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Evaluation of the genetic effects of meiact alone or in combination with carnitine on pregnant female mice and embryos

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Abstract : Pivalate-generating prod rugs such as cefditoren pivoxil (meiact), a new-third generation cephalosporin antibiotic which shows important activity over a large part of the pathogens causing skin and respiratory tract infections, including Gram-positive and Gram-negative bacteria has been suggested to cause significantly hypo-carnitinemia. Also, many studies have shown that carnitine is critical in fetal growth and fetal maturation during pregnancy. So, this study was performed to evaluate the genetic effect of cefditoren pivoxil alone or plus carnitine on embryonic toxicity, micronuclei formations and chromosomal aberrations in the pregnant females and their embryos throughout pregnancy. Pregnant female mice were administrated orally with three dosing regiments of meiact (5, 10 and 20 mg/kg) and meiact plus carnitine (5, 10 and 20mg/kg) twice daily for 14 days from day 3 to day 17 of pregnancy and on day 18 of pregnancy. Pregnant females were killed and examined for evidence of embryonic toxicity and cytogenetic effects including micronuclei formation and chromosomal aberrations in the maternal and embryonic cells.

It was observed that there were significant increases in the frequencies of embryonic toxicity, the micronucleus formation and the chromosomal aberrations in pregnant female mice as well as their embryos treated with the three doses of meiact (5,10 and 20mg/kg) in dose dependent-manner but this increase in the low dose (5mg/kg) was close to the control group. On the other hand the results showed that in the three doses of meiact plus carnitine (5, 10 and 20+5mg/kg) the frequencies of embryonic toxicity, micronucleus formation and chromosomal aberrations were also increased significantly over the control group but these increase were decreased significantly comparing with the groups of meiact alone and became relatively similar to those in controls in the low dose of meiact plus carnitine (5+5 mg/kg).

The results suggest that meiact seems to be safe at the low dose but by increasing its concentration it caused genetic and embryonic toxicity, on the other hand, the administration of pregnant females with meiact plus carnitine caused significant decreases in the frequencies of embryonic toxicity, micronuclei formation and chromosomal aberrations when comparing with the pregnant females administrated with meiact alone and the frequency of the low dose of meiact plus carnitine become in the limit of the control. This is may be due to that the administration of meiact especially in high doses during pregnancy caused a decrease in the concentration of carnitine under the normal level and this decrease is dose-dependent The administration of carnitine is responsible for removing toxic substances from the body and improves embryonic and fetal growth.

Key words: Meiact, cefditoren pivoxil, micronucleus test, embryonic toxicity, chromosomal aberrations, mice, embryos.