**Metformin use in pregnancy and lactation. A preclinical investigation of short and long-term effects for mother and offspring.**

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Gestational or pre-existing diabetes during pregnancy carries risks for both the mother (excessive weight gain, cardiovascular disease, pre-eclampsia) and child (Large for Gestational Age, birth trauma). In addition, there is increased risk of the child developing obesity, diabetes and cardiovascular disease later in life. Therefore, effective treatment is paramount.

Metformin is the first-line pharmacological treatment for type 2 diabetes and has been increasingly used for gestational diabetes. It effectively reduces hyperglycaemia and the occurrence of diabetes-associated pregnancy risks. However, metformin crosses the placenta, raising concern over potential impacts on the developing embryo that could impact the offspring later in life. In addition, as metformin-induced glucose lowering in the mother results in large beneficial effects, it is difficult to determine any effects of metformin independent of glycaemia that should be considered when choosing treatments.

*Aim*: To determine the short and long-term effects of metformin treatment during pregnancy and lactation independent of glycaemia.

*Methods*: We treated non-diabetic mice with 5 mg/L metformin or vehicle control in their drinking water throughout pregnancy and/or lactation and analysed a wide range of outcomes.

*Results*: All dams maintained euglycaemia therefore any effects of metformin were independent of glucose-lowering. We found a significant effect of metformin treatment during lactation, but not pregnancy, to restrict post-natal growth, that was associated with changes in milk composition. We also found effects of gestational metformin exposure to slightly reduce weight gain in response to a high-fat diet, alter gonadal and infrarenal fat distribution in a sex-specific manner and sex-specific differences in glucose tolerance in the offspring.

*Conclusion*: This study provides evidence of the potential effects of metformin on both mother and child independent of its glucose lowering effects. This will help determine the safety of metformin’s use in pregnancy and lactation as well as potential benefits in addition to glycaemic management.