Effect of propranolol and its dosages on maternal-fetal heart rates coupling in pregnant mice and fetuses

Beta-blockers are well known drugs that are frequently used during pregnancy in the treatment of hypertension, cardiomyopathy and maternal-fetal tachycardia. In complicated pregnancies such as hypertension, treatment with propranolol did not show any congenital abnormalities have been observed. The aim of this preliminary study is to look how maternal-fetal heart rates and their beat to beat coupling patterns (λ for f1:m3~10) [f=fetal(beat):m=maternal(beat)] (Khandoker et al, 2018) are influenced by injection of β blocker(propranolol) into pregnant mice. Total of 9 fetuses from 9 pregnant female mice type of C57BL/6J were divided into three groups [control (3), β blockade (3) (4 mg), β blockade (3) (10 mg)]. On 17.5-day beat-to-beat maternal and fetal heart rates (MHR and FHR) were simultaneously measured for 20 minutes (10 minutes under normal condition and 10 minutes with saline (to control group) and propranolol (to the β blockade groups) solution by using an invasive maternal and fetal electrocardiogram techniques with needle electrodes. Results show that FHR decrease (151±60 bpm (pre); 110±34 bpm (post); $p<0.05$ Wilcoxon's signed rank test for 10 mg) and maternal-fetal heart rate coupling (λ) patterns changed [$\lambda_{f1:m3}$ decreases 20%(±7) but $\lambda_{f1:m4}$ increases by 12%(±6) for 10 mg; $p<0.05$ and no significant changes for 4mg] followed by propranolol infusion (no change with saline). Fisher's exact test showed that changes (increase/decrease from pre to post values) in mean and rmssd of MHR and FHR, and $\lambda_{f1:m3\text{-}7}$ were found to be significantly associated with treatment types (saline to propranolol_10mg only). These changes could be caused by propranolol (dosage of 10 mg caused significant changes) which could have transmitted through the placental barrier. The presented results allow for assessment of the dosages of β adrenergic control of maternal and fetal heart, which will further enhance the value of the mouse as a model of heritable human pregnancy and hypertension.