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Influence of maternal folate status on the developmental toxicity of methanol in the CD-1 mouse.

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Methanol, which is detoxified via a folic acid-dependent pathway, has been shown to be teratogenic in mice. Given recent observations that the level of dietary folic acid intake may be inversely related to the occurrence of select birth defects in humans, we tested the hypothesis that dietary folic acid intake would influence the developmental toxicity of methanol. Virgin female mice were fed one of three diets containing 400 (low), 600 (marginal), or 1,200 (adequate) nmol folic acid/kg diet for 5 weeks prior to and following mating. On gestation days (GD) 6-15, dams were administered by gavage either vehicle (distilled, deionized water) or methanol at 2.0 or 2.5 g/kg body weight, twice daily. On GD 18, mice were weighed and killed and the liver, kidneys, and gravid uteri removed and weighed. Implantation sites, live and dead fetuses, and resorptions were counted; fetuses were weighed individually and examined for cleft palate and exencephaly. One third of the fetuses in each litter were examined for skeletal morphology. Maternal liver folate concentrations were approximately 40-50% lower in the low dietary folic acid groups than in the marginal and adequate groups; methanol did not affect maternal liver folate concentration at term. Maternal net gestational weight gain was lowest at the lowest dietary folate level but was not affected by methanol. Gravid uterus weights were lowest in the low dietary folic acid groups exposed to the high methanol dose and the number of live fetuses per litter was lowest in the low folic acid groups. Fetal body weights were lowest in the low folic acid groups and significantly lower in the methanol groups relative to vehicle-treated animals. Fetal crown-rump lengths were shorter in the methanol-treated groups; this parameter was not affected by folic acid treatment. Both methanol and low dietary folic acid increased the incidence of cleft palate, with the highest number of affected litters in the low dietary folic acid group. These results support the concept that maternal folate status can modulate the developmental toxicity of methanol.

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