The effects of short-term and chronic daily propylparaben exposure on estrous cyclicity and fertility in mice

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Parabens are a group of chemicals widely used as preservatives in cosmetics, prescription medications, and personal care products. Evidence suggests that parabens have weak estrogenic endocrine-disrupting properties. This is concerning because altered signaling of reproductive-related hormones can have marked effects on estrous cyclicity and fertility outcomes in females. The effects of propylparaben, one of the most commonly used paraben, on mouse estrous cyclicity and fertility are unknown. Here we hypothesized that propylparaben at low levels of exposure can negatively affect estrous cyclicity and fertility outcomes in mice. Thus, adult female CD-1 mice were treated with propylparaben at 0, 2, 20, and 200 µg/kg/day over the course of one, three, and six months. Estrous cyclicity was evaluated over three weeks prior to the end of each dosing period to compare cycle lengths and numbers, and time spent in each estrous stage. Fertility studies were conducted after 6 months of chronic propylparaben exposure (n=7-8 per group). Analysis of variance of cyclicity outcomes (cycle length in days and numbers of cycles in 21 days) was performed with a linear mixed model for repeated measures. The model included treatment as a fixed effect and mouse as a random effect to account for repeated measures on the same mouse. The effect of treatment on the marginal means of the outcome variables was compared using Fisher's Least Significant Difference test. Overall, significant statistical differences were limited, likely due to relatively high biological variability between groups and small numbers of mice per group (n=6-9/group). The mean (±SEM) 'numbers of cycles' at 3 months differed between groups (p=0.055) and was higher in the control group (2.11±0.27) compared to the 2 µg/kg/day (1.27±0.32; p=0.055) and the 200 µg/kg/day (1.13±0.33; p=0.031). Further, we observed reduced neonatal survival along with a higher incidence of pups' death per litter following propylparaben exposure. Specifically, percentages of total live pups/total pups were 91% (controls), 90% (2µg/kg), 77% (20 µg/kg), and 83% (200µg/kg). Incidences of dead pups were 3/7 (controls), 6/8 (2µg/kg), 5/8 (20 µg/kg), and 2/8 (200µg/kg). Yet, statistical analysis of fertility outcomes did not result in significant differences between the groups, including averages of pup's weight (1.66gr-1.71gr), litter size (10-12), or number of dead pups per litter. Overall, our finding suggests that environmentally relevant propylparaben exposure had a limited impact on estrous cyclicity and fertility in female mice.