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Toxicological Effects of Acrylamide on Mice and Rats : Mutagenicity, Neurotoxicity and Reproductive Toxicity

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Introduction

Acrylamide (AA) has been issued because of its finding in a variety of fried and oven-baked food or contaminated water which means the public can be exposed to AA. Also laboratory researchers or workers in factories can be exposed to AA in their workplace. Exposure to AA is a concern because it is a possible human carcinogen with genotoxicity based on high-dose animal studies. Also it has the neurotoxicity which causes several nuerological sign such as drowsiness, incoordination, and confusion. Furthermore, it has been repoted that AA has the toxicity for the male reproductive system. In this study, mutagenicity and neurotoxicity of AA were observed in mice, and reproductive toxicity of AA was examined in rats. Also the up/down regulations of the potential gene by AA were evaluated through micro-array test.

Materials & methods

Male ICR mice, aged 45-50 days (25-30 g), were divided into six groups and AA was administered orally everyday at doses of 0, 5, 15, 30, 45, and 60 mg/kg of body weight for 10 consecutive days. The mutagenicity of AA was examined using Ames test, micronucleus test, and chromosomal abbreviation test. Rota-rod test and spontaneous activity test were performed to observe the neurotoxicity of AA. For reproductive toxicological studies, adult male Sprague-Dawley rats, aged 50-60 days (200-250 g), were divided into six groups and AA was administered for 5 consecutive days. Leydig cells were isolated from rats and their cell viabilities were observed. Also testosterone levels were evaluated and the numbers of sperm were counted from rat cauda epididymis.

For histological features of testis and epididymis were observed with hematoxylin & eosin staining and TUNEL method. Micro-array analysis were performed to observe the effects of AA

on the regulation of potential gene in mouse brain, mouse liver, rat brain, rat liver, and rat testis.

Results

Based on rota-rod test and spontaneous activity test, the motor activity of mice was decreased in AA concentration-dependent manner (approximate IC50 of 45 mg/kg of body weight). AA raised the number of micronucleus over 2 out of 1,000 in its concentration of >100 mg/kg of body weight. In AA treated CHL cells, chromosomal abbreviations such as breakage, gap and exchange of chromosomes were observed during the metaphase of cell division. Leydig cells isolated from AA administered rat testis showed decreased cell viability in an AA dose-dependent manner. In related to this, the numbers of sperm in cauda epididymis from AA treated rats were reduced significantly, and they have several abnormal features (e.g. broken tails or cleaved head from its tail). Histological features of testis from AA treated rats presented vacuolations, multinucleate giant cells, and apoptosis. Micro-array analysis evaluated the effects of AA on the up and down regulations of the genes in mouse brain, mouse liver, rat brain, rat liver, and rat testis.

Discussion

In this study, various toxicological effects of AA on mice and rats were examined. Also the potential gene over/down expression by AA was evaluated through micro-array test.

Interestingly, both global ischemia induced protein GIIG15B gene and glucocorticoid regulated kinase gene were up-regulated in AA treated rat brain which suggest that AA causes neurotoxicity by regulating protein levels in central nerve system. Cytochrome p-450 gene was down-regulated in AA treated rat liver based on micro-array test which indicates that AA affects the detoxication system in liver. Most striking feature of AA toxicity can be observed in reproductive system in rats. At least 151 genes related signals to apoptosis were up-regulated and 16 genes were down-regulated in AA treated rat testis. Based on TUNEL method, histological signs of apoptosis were observed in rat testis. Therefore, it is worth to try to make more examinations for those genes related to spermatogenesis or other factors including apoptosis. Recently, AA has been issued because of its finding in a variety of fried and oven-baked food or contaminated water. To solve the problem, Global efforts for reducing potential risk of AA are needed for public health in the World.

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