Cardiorenal pregnancy adaptations in females born small on a high fat diet and benefits of endurance exercise training

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Intrauterine growth restriction programs adult cardiorenal disease, which is exacerbated with "second hits" such as pregnancy and obesity in females born small. Importantly, exercise is reported to have a positive effect in those born small. The aim of this study was to determine if a high fat diet (HFD) exacerbates the known adverse cardiorenal adaptations to pregnancy in rats born small and whether exercise before and during pregnancy is more beneficial in preventing these complications than exercise during pregnancy alone.

Uteroplacental insufficiency resulting in growth restriction was induced by bilateral uterine vessel ligation (Restricted) or sham (Control) surgery on embryonic day 18 (E18) in Wistar-Kyoto rats (4% isoflurane and 650ml.min^{-1} oxygen flow, reduced to 3.2% isoflurane and 250ml.min^{-1} when suturing). Female offspring consumed a Chow or HFD (23% fat) from 5 weeks and were mated at 20 weeks. Female rats were exercised on motorized treadmills for 4 weeks before pregnancy and throughout pregnancy or during the last two thirds of pregnancy only. Systolic blood pressure was measured by tail cuff at E18. At E12 and E19, rats were individually placed in a metabolic cage for 24 hours to collect urine and plasma was taken by tail vein to calculate estimated glomerular filtration rate (eGFR). At E20, rats were anaesthethised with an intraperitoneal injection of Ketamine (100mg.kg^{-1}) and Ilium Xylazil-20 (30mg.kg^{-1}) and plasma was collected.

Control and Restricted rats consuming a HFD were significantly heavier with higher plasma leptin concentrations compared to Chow-fed rats irrespective of exercise interventions. No changes in pre-pregnancy systolic blood pressure were measured in all groups. Restricted Chow-fed rats, and both Control and Restricted females on a HFD had an adverse cardiovascular adaptation to pregnancy with a greater reduction in systolic blood pressure during late gestation (P<0.05). Importantly, exercise before and during pregnancy prevented this adverse cardiovascular adaptation (P<0.05). Additionally, at E20, Control and Restricted rats that exercised prior to and during pregnancy had an increased heart weight (normalized to tibial length) irrespective of diets indicative of physiological cardiac hypertrophy.

No changes in renal function at E12 were detected in all groups. At E20, Restricted females on a Chow diet and Control females on a HFD that remained Sedentary had adverse renal function (+50-56% eGFR; P<0.05) with no difference in urinary sodium excretion. HFD reduced water intake, urine flow rate and albumin excretion in both Control and Restricted females (P<0.05). There was no effect of either exercise intervention on renal function for any groups.

In summary, pregnant females born small and on a HFD are at a greater risk of cardiorenal alterations during pregnancy. Although cardiovascular dysfunction was prevented by exercise prior to and during pregnancy, renal dysfunction was not affected by exercise interventions. This study highlights that modifiable risk factors such as diet and exercise can have beneficial effect in the mother during pregnancy.