Neonicotinoids are cytotoxic to human trophoblast cells

Ezinne K OKORO, Wataru MIYAZAKI, Yuki FUJIWARA, Takahiko KATOH

Department of Public Health, Faculty of Life Sciences, Kumamoto University, Japan

The neonicotinoids are a new class of widely used potent insecticides accounting for over 17% of the global insecticide market. They were developed from the modification of nicotinoids and are thus similar to nicotine in structure and function. Acting primarily and selectively at insect nicotinic acetylcholine receptor (nAChR) in the central nervous system (CNS), they are believed to possess low toxicity to vertebrates. However, several in vivo and in vitro mammalian studies (mouse) have reported neonicotinoids to impair reproduction at almost all levels. The adverse effects of nicotine on pregnancy have also been reported severally and are known to be mediated via the nAChR hence, we investigated for the adverse effects of neonicotinoids on human trophoblast cells and the underlying signaling mechanisms using human choriocarcinoma NJG and BeWo cells. Cells were treated with neonicotinoids for 24, 48 and 72 h with re-exposures every 24 h. This resulted in a time and concentration-dependent growth inhibition in both cell lines. Increased generation of reactive oxygen species (ROS) suggested involvement of oxidative stress in the cytotoxicity of neonicotinoids. Western blot data revealed that neonicotinoid exposure also induced a dose and time dependent activation of ERK1/2 which was inhibited by mecamylamine (a non-selective inhibitor of nAChR). Cleaved caspase-3 expression substantiated neonicotinoid induced cytotoxicity and suggests apoptosis as the pathway through which cell death occurs. Overall, these findings suggest that neonicotinoids and nicotine exert similar cytotoxic effect to human trophoblasts and may adversely affect reproduction in humans through disruption of essential signaling pathways.

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