Can voluntary exercise improve renal changes in offspring induced by maternal obesity

ABSTRACT

Obesity in the mother is known to affect offspring, making them more prone to obesity, diabetes, and kidney disease. A recent study reported that children of obese mothers have a 22% increased risk of developing kidney disease suggesting that its development may be programmed in utero. However, the link between maternal obesity and offspring kidney disease remains unclear. Exercise is known to be beneficial in kidney disease, but whether it impacts renal effects of maternal obesity is not known. Thus we studied the impact of maternal obesity on siblings that were either sedentary or given access to a running wheel. Female Sprague-Dawley rats were fed either chow diet or high-fat diet (HFD) for 6 weeks before mating. Female offspring were weaned onto either chow diet or HFD and after 7 weeks, half of offspring were exercised for 5 weeks. Offspring were killed at 15 weeks; kidneys were collected for gene expression. The body weight, kidney mass, and kidney triglyceride levels were measured. Offspring of obese mothers had significantly increased body weight which was reduced by exercise in offspring consuming HFD. Kidney weight was significantly increased by maternal diet and post-weaning HFD. Maternal diet was associated with a significant increase in kidney triglyceride accumulation; chow fed offspring of obese mother showed a 91% increase in renal triglyceride content ($P<0.001$). Post-weaning HFD consumption also increased kidney triglyceride content by 37% and 20% in offspring of lean and obese mothers, respectively ($P<0.01$). However, exercise also increases renal triglyceride accumulation in offspring of both obese and lean mother consuming HFD. Lipid accumulation was associated with dysregulation of lipid metabolism genes. Maternal diet was associated with an upregulation of fatty acid transporter Cd36. Ldl receptor (Ldlr), involved in uptake of fat, was significantly upregulated by both post-weaning HFD and exercise. Downregulation of renal lipoprotein lipase (Lpl) which is involved in hydrolyzing circulating triglyceride was observed by current HFD and upregulated by exercise. Sterol regulatory element binding protein 1 (Srebp 1) and acetyl-CoA carboxylase alpha (Acaca), involve in lipogenesis, were upregulated by exercise. Significant upregulation of kidney injury molecule 1 (Kim 1) and neutrophil gelatinase-associated lipocalin (Ngal) was also induced by post-weaning HFD. Our data suggest that maternal diet has a greater effect than current HFD consumption on triglyceride accumulation in offspring kidney. Voluntary exercise in offspring did not reduce this triglyceride content in the kidney. Dysregulation of lipid metabolism genes may explain renal lipid accumulation which may further result in renal injury.