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Lactational exposure to atypical antipsychotic drugs disrupt pituitary-ovarian axis of mice

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Sexual and reproductive dysfunctions induced by atypical antipsychotic drugs olanzapine (OLNZ) and risperidone (RISP) have been recognized both in clinics and in preclinical studies. As both these drugs transfers through milk, the neonates are susceptible to their adverse side effects. The pituitary-ovarian axis of mice lactationally exposed to olanzapine (OLNZ; 4, 8, 10 mg/kg) and risperidone (RISP; 1, 2 mg/kg), was examined to evaluate the adverse drug effects on the reproductive axis during postnatal development.

The assessment was done at postnatal day 28 (pre pubertal age) to see the direct exposure effect through milk and at postnatal day 63 (post pubertal age) to address the persistence of the adverse effect to adulthood. Weight analysis, histopathology and follicular dynamics study of ovary, immunocharacteristics and morphometry of pituitary PRL and LH cells, and plasma levels of PRL, LH, Estradiol and corticosterone were carried out.

Ovarian regression was revealed as weight and the numbers of healthy follicles were significantly reduced with a parallel increase of follicular atresia. Lactotrophs immunointensity was increased along with plasma elevation of PRL levels. On the contrary, immunointensity of LH cells and plasma levels of LH were decreased. The plasma estradiol levels were decreased as well. Effects were more prominent in risperidone-exposed groups than olanzapine groups. The antigonadal effects of the drugs might have mediated through their hyperprolactinemic effects which further inhibited LH and estradiol synthesis/secretions ultimately affecting the follicular development. The adverse impact was persisted to adulthood with higher doses of the drugs.

Key Words: Lactational exposure, Olanzapine, Risperidone, Pituitary-ovarian axis, Mice

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