased compared to the CCl_4 groups. CCl_4 intoxication and lipid peroxidation in the liver caused by experimental application, the level, depending on the NAS application and time were reduced.

Serum analysis of TAS, the levels decreased in the group CCl_4 6. hour compared to the control groups, 72. hour there was an decreased but were increased compared to 6. hour. In the group with CCl_4+NAC 6. and 72. hours there were an decreased level

compared with control groups but levels were increased compared to the CCl_4 group. Analysis of the TOS, the levels increased CCl_4 in the group 6. hour compared to control groups, 72. hour difference between the groups was not identified. CCl_4+NAC treated group compared with the control group 6 hours, there was an increased, but the level decreased compared to CCl_4 group, the difference was not identified in 72. hour.

The 8-hydroxy-2-deoxyguanosine and Histone Acetyl Transferase analysis in nuclear extract, the CCl_4 treated group, the level was increased compared to control groups the in 6 hours, 72. hour, but also there was an increased level compared to 6. hour were reduced. CCl_4+NAC treated group, the level was increased compared with control groups in the 6. and 72. hours, but decreased levels were determined according to CCl_4 group. The level of histone deacetylase, CCl_4 treated group 6. hour level was decreased than the control groups, 72. hour there was an decreased but were increased compared to 6. hour. CCl_4+NAC treated group was decreased compared with control groups in the 6. and 72. hours, but increased levels were determined according to CCl_4 group.

In the analysis of apoptotic DNA fragmentation, the levels increased in the group CCl_4 6. hour than the control groups, 72. hour there was an increased but were decreased compared to 6. hour. In the group with CCl_4+NAC 6. and 72. hour there was an increased level compared with control groups, but levels were decreased compared to the CCl_4 groups. Apoptosis also was evaluated by TUNEL assay in liver tissue, and 6. hour, apoptotic cells increased in CCl_4 treated group than the control groups, the NAS was added to the group decreased compared to the CCl_4 group, 72. hour is an increase compared with the control groups but decreased levels were determined compared with 6. hour.

Toxicity model of CCl_4 in the liver was performed to generate free radicals. Oxidative stress, DNA damage and DNA breakage occurred and formed and consequently, increased histone acetylation, decreased histone deacetylation and increased apoptosis were determined. At the same time, that the protective role of N acetyl cysteine on DNA damage and reduced oxidative stress and apoptosis were determined.

Key Words; Carbon tetrachloride, N acetyl cysteine, oxidative DNA damage, histone acetylation, free radicals, apoptosis