Effects of Topiramate on Pregnancy Outcome in Rats

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Background: Anti-epileptics taken during pregnancy might lead to low birth-weight and birth defects which could be associated with neonatal morbidity and mortality.

Objective: To evaluate the effects of maternal exposure to therapeutic doses of topiramate on the growth of 20day rat fetuses.

Design: An Experimental Animal Study.

Setting: Teratology Laboratory, Anatomy Department, College of Medicine and Medical Sciences, Arabian Gulf University, Bahrain.

Method: Three groups of Sprague-Dawley pregnant rats were used in the experiment: control, Topiramate 50mg/Kg BW and Topiramate 100 mg/Kg BW. Topiramate was administered by intragastric intubation from day 6 through day 19 of gestation. Cesarean section was performed on day 20. Resorption was calculated, placental weight and umbilical cord length were measured. Fetuses were collected to assess their growth parameters: fetal weight (FW), biparietal diameter (BPD), crown-rump length (CRL) and head length (HL). Ponderal index and CRL/HL ratio were calculated to indicate the type of growth restriction.

Result: The Topiramate treated groups showed an insignificant increase in the rate of resorption, a significant decrease in umbilical cord length, placental weight and highly significant reduction in fetal growth parameters. No significant changes were noticed in fetal growth parameters between Topiramate groups. A positive correlation was found between FW and UCL, PW, CRL, HL and BPD in all examined groups. Ponderal index and CRL/HL ratio indicate symmetrical growth restriction of the fetuses in both treated Topiramate groups.

Conclusion: The doses of Topiramate, which were given to pregnant rats were equivalent to the human therapeutic range; the drug led to symmetrical fetal gross restriction with few abnormal fetuses and placentae. Topiramate attributed effects were not dose related. The drug should be taken with caution during pregnancy.

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