Interaction between 17β-estradiol and 2,3,7,8-tetrachlorodibenzo-p-dioxin in Proliferation and Na+/glucose Cotransporter Activity of Renal Proximal Tubule Cells

Department of Veterinary Physiology, College of Veterinary Medicine,
Chonnam National University, Gwangju 500-757 Korea

Min Jin Lim, Yun Jung Lee, Su Hyung Park, Eun Jung Kim, Ran Jeong, Ho Jae Han

Background: The 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is a highly toxic environmental toxicant that is a byproduct of industrial processes and combustion of organic materials including municipal garbage. It has been proposed that many TCDD-induced effects are mediated through initial binding to an intracellular cytosolic protein, aryl hydrocarbon receptor. However, interaction between 17β-estradiol (E2) and TCDD on [3H]-thymidine incorporation and Na+/glucose co-transpoter activity is not yet elucidated in primary cultured rabbit renal proximal tubule cells (PTCs).

Methods: PTCs were exposed to TCDD in the presence or absence of agonists (β-naphthoflavone; β-NF, polychlorinated biphenyl congener; PCBs), antagonist (α-naphthoflavone; α-NF), and E2. Cell proliferation and Na+/glucose cotransporter activity were assessed by [3H]-thymidine incorporation and 14C-α-methyl-D- glucopyranoside (α-MG) uptake, respectively.

Results: TCDD (10-8 M) bited [3H]-thymidine incorporation from 1 hr and this response was sustained over 24 hr. Thus, the treatment of 10-8 M TCDD for 24 hr was used for this study. The β-NF and PCBs were seen synergistic effects and the α-NF were seen suppressed effect on TCDD-induced inhibition of [3H]-thymidine incorporation. In addition, TCDD inhibited E2-induced stimulation of [3H]-thymidine incorporation. And in the experiments to examine specificity of the TCDD on apical membrane transporters, TCDD inhibited α-MG uptake, a typical marker of Na+/glucose cotransporter, not L-arginine, alanine, fructose, or Pi uptake. 10-8 M TCDD (≥48 hr) significantly inhibited α-MG uptake compared to control but 10-8 M TCDD for 24 hr did not affect. TCDD-induced inhibition of α-MG uptake slightly increased by β-NF or PCBs and blocked by α-NF. E2 did not affect α-MG uptake but blocked TCDD-induced inhibition of α-MG uptake.

Conclusion: TCDD inhibited Na+/glucose cotransporter activity and inhibited E2-induced stimulation of cell proliferation through aryl hydrocarbon receptor and E2 inhibited TCDD-induced inhibition of α-MG uptake.