P-11 Effects of Acute Exposure to Triphenyltin Chloride on the Fas-Mediated Apoptosis in Mouse Liver and Ovary

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Background & Objectives: Organotin compounds have been implicated as reproductive toxicants and endocrine disruptors and there effects in some cases of occupational poisoning, hepatic injury, acute nephropathy also have been reported. Present study investigated whether triphenyltin chloride (TPT) causes apoptosis in ovarian and liver cells and to delineate further the pathways involved, we examined the changes of the expression of FasL and Fas.

Method: Immature female ICR mice were given a single oral dose of 2.5, 12.5, 25, or 50 mg/kg BW of TPT and sacrificed 24 hours after the treatment. The frequency of apoptosis of ovarian and liver cells was demonstrated by the in situ 3'-end-labelling method. Serum estradiol concentration was measured by radioimmunoassay and the mRNA and protein expressions of FasL and Fas were determined by RT-PCR analyses and immunohistochemistry, respectively.

Results: Serum estradiol concentration was slightly decreased in the TPT-treated groups. The numbers of apoptotic cells, visualized by in situ 3' end labeling, were dose-dependently increased in the liver of TPT treated groups and the Kupffer cells were shown to be the target cells for TPT exposure. In contrast, no significant change on the number of apoptotic cells was observed in the ovary. Result from RT-PCR analysis demonstrated that expressions of Fas and FasL mRNAs were significantly increased in the liver from TPT-treated mice while those in ovary were not significantly changed. Immunohistochemical analyses also revealed increased immunostaining of Fas and FasL in liver, especially in the Kupffer cells.

Conclusions: Taken together, the present study demonstrates that acute exposure to TPT induces apoptosis of Kupffer cells through upregulation of Fas and FasL system. As the Kupffer cells are considered to play a part in mediating normal liver function and hepatocellular activity, it is suggested that TPT may cause liver injury and hence, alter the defense mechanisms of the body. In the ovary, no significant effects of TPT were observed in the present study, however, further study for the effects of chronic exposure to TPT are needed to characterize its reproductive toxicity.

KOSEF, ABRL; R14-2003-036-010020