**Effects of Timing and Exposure Patterns of Ritodrine Administration to Pregnant Rats on Neonatal Glucose Levels**

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**Background and aims.** Ritodrine (RD), a β₂-adrenergic agonist used for tocolysis, causes maternal and fetal hyperglycemia, but paradoxically induces neonatal hypoglycemia. A short interval (<6 hours) between stopping maternal RD administration and delivery is a known risk factor for neonatal hypoglycemia (1). While RD crosses the placenta, whether it directly causes neonatal hypoglycemia remains unclear. This study aimed to clarify how RD exposure duration and patterns affect neonatal glucose levels using a rat model.

**Methods.** On gestational day 21, pregnant SD rats were administered RD (16 mg/kg body weight) or PBS as control. Fetal blood glucose levels and fetal plasma RD concentrations were measured up to 3 hours post-administration. Cesarean sections were performed at 1, 2, 3, and 6 hours after maternal RD or PBS administration, and neonatal blood glucose was measured up to 3 hours after birth. Finally, RD (1.6 mg/kg or 0.1 mg/kg) or PBS was administered directly to neonates delivered from untreated pregnant rats, and blood glucose levels were monitored for 3 hours after birth.

**Results.** Maternal RD administration significantly increased fetal glucose levels at 1-2 hours compared to PBS group. Fetal plasma RD concentrations at 3 hours post-administration were comparable to clinical settings. Neonates delivered 1 and 6 hours post-administration did not observe hypoglycemia. In contrast, neonates delivered at 2 and 3 hours post-administration showed significantly lower glucose levels compared to the PBS group at 2 hours and 2 to 3 hours after birth, respectively. Direct neonatal RD administraiton at concentrations equivalent to those observed at 1 and 3 hours after maternal RD administration did not induce hypoglycemia.

**Conclusion/Discussion.** RD elevates glucose levels in fetuses and neonates but induces neonatal hypoglycemia within clinical RD concentration. Neonatal hypoglycemia induced only by maternal RD administration is reversible, as a prolonged intervals between administration and birth may prevent its development.

**References:**

1. Shimokawa, S. et al. (2019) J Pharm Health Care Sci. 16:5:7